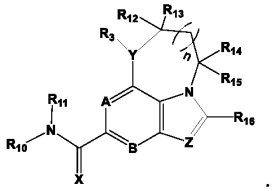
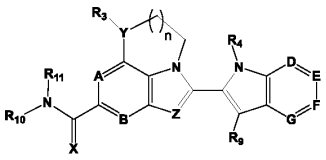
# HETEROCYCLIC COMPOUNDS AS PAD INHIBITORS

## TECHNICAL FIELD OF THE INVENTION

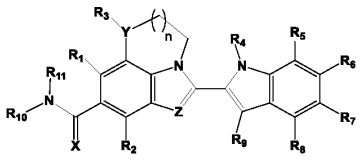
**[0001]** The present disclosure is directed to novel heterocyclic compounds of Formula (I), (II), and (III) along with their polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof which act as PAD4 inhibitors.



**Formula (I)**



**Formula (II)**



**Formula (III)**

The process for the preparation of the above heterocyclic compounds of the Formula (I), (II), and (III), their polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, pharmaceutical compositions, and metabolites, are also described herein which are useful in the preparation of such compounds.

**[0002]** The compounds described herein are PAD4 inhibitors and may be useful in the treatment of various disorders, for example rheumatoid arthritis, vasculitis, systemic lupus erythematosis, cutaneous lupus erythematosis, ulcerative colitis, cancer, cystic fibrosis, asthma, multiple sclerosis, and psoriasis.

## BACKGROUND OF THE INVENTION

**[0003]** The PAD (protein arginine de-iminase) consists of a family of enzymes that convert peptidyl-arginine to peptidyl citrulline. The process for this conversion is known as citrullination (J. E. Jones, et al. Curr. Opin. Drug Discov. Devel., 2009, 12, 616-627). There are five isozymes of the PAD family found in mammals, *viz*. PAD1, PAD2, PAD3, PAD4, and PAD6. The amino acid sequence of these isozymes share a sequence similarity of 70 – 95 % with mammals. Citrullination which is a post-translational modification of arginine to citrulline by the closely related enzymes of PAD family affect numerous physiological and pathological processes.

**[0004]** Citrullination has been implicated in various ailments, for example, cell differentiation (K. Nakashima et al., J. Biol. Chem., 1999, 274, 27786-27792), stem cell pluripotency (M. A. Christophorou et al., Nature, 2014, 507, 104-108), apoptosis (G. Y.

Liu, Apoptosis, 2006, 11, 183-196), neutrophil extracellular trap (NET) formation (Y. Wang et al., J. Cell Biol., 2009, 184, 205-213), transcriptional regulation (P. Li et al., Mol. Cell Biol., 2008, 28, 4745-4758), antigen processing in autophagy (J. M. Ireland et al., J. Exp. Med., 2011, 208, 2625-2632), inflammation (D. Makrygiannakis et al., Ann. Rheum. Dis., 2006, 65, 1219-1222), the cornification of skin (E. Candi et al., Nat. Rev. Mol. Cell Biol., 2005, 6, 328-340), demyelination in multiple sclerosis (F. G. Mastronardi et al., J. Neurosci., 2006, 26, 11387-11396), chemokine regulation (T. Loos et al., Blood, 2008, 112, 2648-2656), spinal cord injury repair (S. Lange et al., Dev. Biol., 2011, 355, 205-214), and various normal cellular processes.

**[0005]** The role of PAD in pathogenesis of many diseases has become increasingly evident as the enzymes that catalyze citrullination, also produce autoantibodies that recognize the citrullinated proteins. The introduction of citrulline, resultant of PAD activity, changes both the structure and function of proteins. At physiological activity levels, PADs regulate many cell-signaling pathways like cell differentiation, apoptosis, and gene transcription (György et al. Int. J. Biochem. Cell Biol., 2006, 38, 1662-1677). Over the past decade, it is becoming increasingly apparent that aberrant PAD activity is involved in many human inflammatory diseases such as, rheumatoid arthritis (RA), Alzheimer's disease, and multiple sclerosis (N. K. Acharya, J. Autoimmun., 2012, 38, 369-380).

**[0006]** PAD4 have also been known for the deamination or citrullination of a variety of proteins both *in vitro* and *in vivo*, with consequences of diverse functional response in a variety of diseases, such as, rheumatoid arthritis (RA), diseases with neutrophilic contributions to pathogenesis (for example, vasculitis, systemic lupus erythematosus, ulcerative colitis), along with oncology indications (J. E. Jones, et al. Curr. Opin. Drug Discov. Devel., 2009, 12, 616-627). PAD4 has been found to be involved in the formation of neutrophil extracellular traps (NETs) and more specifically in the histone citrullination that occurs during NETosis (J. Cedervall, A. -K. Olsson, Oncoscience, 2015, 2(11), 900-901). Thus, PAD4 enzyme is linked to diseases characterized by abnormal levels of neutrophil extracellular traps (NETs). The proposed role of PAD4 in NETosis is pertinent for rheumatoid arthritis (RA) as NETs are deficient in the absence of PAD4 and PAD4 is released extracellulary in RA joints, probably due to the pathological status of RA neutrophils.

**[0007]** Considering the fact that NETs are implicated in many diseases, the therapeutic potential of PAD inhibitor drugs would be significant. PAD4 inhibitors may also have

wider applicability as tools and therapeutics for human disease through epigenetic mechanisms.

**[0008]** In literature, a number of PAD inhibitors that are selective for PAD4 are known (H. D. Lewis *et al.*, Nature Chemical Biology, 2015, 11, 189-191). Some of these compounds are chloro-amidine, fluoro-chloridine and their related analogs act as mechanism-based inhibitors that irreversibly inactivate PAD4 and other PAD isozymes. The PAD4 inhibitor compounds have utility against rheumatoid arthritis (RA). PAD4, detected in synovial tissue, has been found to be responsible for citrullination of a variety of joint proteins. These citrullinated protein substrates produce anti-citrullinated antibodies which are responsible for disease pathogenesis (Y. Kochi et al., Ann. Rheum. Dis., 2011, 70, 512-515).

**[0009]** PAD4 inhibitors have also been known for alleviating pathological activity in a variety of diseases. Some specific studies show that the defence mechanism of neutrophils to eliminate pathogens, also known as NET formation is associated with histone citrullination (I. Neeli et al., J. Immunol., 2008, 180, 1895-1902). Therefore, PAD4 inhibitor compounds can be utilized in injuries and disease pathologies where NET formation in tissues occurs. In addition, PAD4 inhibitors have wider applicability to neutrophilic diseases.

**[00010]** US20170105971 discloses the alleviation, treatment and/ or prevention of auto immune diseases like, rheumatoid arthritis, osteoarthritis and arthralgia by using amidines as PAD inhibitor compounds. Another application US20050159334 also discusses the treatment of rheumatoid arthritis (RA) with the administration of suitable PAD inhibitor.

**[00011]** The PAD inhibitor compound chloro-amidine, has been widely studied to demonstrate their efficacy in several animal disease models like, collagen-induced arthritis (V. C. Willis et al., J. Immunol., 2011, 186(7), 4396-4404), dextran sulfate sodium (DSS)-induced experimental colitis (A. A. Chumanevich et al., Am. J. Physiol. Gastrointest. Liver Physiol., 2011, 300(6), G929-G938), lupus-prone MRL/lpr mice atherosclerosis and arterial thrombosis (J. S. Knight et al., Circ. Res., 2014, 114(6), 947-956), spinal cord injury repair (S. Lange et al., Dev. Biol., 2011, 355(2), 205-214), and experimental autoimmune encephalomyelitis (EAE). The study on DSS colitis demonstrated that chloro-amidine drives *in vitro* and *in vivo* apoptosis of inflammatory cells, indicating the efficacy of PAD4 inhibitors in treating inflammatory diseases.

demonstrated that chloro-amidine drives *in vitro* and *in vivo* apoptosis of inflammatory cells, indicating the efficacy of PAD4 inhibitors in treating inflammatory diseases.

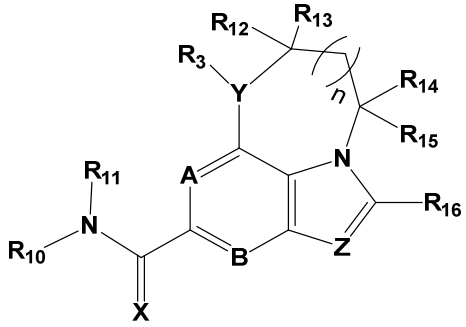
**[00012]** PAD4 is predominantly expressed in granulocytes and is strongly linked to diverse diseases. In multiple tumors, PAD4 is found to be overexpressed affecting the p53 function and downstream pathways. Calcium binding to PAD promotes the bioactive conformation, increasing PAD4 activity by ten thousand times.

**[00013]** Slack *et al.* demonstrated the use of PAD4 inhibitors in the treatment of cancers (J. L. Slack et al., Cellular and Molecular Life Sciences, 2011, 68(4), 709-720). Overexpression of PAD4 had already been demonstrated in numerous cancers (X. Chang et al., BMC Cancer, 2009, 9, 40). It is suggested that PAD4 inhibitors have an anti-proliferative role as well. PAD4 deiminases arginine residues in histones at the promoters of p53- target genes such as p21, which are involved in cell cycle arrest and induction of apoptosis (P. Li et al., Molecular & Cell Biology, 2008, 28(15), 4745-4758).

**[00014]** PAD inhibition is a viable strategy for the treatment of numerous diseases mentioned above. The use of PAD inhibitors in various other diseases where dysregulated PAD activity is implicated needs to be explored. Although a definitive role for dysregulated PAD activity in these diseases has not been established, a direct link is plausible. However, there remains an unmet need to identify and develop PAD4 inhibitors which may treat PAD4 mediated disorders with efficacy.

**SUMMARY**

**[00015]** The present invention refers to subject matter as defined in the attached set of claims. In one example, present disclosure discloses a compound of Formula (I)




**Formula (I)**

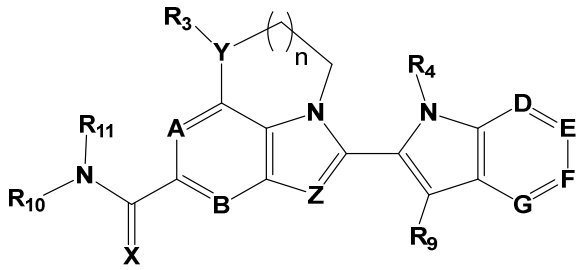
their polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof,

wherein X is selected from O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy,

$C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10

membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00016]** In another example, present disclosure also discloses compound of Formula (II)




**Formula (II)**

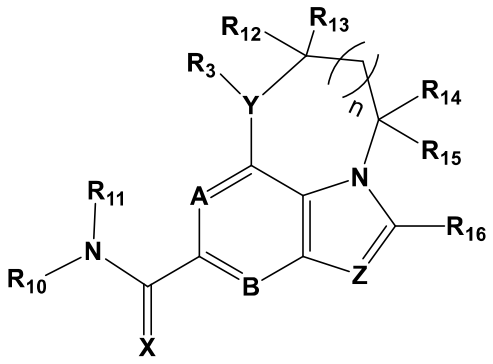
their polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof,

wherein

X is selected from O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; D is selected from N or $CR_5$; E is selected from N or $CR_6$; F is selected from N or $CR_7$; G is selected from N or $CR_8$; n is 0-2; $R_1$, $R_2$, $R_5$, $R_6$, $R_7$, $R_8$, and $R_9$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl,

wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_4$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, -COOH, and cyano; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of $C_{1-6}$ alkylamino, and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00016a]** In another aspect, there is provided a compound of Formula (I)




Formula (I)

their stereoisomers and pharmaceutically acceptable salts thereof, wherein

X is O or S;

Y is O or N;

Z is N;

A is $CR_1$;

B is $CR_2$;

n is 0-1;

$R_1$ and $R_2$ are independently selected from hydrogen;

$R_3$ is absent or is selected from hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2C_6$ aryl, and $SO_2C_{1-6}$ alkyl, wherein $SO_2C_{1-6}$ alkyl, and $SO_2C_6$ aryl is optionally substituted with $C_{1-6}$ alkoxy, halogen, and $C_6$ aryl;

$R_{10}$ and $R_{11}$ are taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein,

the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from amino, $-NHC(O)CH=CHCH_2N(CH_3)_2$, or $C_{1-6}$ alkylamino;

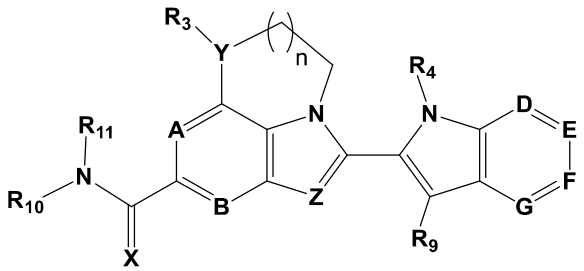
$R_{12}$, $R_{13}$, $R_{14}$ and $R_{15}$ are independently selected from hydrogen or $C_{1-6}$ alkyl; and

$R_{16}$ is 5-10 membered bicyclic heteroaryl with 1-2 heteroatoms selected from N or S, wherein,

5-10 membered bicyclic heteroaryl is optionally substituted with 1-3 substituents selected from the group consisting of halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl- $C_6$ aryl, $C_{2-6}$ alkenyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one

or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and -COOH.

**[00016b]** In another aspect, there is provided a compound of Formula (II)




Formula (II)

their stereoisomers and pharmaceutically acceptable salts thereof,

wherein,

X is O or S;

Y is O or N;

Z is N;

A is $CR_1$;

B is $CR_2$;

D is selected from N or $CR_5$;

E is $CR_6$;

F is $CR_7$;

G is $CR_8$;

n is 1-2;

$R_1$, $R_2$ and $R_9$ are independently selected from hydrogen;

$R_5$, $R_6$, $R_7$ and $R_8$ are independently selected from the group consisting of hydrogen, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{2-6}$ alkenyl- $C_6$ aryl, and $C_{1-6}$ heteroaryl;

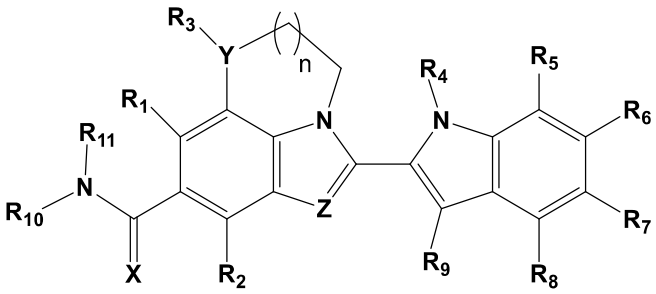
$R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $SO_2C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, and $SO_2C_6$ aryl, wherein, $SO_2C_6$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, and $C_6$ aryl;

$R_4$ is selected from the group consisting of $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and -COOH; and

$R_{10}$ and $R_{11}$ are taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein,

the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, and -$NHC(O)CH=CHCH_2N(CH_3)_2$.

**[00016c]** In another aspect, there is provided a compound of Formula (III)




Formula (III)

their stereoisomers and pharmaceutically acceptable salts thereof,

wherein,

X is O or S;

Y is O or N;

Z is N;

n is 1-2;

$R_1$, $R_2$ and $R_9$ are independently selected from hydrogen;

$R_5$, $R_6$, $R_7$ and $R_8$ are independently selected from the group consisting of hydrogen, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{2-6}$ alkenyl- $C_6$ aryl, and $C_{1-6}$ heteroaryl;

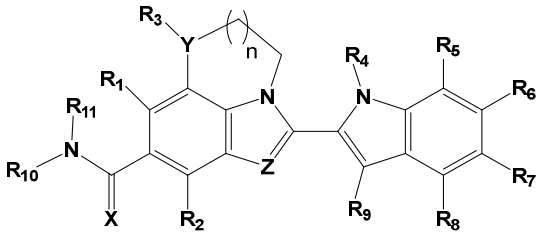
$R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $SO_2C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, and $SO_2C_6$ aryl, wherein, $SO_2C_6$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, and $C_6$ aryl;

$R_4$ is selected from the group consisting of $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and -COOH; and

$R_{10}$ and $R_{11}$ are taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein,

the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, and -$NHC(O)CH=CHCH_2N(CH_3)_2$.

combinations thereof.In yet another example, present disclosure further dislcoses compound of Formula (III)



**Formula (III)**

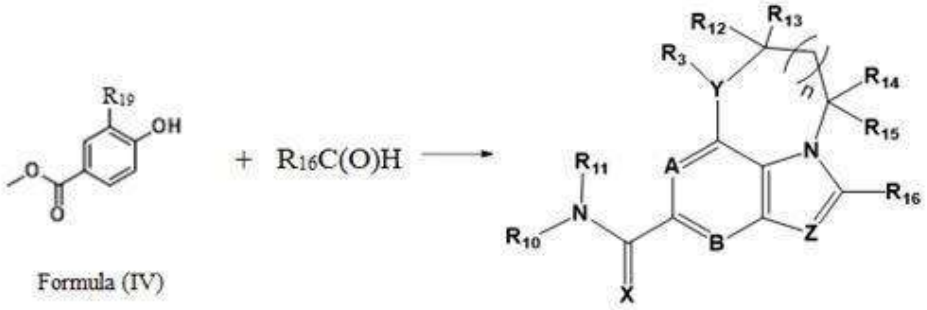
their polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof, wherein X is selected from O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; n is 0-2; $R_1$, $R_2$, $R_5$, $R_6$, $R_7$, $R_8$, and $R_9$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_4$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $CH_2OH$, COOH, and cyano; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$

alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $-NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00018]** The present disclosure further describes the process of preparation of compounds of Formula (I), Formula (II), and Formula (III) or its polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof.

**[00019]** The present disclosure further discloses a pharmaceutical composition comprising a compound of Formula (I), Formula (II), and Formula (III) or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier, optionally in combination with one or more other pharmaceutical compositions.

**[00019a]** In an aspect, there is provided a process of preparation of compounds of Formula (I) as defined above or its stereoisomers and pharmaceutically acceptable salts thereof, the process comprising reacting Formula (IV) and $R_{16}C(O)H$



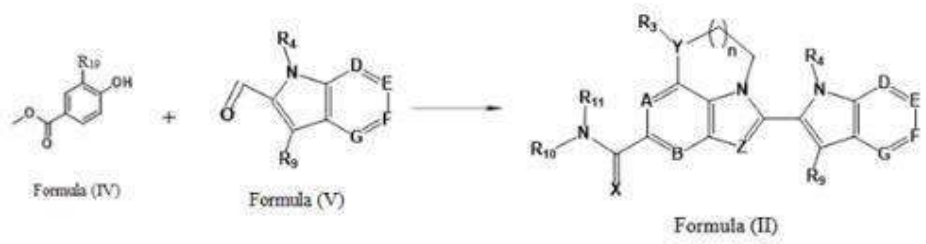

Formula (IV)

Formula (I)

wherein $R_{19}$ of Formula (IV) is selected from nitro and $C_{1-6}$ alkoxy; $R_{16}$ of $R_{16}C(O)H$ is 5-10 membered bicyclic heteroaryl with 1-2 heteroatoms selected from N or S, wherein, 5-10 membered bicyclic heteroaryl is optionally substituted with 1-3 substituents selected from the group consisting of halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{2-6}$ alkenyl- $C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and -COOH; X of Formula (I) is selected from O or S; Y is selected from O or N; Z is N; A is $CR_1$; B is $CR_2$; n is 0-1; $R_1$ and $R_2$ are independently selected from hydrogen; $R_3$ is absent or is selected from hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $SO_2C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, and $SO_2C_6$ aryl, wherein, $SO_2C_6$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, and $C_6$ aryl; $R_{10}$ and $R_{11}$ are taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein, the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from amino, $C_{1-6}$ alkylamino, and -$NHC(O)CH=CHCH_2N(CH_3)_2$; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from hydrogen and $C_{1-6}$ alkyl; $R_{16}$ is 5-10 membered bicyclic heteroaryl with 1-2 heteroatoms selected from N or S, wherein, 5-10 membered bicyclic heteroaryl is optionally substituted with 1-3 substituents selected from the group consisting of halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{2-6}$ alkenyl- $C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and

$C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and -COOH.

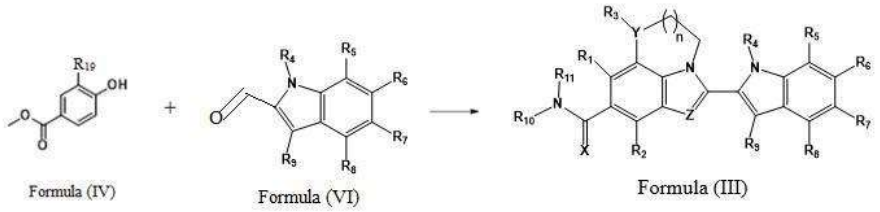
**[00019b]** In another aspect, there is provided a process of preparation of compounds of Formula (II) as defined above or its stereoisomers and pharmaceutically acceptable salts thereof, the process comprising reacting Formula (IV) and Formula (V)




wherein $R_{19}$ of Formula (IV) is selected from nitro and $C_{1-6}$ alkoxy; X of Formula (II) is selected from O or S; Y is selected from O or N; Z is N; A is $CR_1$; B is $CR_2$; D is selected from N or $CR_5$; E is $CR_6$; F is $CR_7$; G is $CR_8$; n is 1-2; $R_1$, $R_2$ and $R_9$ are independently selected from hydrogen; $R_5$, $R_6$, $R_7$ and $R_8$ are independently selected from the group consisting of hydrogen, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{2-6}$ alkenyl- $C_6$ aryl, and $C_{1-6}$ heteroaryl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $SO_2C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, and $SO_2C_6$ aryl, wherein, $SO_2C_6$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, and $C_6$ aryl; $R_4$ is selected from the group consisting of $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and -COOH; $R_{10}$ and $R_{11}$ are taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, and -$NHC(O)CH=CHCH_2N(CH_3)_2$; D of Formula (V) is selected from N or $CR_5$; E is $CR_6$; F is $CR_7$; G is $CR_8$, $R_9$ is H; and $R_4$ is selected from the group consisting of $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, is

optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and -COOH.

**[00019c]** In another aspect, there is provided a process of preparation of compounds of Formula (III) as defined above or its stereoisomers and pharmaceutically acceptable salts thereof, the process comprising reacting Formula (IV) and Formula (VI)




wherein $R_{19}$ of Formula (IV) is selected from nitro and $C_{1-6}$ alkoxy; X of Formula (III) is selected from O or S; Y is O or N; Z is N; n is 1-2; $R_1$, $R_2$ and $R_9$ are independently selected from hydrogen; $R_5$, $R_6$, $R_7$ and $R_8$ are independently selected from the group consisting of hydrogen, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{2-6}$ alkenyl- $C_6$ aryl, and $C_{1-6}$ heteroaryl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $SO_2C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, and $SO_2C_6$ aryl, wherein, $SO_2C_6$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, and $C_6$ aryl; $R_4$ is selected from the group consisting of $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and COOH; $R_{10}$ and $R_{11}$ are taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein, the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, and -$NHC(O)CH=CHCH_2N(CH_3)_2$; and $R_9$ of formula (VI) is hydrogen; $R_5$, $R_6$, $R_7$ and $R_8$ are independently selected from the group consisting of hydrogen, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{2-6}$ alkenyl- $C_6$ aryl, and $C_{1-6}$ heteroaryl; $R_4$ is selected from the group consisting of $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and COOH.

**[00019d]** In yet another aspect, the present disclosure provides a pharmaceutical composition comprising a compound of Formula (I), Formula (II), and Formula (III) or a pharmaceutically acceptable salt thereof as provided herein with a pharmaceutically acceptable carrier, optionally in combination with one or more other pharmaceutical compositions.

**[0019e]** In yet another aspect, the present disclosure provides compounds as claimed herein or a pharmaceutically acceptable salt thereof for use as a medicament

**[00020]** In yet another example, the present disclosure further discloses a method for inhibiting one or more PAD family in a cell with an effective amount of the compound of the present disclosure.

**[0020a]** In yet another aspect, there is provided an *in vitro* method for inhibiting one or more PAD family in a cell with an effective amount of the compound as defined herein.

**[00021]** The present disclosure further discloses a method of treating a condition mediated by one or more PAD's, the method comprising administering to a subject suffering from a condition mediated by one or more PAD family, a therapeutically effective amount of the compound of Formula (I), Formula (II), and Formula (III) or the pharmaceutical composition of the present disclosure with other clinically relevant agents or biological agents to a subject in need thereof.

**[00021a]** In yet another aspect, the present disclosure provides use of a pharmaceutical composition provided herein in the manufacture of a medicament for treating a condition selected from vasculitis, systemic lupus erythematosus, cancer, asthma, rheumatoid arthritis, ulcerative colitis, psoriasis, cystic fibrosis and cutaneous lupus erythematosus

.

**[00021b]** In yet another aspect, the present disclosure provides use of the compound of Formula (I), Formula (II), and Formula (III) as provided herein in the manufacture of a medicament for the treatment of rheumatoid arthritis, vasculitis, systemic lupus erythematosus, ulcerative colitis, cancer, cystic fibrosis, asthma, cutaneous lupus erythematosus and psoriasis.

**[00022]** In yet another aspect, the present disclosure further discloses use of the compound of Formula (I), Formula (II) and Formula (III) as defined above in the manufacture of a medicament for the treatment of rheumatoid arthritis, vasculitis, systemic lupus erythematosus, ulcerative colitis, cancer, cystic fibrosis, asthma, cutaneous lupus erythematosus, and psoriasis.

**[00022a]** In yet another aspect, the present disclosure provides use of the compound provided herein or the pharmaceutical composition provided herein together with other clinically relevant agents or biological agents in the manufacture of a medicament for the treatment and/or prevention of treatment of rheumatoid arthritis, vasculitis, systemic lupus erythematosus, ulcerative colitis, cancer, cystic fibrosis, asthma, cutaneous lupus erythematosus and psoriasis.

**[00022b]** In yet another aspect, the present disclosure provides use of the compound provided herein or the pharmaceutical composition provided herein together with other clinically relevant agents or biological agents in the manufacture of a medicament for the treatment and/or prevention of acid-induced lung injury, respiratory distress syndrome, allergen induced asthma, allergic bronchopulmonary, chronic lung disease of prematurity, chronic obstructive pulmonary disease, colitis, cystic fibrosis, gouty arthritis, inflammatory bowel disease, inflammatory lung disease, inflammatory pain, juvenile rheumatoid arthritis, kidney disease, kidney injury caused by parasitic infections, kidney transplant rejection prophylaxis, lung injury, lupus, lupus nephritis, multiple sclerosis, muscular dystrophy, non-allergen induced asthma, osteoarthritis, periodontitis, peritoneal endometriosis, psoriasis,pulmonary disease, pulmonary fibrosis, pyogenic sterile arthritis, renal disease, rheumatic disease, rheumatoid arthritis, sepsis, severe pain and ulcerative colitis.

**[00022c]** In yet another aspect, the present disclosure provides use of a therapeutically effective amount of the compound provided herein or the pharmaceutical composition provided herein in the manufacture of a medicament for the treatment and/or prevention of a condition selected from acid-induced lung injury, respiratory distress syndrome, allergen induced asthma, allergic bronchopulmonary, chronic lung disease of prematurity, chronic obstructive pulmonary disease, colitis, cystic fibrosis, gouty arthritis, inflammatory bowel disease, inflammatory lung disease, inflammatory pain, juvenile rheumatoid arthritis, kidney disease, kidney injury caused by parasitic

infections, kidney transplant rejection prophylaxis, lung injury, lupus, lupus nephritis, multiple sclerosis, muscular dystrophy, non-allergen induced asthma, osteoarthritis, periodontitis, peritoneal endometriosis, psoriasis, pulmonary disease, pulmonary fibrosis, pyogenic sterile arthritis, renal disease, rheumatic disease, rheumatoid arthritis, sepsis, severe pain and ulcerative colitis.

**[00022d]** In yet another aspect, the present disclosure provides use of a combination of the compounds provided herein or the pharmaceutical composition provided herein with other clinically relevant agents or biological agents in the manufacture of a medicament for the treatment of rheumatoid arthritis.

**[00022e]** In yet another aspect, the present disclosure provides use of a combination of the compounds provided herein or the pharmaceutical composition provided herein with other clinically relevant immune modulators agents in the manufacture of a medicament for the treatment of cancer.

**[00023]** These and other features, aspects, and advantages of the present subject matter will become better understood with reference to the following description. This summary is provided to introduce a selection of concepts in a simplified form. This summary is not intended to identify key features or essential features of the disclosure, nor is it intended to be used to limit the scope of the subject matter.

## DETAILED DESCRIPTION

**[00024]** Those skilled in the art will be aware that the present disclosure is subject to variations and modifications other than those specifically described. It is to be understood that the present disclosure includes all such variations and modifications. The disclosure also includes all such steps, features, compositions and compounds referred to or indicated in this specification, individually or collectively, and any and all combinations of any or more of such steps or features.

*Definitions*

**[00025]** For convenience, before further description of the present disclosure, certain terms employed in the specification, and examples are collected here. These definitions should be read in the light of the remainder of the disclosure and understood as by a person of skill in the art. The terms used herein have the meanings recognized and known to those of skill in the art, however, for convenience and completeness, particular terms and their meanings are set forth below.

**[00026]** The articles “a”, “an” and “the” are used to refer to one or to more than one (i.e., to at least one) of the grammatical object of the article.

**[00027]** Throughout the description and the claims which follow, unless the context requires otherwise, the word “comprise”, and variations such as “comprises” and “comprising”, will be understood to imply the inclusion of a stated integer or step or group of integers but not to the exclusion of any other integer or step or group of integers or steps.

**[00028]** The term “including” is used to mean “including but not limited to”. “Including” and “including but not limited to” are used interchangeably.

**[00029]** In the structural formulae given herein and throughout the present disclosure, the following terms have been indicated meaning, unless specifically stated otherwise.

**[00030]** Furthermore, the compound of Formula (I), Formula (II), and Formula (III) can be its derivatives, analogs, stereoisomer's, diastereomers, geometrical isomers, polymorphs, solvates, co-crystals, intermediates, metabolites, prodrugs or pharmaceutically acceptable salts and compositions.

**[00031]** The compounds according to Formula (I), Formula (II), and Formula (III) contain one or more asymmetric centres (also referred to as a chiral centres) and may, therefore, exist as individual enantiomers, diastereoisomers, or other stereoisomeric forms, or as mixtures thereof. Chiral centres, such as chiral carbon atoms, may also be present in a substituent such as an alkyl group. Where the stereochemistry of a chiral centre present in Formula (I), Formula (II), and Formula (III), or in any chemical structure illustrated herein, is not specified, the structure is intended to encompass any stereoisomer and all mixtures thereof. Thus, compounds according to Formula (I), Formula (II), and Formula (III) containing one or more chiral centres may be used as racemic modifications including racemic mixtures and racemates, enantiomerically-enriched mixtures, or as enantiomerically-pure individual stereoisomers.

**[00032]** Individual stereoisomers of a compound according to Formula (I), Formula (II), and Formula (III) which contain one or more asymmetric centres may be resolved by methods known to those skilled in the art. For example, such resolution may be carried out (1) by formation of diastereoisomeric salts, complexes or other derivatives; (2) by selective reaction with a stereoisomer-specific reagent, for example by enzymatic oxidation or reduction; or (3) by gas-liquid or liquid chromatography in a chiral environment, for example, on a chiral support such as silica with a bound chiral ligand or in the presence of a chiral solvent. It will be appreciated that where the desired stereoisomer is converted into another chemical entity by one of the separation procedures described above, a further step is required to liberate the desired form.

**[00033]** Alternatively, specific stereoisomers may be synthesised by asymmetric synthesis using optically active reagents, substrates, catalysts or solvents, or by converting one enantiomer to the other by asymmetric transformation.

**[00034]** It is to be understood that the references herein to compounds of Formula (I), Formula (II), and Formula (III) and salts thereof covers the compounds of Formula (I), Formula (II), and Formula (III) as free bases, or as salts thereof, for example as pharmaceutically acceptable salts thereof. Thus, in one embodiment, the disclosure is

directed to compounds of Formula (I), Formula (II), and Formula (III) as the free base. In another embodiment, the disclosure is directed to compounds of Formula (I), Formula (II), and Formula (III) and salts thereof. In a further embodiment, the disclosure is directed to compounds of Formula (I), Formula (II), and Formula (III) and pharmaceutically acceptable salts thereof.

**[00035]** It will be appreciated that pharmaceutically acceptable salts of the compounds according to Formula (I, II and III) may be prepared. Indeed, in certain embodiments of the disclosure, pharmaceutically acceptable salts of the compounds according to Formula (I), Formula (II), and Formula (III) may be preferred over the respective free base because such salts impart greater stability or solubility to the molecule thereby facilitating formulation into a dosage form. Accordingly, the disclosure is further directed to compounds of Formula (I), Formula (II), and Formula (III) and pharmaceutically acceptable salts thereof.

**[00036]** "Enantiomeric excess" (ee) is the excess of one enantiomer over the other expressed as a percentage. In a racemic modification, since both enantiomers are present in equal amounts, the enantiomeric excess is zero (0% ee). However, if one enantiomer were enriched such that it constitutes 95% of the product, then the enantiomeric excess would be 90% ee (the amount of the enriched enantiomer, 95%, minus the amount of the other enantiomer, 5%).

**[00037]** "Enantiomerically enriched" refers to products whose enantiomeric excess (ee) is greater than zero. For example, 'enantiomerically enriched' refers to products whose enantiomeric excess is greater than 50% ee, greater than 75% ee, and greater than 90% ee. 'Enantiomerically pure' refers to products whose enantiomeric excess is 99% or greater.

**[00038]** Included within the scope of the 'compounds of the disclosure' are all solvates (including hydrates), complexes, polymorphs, prodrugs, radiolabelled derivatives, and stereoisomers of the compounds of Formula (I), Formula (II), and Formula (III) and salts thereof.

**[00039]** The compounds of the disclosure may exist in solid or liquid form. In the solid state, the compounds of the disclosure may exist in crystalline or non-crystalline form, or as a mixture thereof. For compounds of the disclosure that are in crystalline form, the skilled artisan will appreciate that pharmaceutically acceptable solvates may be formed wherein solvent molecules are incorporated into the crystalline lattice during crystallization. Solvates may involve non-aqueous solvents such as ethanol, iso-propyl

alcohol, N,N- dimethylsulfoxide (DMSO), acetic acid, ethanolamine, and ethyl acetate, or they may involve water as the solvent that is incorporated into the crystalline lattice. Solvates wherein water is the solvent that is incorporated into the crystalline lattice are typically referred to as 'hydrates'. Hydrates include stoichiometric hydrates as well as compositions containing variable amounts of water. The disclosure includes all such solvates.

**[00040]** It will be further appreciated that certain compounds of the disclosure that exist in crystalline form, including the various solvates thereof, may exhibit polymorphism (i.e. the capacity to occur in different crystalline structures). These different crystalline forms are typically known as 'polymorphs'. The disclosure includes such polymorphs. Polymorphs have the same chemical composition but differ in packing, geometrical arrangement, and other descriptive properties of the crystalline solid state. Polymorphs, therefore, may have different physical properties such as shape, density, hardness, deformability, stability, and dissolution properties. Polymorphs typically exhibit different melting points, IR spectra, and X-ray powder diffraction patterns, which may be used for identification. It will be appreciated that different polymorphs may be produced, for example, by changing or adjusting the reaction conditions or reagents, used in making the compound. For example, changes in temperature, pressure, or solvent may result in polymorphs. In addition, one polymorph may spontaneously convert to another polymorph under certain conditions.

**[00041]** The disclosure also includes isotopically-labelled compounds, which are identical to the compounds of Formula (I, II and III) and salts thereof, but for the fact that one or more atoms are replaced by an atom having an atomic mass or mass number different from the atomic mass or mass number most commonly found in nature. Examples of isotopes that can be incorporated into the compounds of the disclosure include isotopes of hydrogen, carbon, nitrogen, oxygen and fluorine, such as $^{3}H$, $^{11}C$, $^{14}C$ and $^{18}F$.

**[00042]** The term "co-crystals" refers to solids that are crystalline single-phase materials composed of two or more different molecular and/or ionic compounds generally in a stoichiometric ratio which are neither solvates nor simple salts.

**[00043]** The term "substituted" in reference to a group indicates that a hydrogen atom attached to a member atom within a group is replaced. It should be understood that the term 'substituted' includes the implicit provision that such substitution be in accordance with the permitted valence of the substituted atom and the substituent and that the

substitution results in a stable compound (i.e. one that does not spontaneously undergo transformation such as rearrangement, cyclisation, or elimination). In certain embodiments, a single atom may be substituted with more than one substituent as long as such substitution is in accordance with the permitted valence of the atom. Suitable substituents are defined herein for each substituted or optionally substituted group.

**[00044]** The term "polymorphs" refers to crystal forms of the same molecule, and different polymorphs may have different physical properties such as, for example, melting temperatures, heats of fusion, solubilities, dissolution rates and/or vibrational spectra as a result of the arrangement or conformation of the molecules in the crystal lattice.

**[00045]** The term "prodrugs" refers to the precursor of the compound of Formula (I, II, and III) which on administration undergoes chemical conversion by metabolic processes before becoming active pharmacological substances. In general, such prodrugs will be functional derivatives of a compound of the disclosure, which are readily convertible *in vivo* into a compound of the disclosure.

**[00046]** The term "alkyl" refers to a saturated hydrocarbon chain having the specified number of carbon atoms. For example, which are not limited, $C_{1\text{-}6}$ alkyl refers to an alkyl group having from 1 – 6 carbon atoms, or 1 – 3 carbon atoms. Alkyl groups may be straight or branched chained groups. Representative branched alkyl groups have one, two, or three branches. Preferred alkyl groups include, without limitation, methyl, ethyl, n-propyl, isopropyl, butyl, and isobutyl.

**[00047]** The term "C(O) alkyl" refers to an alkyl group as defined above attached via carbonyl linkage to the rest of the molecule. For example, $C(O)C_{1\text{-}6}$ alkyl refers to an alkyl group having from 1 – 6 carbon atoms, or 1 – 3 carbon atoms attached via carbonyl linkage to the rest of the molecule. Preferred C(O) alkyl groups include, without limitation, $-C(O)CH_3$, $-C(O)CH_2CH_3$, and the like.

**[00048]** The term "$SO_2$ alkyl" refers to an alkyl group as defined above attached via sulfonyl linkage to the rest of the molecule. For example, $SO_2C_{1\text{-}6}$ alkyl refers to an alkyl group having from 1 – 6 carbon atoms, or 1 – 3 carbon atoms attached via sulfonyl linkage to the rest of the molecule. Preferred $SO_2$ alkyl groups include, without limitation, $-SO_2CH_3$, $-SO_2CH_2CH_3$, and the like.

**[00049]** The term "alkoxy" refers to an alkyl group attached via an oxygen linkage to the rest of the molecule. For example, $C_{1\text{-}6}$ alkoxy refers to an alkyl group having from 1 – 6 carbon atoms, or 1 – 3 carbon atoms attached via an oxygen linkage to the rest of the

molecule. Preferred alkoxy groups include, without limitation, –$OCH_3$ (methoxy), –$OC_2H_5$ (ethoxy) and the like.

**[00050]** The term "alkylamino" refers to an alkyl group as defined above attached via amino linkage to the rest of the molecule. For example, $C_{1-6}$ alkylamino refers to an alkyl group having from 1 – 6 carbon atoms, or 1 – 3 carbon atoms attached via amino linkage to the rest of the molecule. Preferred alkylamino groups include, without limitation, -$NHCH_3$, -$N(CH_3)_2$, and the like.

**[00051]** The term "C(O)NR" refers to an alkylamino group as defined above attached via a carbonyl linkage to the rest of the molecule. Preferred C(O)NR groups include, $C(O)NCH_3$, $C(O)NCH_2CH_3$, and the like.

**[00052]** The term "$SO_2NR$" refers to an alkylamino group as defined above attached via a sulfonyl linkage to the rest of the molecule. Preferred $SO_2NR$ groups include, $SO_2NCH_3$, $SO_2NCH_2CH_3$, and the like.

**[00053]** The term "C(O) alkylamino" refers to an alkylamino group as defined above attached via carbonyl linkage to the rest of the molecule. For example, $C(O)C_{1-6}$ alkylamino refers to an alkylamino group having from 1 – 6 carbon atoms, or 1 – 3 carbon atoms attached via carbonyl linkage to the rest of the molecule. Preferred C(O) alkylamino groups include, without limitation, -$C(O)NHCH_3$, -$C(O)N(CH_3)_2$, and the like.

**[00054]** The term "$SO_2$ alkylamino" refers to an alkylamino group as defined above attached via sulfonyl linkage to the rest of the molecule. For example, $SO_2C_{1-6}$ alkylamino refers to an alkylamino group having from 1 – 6 carbon atoms, or 1 – 3 carbon atoms attached via sulfonyl linkage to the rest of the molecule. Preferred $SO_2$ alkylamino groups include, without limitation, -$SO_2NHCH_3$, -$SO_2N(CH_3)_2$, and the like.

**[00055]** The term "acylamino" refers to an acyl group attached via amino linkage to the rest of the molecule. For example, $C_{1-6}$ acylamino refers to an acyl group having from 1 – 6 carbon atoms, or 1 – 3 carbon atoms attached via amino linkage to the rest of the molecule. Preferred acylamino groups include, without limitation, -$(CO)NHCH_3$, -$(CO)N(CH_3)_2$, and the like.

**[00056]** The term "haloalkyl" refers to an alkyl group as defined above attached via halo linkage to the rest of the molecule. For example, $C_{1-6}$ haloalkyl refers to an alkyl group having from 1 – 6 carbon atoms, or 1 – 3 carbon atoms attached via halo linkage to the rest of the molecule. Preferred haloalkyl groups include, without limitation, -$CH_2Cl$, -$CHCl_2$, and the like.

**[00057]** The term "C(O) haloalkyl" refers to an haloalkyl group as defined above attached via carbonyl linkage to the rest of the molecule. For example, $C(O)C_{1-6}$ haloalkyl refers to an haloalkyl group having from 1 – 6 carbon atoms, or 1 – 3 carbon atoms attached via carbonyl linkage to the rest of the molecule. Preferred C(O) haloalkyl groups include, without limitation, $-(CO)CH_2Cl$, $-C(O)CHCl_2$, and the like.

**[00058]** The term "$SO_2$ haloalkyl" refers to an haloalkyl group as defined above attached via sulfonyl linkage to the rest of the molecule. For example, $SO_2C_{1-6}$ haloalkyl refers to an haloalkyl group having from 1 – 6 carbon atoms, or 1 – 3 carbon atoms attached via sulfonyl linkage to the rest of the molecule. Preferred $SO_2$ haloalkyl groups include, without limitation, $-SO_2CH_2Cl$, $-SO_2CHCl_2$, and the like.

**[00059]** The term "haloalkoxy" refers to an alkoxy group as defined above attached via oxygen linkage of the haloalkoxy group to the rest of the molecule. For example, $C_{1-6}$ haloalkoxy refers to an alkoxy group having from 1 – 6 carbon atoms, or 1 – 3 carbon atoms attached via oxygen linkage to the rest of the molecule. Preferred haloalkoxy groups include, without limitation, $-OCH_2Cl$, $-OCHCl_2$, and the like.

**[00060]** The term "halogen" refers to a halogen radical, for example, fluoro, chloro, bromo, or iodo. "Haloalkyl" refers to an alkyl group, as herein before defined, in which at least one of the hydrogen atoms has been replaced with a halogen radical. "$C_{1-6}$ haloalkyl" refers to a $C_{1-6}$ alkyl group in which at least one of the hydrogen atoms has been replaced with a halogen radical. An example of 'haloalkyl' is trifluoromethyl or 2,2,2-trifluoroethyl.

**[00061]** The term "cycloalkyl" refers to a saturated hydrocarbon ring having a specified number of carbon atoms. For example, which are not limited, $C_{3-6}$ cycloalkyl refers to a cycloalkyl group having from 3 to 6 member atoms, or 3 member atoms. Preferred cycloalkyl groups include, without limitation, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, groups and the like.

**[00062]** The term "$SO_2C_{3-6}$ cycloalkyl" refers to a cycloalkyl group as defined above attached via sulfonyl linkage to the rest of the molecule. For example, $SO_2C_{3-6}$ cycloalkyl refers to a cycloalkyl group having from 3 – 6 carbon atoms attached via sulfonyl linkage to the rest of the molecule. Preferred $SO_2$ cycloalkyl groups include, without limitation, $-SO_2C_3$ cycloalkyl, and the like.

**[00063]** The term "aryl" refers to aromatic ring having a specified number of carbon atoms. For example, $C_{5-6}$ aryl refers to a aryl group having 5 or 6 member atoms, or 6 member atoms. Preferred aryl groups include, without limitation, phenyl, and the like.

**[00064]** The term "C(O) aryl" refers to an aryl group as defined above attached via carbonyl linkage to the rest of the molecule. For example, $C(O)C_{5-6}$ aryl refers to an aryl group having from 5 – 6 carbon atoms attached via carbonyl linkage to the rest of the molecule. Preferred C(O) aryl groups include, without limitation, -C(O) $C_6H_5$, -C(O) $C_5H_5$, and the like.

**[00065]** The term "$SO_2$ aryl" refers to an aryl group as defined above attached via sulfonyl linkage to the rest of the molecule. For example, $SO_2C_{5-6}$ aryl refers to an aryl group having from 5 – 6 carbon atoms attached via sulfonyl linkage to the rest of the molecule. Preferred $SO_2$ aryl groups include, without limitation, -$SO_2$ $C_6H_5$, -$SO_2$ $C_5H_5$, and the like.

**[00066]** The term "heteroaryl" refers to aromatic rings containing from 1 to 5 heteroatoms in the ring. "Heteroaryl" groups may be substituted with one or one or more substituents if so defined herein. The "$C_{1-6}$ heteroaryl" rings having 1 or 6 carbon as member atoms. The "heteroaryl" includes pyridinyl, tetrazolyl and pyrazolyl. "Heteroatom" refers to a nitrogen, sulfur, or oxygen atom, for example a nitrogen atom or an oxygen atom.

**[00067]** The term "C(O) heteroaryl" refers to an heteroaryl group as defined above attached via carbonyl linkage to the rest of the molecule. For example, $C(O)C_{1-6}$ heteroaryl refers to an alkyl group having from 1 – 6 carbon atoms attached via carbonyl linkage to the rest of the molecule. Preferred C(O) heteroaryl groups include, without limitation, -C(O) pyridinyl, -C(O) pyrazolyl, and the like.

**[00068]** The term "$SO_2$ heteroaryl" refers to an aryl group as defined above attached via sulfonyl linkage to the rest of the molecule. For example, $SO_2C_{1-6}$ heteroaryl refers to an aryl group having from 1 – 6 carbon atoms attached via sulfonyl linkage to the rest of the molecule. Preferred $SO_2$ heteroaryl groups include, without limitation, -$SO_2$ pyridinyl, -$SO_2$ pyrazolyl, and the like.

**[00069]** The term "heterocyclic" and "heterocyclyl" refer to saturated or unsaturated monocyclic aliphatic rings containing 5, 6, or 7 ring members including 1-5 heteroatoms or to saturated or unsaturated bicyclic aliphatic rings containing 5, 6 or 7 ring members each including 1-5 heteroatoms. In certain embodiments, 'heterocyclyl' groups are saturated. In other embodiments, 'heterocyclyl' groups are unsaturated. 'Heterocyclyl' groups containing more than one heteroatom may contain different heteroatoms. 'Heterocyclyl' groups may be substituted with one or more substituents as defined herein.

'Heterocyclyl' includes piperidinyl, tetrahydropyranyl, azepinyl, oxazepinyl, azabicyclo[3.1.0]hexanyl.

**[00070]** The phrase "pharmaceutically acceptable" refers to those compounds, materials, compositions, and dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and animals without excessive toxicity, irritation, or other problem or complication, commensurate with a reasonable benefit/risk ratio.

**[00071]** As used herein, the term "pharmaceutically acceptable salts" refers to salts that retain the desired biological activity of the subject compound and exhibit minimal undesired toxicological effects. These pharmaceutically acceptable salts may be prepared in situ during the final isolation and purification of the compound, or by separately reacting the purified compound in its free base form with a suitable acid. The pharmaceutically acceptable salt selected derived from inorganic bases such as like Li, Na, K, Ca, Mg, Fe, Cu, Zn and Mn; salts of organic bases such as N, N'-diacetylethylenediamine, glucamine, triethylamine, choline, dicyclohexylamine, benzylamine, trialkylamine, thiamine, guanidine, diethanolamine, α-phenylethylamine, piperidine, morpholine, pyridine, hydroxyethylpyrrolidine, hydroxyethylpiperidine, ammonium, substituted ammonium salts, aluminum salts and the like. Salts also include amino acid salts such as glycine, alanine, cystine, cysteine, lysine, arginine, phenylalanine, and guanidine. Salts may include acid addition salts where appropriate which are sulphates, nitrates, phosphates, perchlorates, borates, hydrohalides, acetates, tartrates, maleates, citrates, succinates, palmoates, methanesulphonates, tosylates, benzoates, salicylates, hydroxynaphthoates, benzenesulfonates, ascorbates, glycerophosphates, ketoglutarates.

**[00072]** Salts and solvates having non-pharmaceutically acceptable counter-ions or associated solvents are within the scope of the present disclosure, for example, for use as intermediates in the preparation of other compounds of Formula (I), Formula (II), and Formula (III) and their pharmaceutically acceptable salts. Thus, one embodiment of the disclosure embraces compounds of Formula (I), Formula (II), and Formula (III) and salts thereof. Compounds according to Formula (I), Formula (II), and Formula (III) contain a basic functional group and are therefore capable of forming pharmaceutically acceptable acid addition salts by treatment with a suitable acid. Suitable acids include pharmaceutically acceptable inorganic acids and pharmaceutically acceptable organic acids. Representative pharmaceutically acceptable acid addition salts include

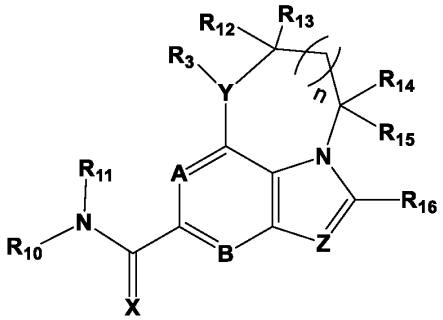
hydrochloride, hydrobromide, nitrate, methylnitrate, sulfate, bisulfate, sulfamate, phosphate, acetate, hydroxyacetate, phenyl acetate, propionate, butyrate, iso-butyrate, valerate, maleate, hydroxymaleate, acrylate, fumarate, malate, tartrate, citrate, salicylate, glycollate, lactate, heptanoate, phthalate, oxalate, succinate, benzoate, o-acetoxybenzoate, chlorobenzoate, methylbenzoate, dinitrobenzoate, hydroxybenzoate, methoxybenzoate, naphthoate, hydroxynaphthoate, mandelate, tannate, formate, stearate, ascorbate, palmitate, oleate, pyruvate, pamoate, malonate, laurate, glutarate, glutamate, estolate, methanesulfonate (mesylate), ethanesulfonate (esylate), 2-hydroxyethanesulfonate, benzenesulfonate (besylate), aminobenzenesulfonate, p-toluenesulfonate (tosylate), and naphthalene-2-sulfonate.

**[00073]** The term "PAD inhibitor" or "inhibitor of PAD" is used to identify a compound, which is capable of interacting with neutrophil extracellular traps (NETs) and more specifically in the histone citrullination that occurs during NETosis. Inhibiting PAD4 enzymatic activity means reducing the ability of PAD4 enzyme so as to inhibit the formation of citrulline through citrullination process. Preferably, such inhibition is specific to PAD4 enzyme.

**[00074]** A term once described, the same meaning applies for it, throughout the patent.

**[00075]** The utility of PAD4 inhibitors is vast as described in the background section. However, the identification and development of PAD4 inhibitor compounds still remains a problem, despite of their vast utility. Therefore, new PAD4 inhibitor compounds treating PAD4 mediated disorders are required.

**[00076]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) their polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof, wherein




Formula (I)

X is selected from O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -$NHC(NH)CH_2Cl$, $NHC(O)CH{=}CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-}$

$_6$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00077]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, C(O)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, C(O)$NR_{18}$, C(O)$C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, C(O)$C_{5-6}$ aryl, C(O)$C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, (CO)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, C(O)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, C(O)$NR_{18}$, C(O)$C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, C(O)$C_{5-6}$ aryl, C(O)$C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, (CO)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-

10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -NHC(NH)$CH_2$Cl, NHC(O)CH=$CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00078]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$

alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$

heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00079]**

**[00080]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O or N; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10

membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -NHC(NH)$CH_2Cl$, NHC(O)CH=$CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00081]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is O; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$

haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$

haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00082]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is N; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$

and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00083]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is N; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, C(O)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, C(O)$NR_{18}$, C(O)$C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, C(O)$C_{5-6}$ aryl, C(O)$C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, (CO)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen,

$C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, -COOH, and cyano; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00084]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy,

is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of

the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00085]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -

$NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00086]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl,

$C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from

hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00087]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 1; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from

the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00088]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, and $C_{1-4}$ alkyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, C(O)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, C(O)$NR_{18}$, C(O)$C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, C(O)$C_{5-6}$ aryl, C(O)$C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, (CO)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, C(O)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, C(O)$NR_{18}$, C(O)$C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, C(O)$C_{5-6}$ aryl, C(O)$C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, (CO)$C_{1-6}$ alkyl,

$C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -$NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00089]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from hydrogen; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$

alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$

haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00090]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-4}$ alkyl, $C_{3-5}$ cycloalkyl, $C_{1-4}$ alkylamino, $C_{1-4}$ haloalkyl, $C(O)C_{1-4}$ alkyl, $C(O)C_{1-4}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-4}$ alkylamino, $SO_2C_{1-4}$ alkyl, $SO_2C_{1-4}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-4}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-4}$ alkyl, $(CO)C_{1-4}$ alkyl, $C(O)C_{1-4}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-4}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH{=}CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$

alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00091]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O or S; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$

alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -$NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00092]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$

alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is selected from the group consisting of hydrogen, $C_{1-4}$ alkyl, $C_{3-5}$ cycloalkyl, $C_{1-4}$ alkylamino, $C_{1-4}$ haloalkyl, $C(O)C_{1-4}$ alkyl, $C(O)C_{1-4}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-4}$ alkylamino, $SO_2C_{1-4}$ alkyl, $SO_2C_{1-4}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-4}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-4}$ alkyl, $(CO)C_{1-4}$ alkyl, $C(O)C_{1-4}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-4}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$

heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00093]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ and $R_{11}$ are taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -$NHC(NH)CH_2Cl$, -$NHC(O)CH{=}CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or

O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00094]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl,

$SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -$NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-4}$ alkyl, $C_{1-4}$ haloalkyl, $C_{1-4}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00095]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of

hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from hydrogen, and $C_{1-4}$ alkyl; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl

is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00096]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally

substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -NHC(NH)$CH_2Cl$, NHC(O)CH=$CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from hydrogen; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00097]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, C(O)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, C(O)$NR_{18}$, C(O)$C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, C(O)$C_{5-6}$ aryl, C(O)$C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, (CO)$C_{1-6}$

alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered bicyclic aryl, and 5-10 membered bicyclic heteroaryl with 1-2 heteroatoms selected from N or S, wherein 5-10 membered bicyclic aryl, and 5-10 membered bicyclic heteroaryl are optionally substituted with 1-3 substituents selected from the group consisting of halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl- $C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl- $C_{1-6}$ heterocyclyl,$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{5-6}$ aryl, $C_{1-6}$ alkyl- $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00098]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O; Y is O or N; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -$NHC(NH)CH_2Cl$, $NHC(O)CH{=}CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted

with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00099]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is S; Y is O or N; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, C(O)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, C(O)$NR_{18}$, C(O)$C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, C(O)$C_{5-6}$ aryl, C(O)$C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, (CO)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, C(O)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, C(O)$NR_{18}$, C(O)$C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, C(O)$C_{5-6}$ aryl, C(O)$C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, (CO)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$

alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -$NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000100]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O or N; Z is N; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally

substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of

the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000101]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O; Y is selected from O or N; Z is N; A is $CR_1$; B is $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -$NHC(NH)CH_2Cl$, $NHC(O)CH{=}CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10

membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000102]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O or N; Z is N; A is $CR_1$; B is $CR_2$; n is 0-1; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered

monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -NHC(NH)$CH_2Cl$, NHC(O)CH=$CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000103]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O; Y is selected from O or N; Z is N; A is $CR_1$; B is $CR_2$; n is 0; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, C(O)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, C(O)$NR_{18}$, C(O)$C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, C(O)$C_{5-6}$ aryl, C(O)$C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, (CO)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with

$C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, -COOH, and cyano; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000104]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O; Y is O or N; Z is N; A is $CR_1$; B is $CR_2$; n is 1; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$

acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl,

$C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000105]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is O or N; Z is N; A is $CR_1$; B is $CR_2$; n is 0-1; $R_1$, and $R_2$ are independently selected from hydrogen; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -$NHC(NH)CH_2Cl$, $NHC(O)CH{=}CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted

with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000106]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is O or N; Z is N; A is $CR_1$; B is $CR_2$; n is 0-1; $R_1$, and $R_2$ are independently selected from hydrogen; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-4}$ alkyl, $C(O)C_{1-4}$ alkyl, $C_{3-6}$ cycloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, wherein $C_{1-4}$ alkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -$NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; and $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10

membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano.

**[000107]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is O or N; Z is N; A is $CR_1$; B is $CR_2$; n is 0-1; $R_1$, and $R_2$ are independently selected from hydrogen; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-4}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-4}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, wherein $C_{1-4}$ alkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ and $R_{11}$ are taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, and $NHC(O)CH=CHCH_2N(CH_3)_2$; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; and $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups

selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano.

**[000108]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is O or N; Z is N; A is $CR_1$; B is $CR_2$; n is 0-1; $R_1$, and $R_2$ are independently selected from hydrogen; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-4}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-4}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, wherein $C_{1-4}$ alkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ and $R_{11}$ is taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, and $NHC(O)CH=CHCH_2N(CH_3)_2$,; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from hydrogen, and $C_{1-6}$ alkyl; and $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano.

**[000109]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O; Y is O or N; Z is N; A is $CR_1$; B is $CR_2$; n is 0-1; $R_1$, and $R_2$ are independently selected from hydrogen; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-4}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, wherein $C_{1-4}$ alkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ and $R_{11}$ is taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$

alkylamino, and $NHC(O)CH=CHCH_2N(CH_3)_2$; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from hydrogen, and $C_{1-6}$ alkyl; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered bicyclic aryl, and 5-10 membered bicyclic heteroaryl with 1-2 heteroatoms selected from N or S, wherein 5-10 membered bicyclic aryl, and 5-10 membered bicyclic heteroaryl are optionally substituted with 1-3 substituents selected from the group consisting of halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl- $C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl- $C_{1-6}$ heterocyclyl,$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{5-6}$ aryl, $C_{1-6}$ alkyl- $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -COOH, and cyano.

**[000110]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is selected from O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-1; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, and $C_{1-6}$ haloalkoxy, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form

a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -$NHC(NH)CH_2Cl$, -$NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S;

$R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000111]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is selected from O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano,

and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C(O)C_{1-6}$ alkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ and $R_{11}$ are taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{2-4}$ alkylamino, $C_{2-4}$ acylamino, $-NHC(NH)CH_2Cl$, $-NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{2-4}$ alkyl, halogen, $C_{2-4}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

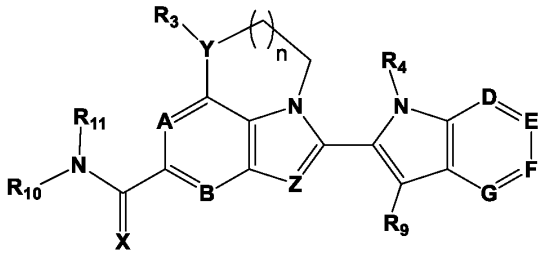
**[000112]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is selected from O or S; Y is selected from O,

N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-1; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, and $C_{1-6}$ haloalkoxy, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ and $R_{11}$ are taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{2-4}$ alkylamino, $C_{2-4}$ acylamino, $-NHC(NH)CH_2Cl$, $-NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{2-4}$ alkyl, halogen, $C_{2-4}$ alkoxy, and hydroxyl; $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, and $C_{1-6}$ haloalkoxy, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$

alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000113]**.In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is $CR_1$; B is $CR_2$; n is 0-1; $R_1$, and $R_2$ are independently selected from hydrogen; $R_3$ is absent or is selected from hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, wherein $SO_2C_{1-6}$ alkyl is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ and $R_{11}$ is taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from amino, $NHC(O)CH=CHCH_2N(CH_3)_2$, or $C_{1-6}$ alkylamino; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from hydrogen or $C_{1-6}$ alkyl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered bicyclic aryl, and 5-10 membered bicyclic heteroaryl with 1-2 heteroatoms selected from N or S, wherein 5-10 membered bicyclic aryl, and 5-10 membered bicyclic heteroaryl are optionally substituted with 1-3 substituents selected from the group consisting of halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl- $C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl- $C_{1-6}$ heterocyclyl,$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{5-6}$ aryl, $C_{1-6}$ alkyl- $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -COOH, and cyano; $R_{17}$ is selected from hydrogen, or $C_{1-6}$ alkyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000114]**In an embodiment of the present disclosure, there is provided a compound of Formula (II) their polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof, wherein



Formula (II)

X is selected from O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; D is selected from N or $CR_5$; E is selected from N or $CR_6$; F is selected from N or $CR_7$; G is selected from N or $CR_8$; n is 0-2; $R_1$, $R_2$, $R_5$, $R_6$, $R_7$, $R_8$, and $R_9$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_4$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, -COOH, and cyano; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of $C_{1-6}$

alkylamino, and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -$NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000115]** In an embodiment of the present disclosure, there is provided a compound of Formula (II) as described herein, wherein X is selected from O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; D is selected from N or $CR_5$; E is selected from N or $CR_6$; F is selected from N or $CR_7$; G is selected from N or $CR_8$; n is 1-2; $R_1$, $R_2$, $R_8$, and $R_9$ are independently selected from the group consisting of hydrogen, halogen, hydroxyl, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, and $C_{1-6}$ haloalkoxy, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_5$, $R_6$, and $R_7$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{2-6}$ alkenyl-$C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_4$ is selected from the group

consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, COOH, and cyano; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000116]** In an embodiment of the present disclosure, there is provided a compound of Formula (II) as described herein, wherein X is selected from O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; D is selected from N or $CR_5$; E is selected from N or $CR_6$; F is selected from N or $CR_7$; G is selected from N or $CR_8$; n is 0-2; $R_1$, $R_2$, $R_8$, and $R_9$ are

independently selected from the group consisting of hydrogen, halogen, hydroxyl, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, and $C_{1-6}$ haloalkoxy, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_5$, $R_6$, and $R_7$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{2-6}$ alkenyl-$C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_4$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, COOH, and cyano; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered

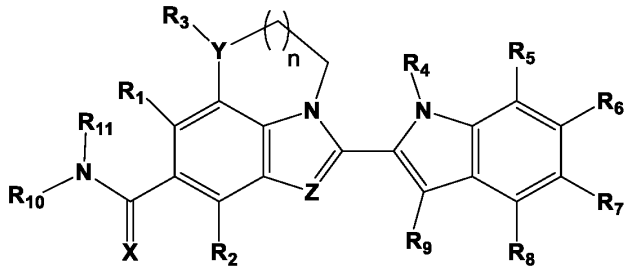
monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -NHC(NH)$CH_2Cl$, NHC(O)CH=$CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000117]** In an embodiment of the present disclosure, there is provided a compound of Formula (II) as described herein, wherein X is selected from O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is $CR_1$; B is $CR_2$; D is selected from N or $CR_5$; E is $CR_6$; F is $CR_7$; G is $CR_8$; n is 0-2; $R_1$, $R_2$, $R_5$, $R_6$, $R_7$, $R_8$, and $R_9$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{2-6}$ alkenyl-$C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_4$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, and $SO_2C_{1-6}$

$_6$ alkyl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, COOH, and cyano; $R_{10}$ and $R_{11}$ are taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{2-4}$ alkylamino, $C_{2-4}$ acylamino, -$NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{2-4}$ alkyl, halogen, $C_{2-4}$ alkoxy, and hydroxyl; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000118]** In an embodiment of the present disclosure, there is provided a compound of Formula (II) as described herein, wherein X is O; Y is selected from O, or N; Z is N; A is $CR_1$; B is $CR_2$; D is selected from N or $CR_5$; E is $CR_6$; F is $CR_7$; G is $CR_8$; n is 1-2; $R_1$, $R_2$, $R_8$, and $R_9$ are independently selected from hydrogen or halogen; $R_5$, $R_6$, and $R_7$ are independently selected from the group consisting of hydrogen, halogen, $C_1$ alkyl, $C_1$ alkoxy, , $C_{2-6}$ alkenyl-$C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_3$ is absent or is selected from hydrogen, $C_{1-6}$ alkyl, $C(O)C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, $C_{3-6}$ cycloalkyl, and $SO_2C_{1-6}$ alkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, wherein $SO_2C_{1-6}$ alkyl, and $SO_2C_{5-6}$ aryl is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_4$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, is optionally substituted with one or more groups selected from hydrogen, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, hydroxyl, -$CH_2OH$, COOH, and halogen; $R_{10}$ and $R_{11}$ are taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from amino, $C_{1-6}$ alkylamino or $NHC(O)CH=CHCH_2N(CH3)_2$; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000119]** In an embodiment of the present disclosure, there is provided a compound of Formula (III) their polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof, wherein




Formula (III)

X is selected from O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; n is 0-2; $R_1$, $R_2$, $R_5$, $R_6$, $R_7$, $R_8$, and $R_9$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_4$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $CH_2OH$, COOH, and cyano; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$

alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $-NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000120]** In an embodiment of the the present disclosure there is provided compound of Formula (I) or its polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof, which is selected from a group consisting of:

**1)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**2)** (R)-(3-aminopyrrolidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**3)** (R)-(3-aminopiperidin-1-yl)(2-(1-ethyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**4)** (2-(aminomethyl)piperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**5)** (R)-(3-aminopiperidin-1-yl)(2-(1-ethyl-1H-pyrrolo[2,3-b]pyridin-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**6)** (R)-(3-aminopiperidin-1-yl)(1-(1-(cyclopropylmethyl)-1H-indol-2-yl)-8,9-dihydro-7H-6-oxa-2,9a-diazabenzo[cd]azulen-4-yl)methanone,

**7)** (R)-(3-aminopyrrolidin-1-yl)(1-(1-(cyclopropylmethyl)-1H-indol-2-yl)-8,9-dihydro-7H-6-oxa-2,9a-diazabenzo[cd]azulen-4-yl)methanone,

**8)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-methyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**9)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**10)** (R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-4-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**11)** (R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-2-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**12)** (R)-(3-aminopiperidin-1-yl)(2-(3-ethylbenzo[b]thiophen-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**13)** (R)-(3-aminopiperidin-1-yl)(2-(1-(4-chlorobenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**14)** (R)-(3-aminopiperidin-1-yl)(2-(1-(2-fluorobenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**15)** (R)-(3-aminopiperidin-1-yl)(2-(1-(4-fluorobenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**16)** (R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-3-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**17)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5,6-dimethoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**18)** (R)-(3-aminopiperidin-1-yl)(2-(1-benzyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**19)** (R)-(3-aminopiperidin-1-yl)(2-(1-(4-methoxybenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**20)** (R)-(3-aminopiperidin-1-yl)(2-(1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**21)** (R)-(3-aminopiperidin-1-yl)(2-(6-methoxy-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**22)** (R)-(3-aminopiperidin-1-yl)(2-(1-(2-hydroxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**23)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-methoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**24)** (R)-(3-aminopiperidin-1-yl)(2-(1-((3-fluoropyridin-4-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**25)** (R)-(3-aminopiperidin-1-yl)(2-(1-(pyrazin-2-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**26)** (R)-(3-aminopiperidin-1-yl)(2-(1-((3-fluoropyridin-2-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**27)** (R)-(3-aminopiperidin-1-yl)(2-(1-(pyrimidin-2-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**28)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**29)** (R)-(3-aminopiperidin-1-yl)(2-(1-(pyrimidin-5-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**30)** (R)-(3-aminopiperidin-1-yl)(2-(1-(pyridazin-3-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**31)** (R)-(3-aminopiperidin-1-yl)(2-(1-isobutyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**32)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5,6-difluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**33)** (R)-(3-aminopiperidin-1-yl)(2-(1-((3-fluoropyridin-2-yl)methyl)-6-methoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**34)** (R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-((3-fluoropyridin-2-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**35)** (R)-(3-aminopiperidin-1-yl)(2-(6-fluoro-1-((3-fluoropyridin-2-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**36)** (*R*)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**37)** (R)-(3-aminopiperidin-1-yl)(2-(1-(4-(hydroxymethyl)benzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone trifluoroacetic acid salt,

**38)** (R,E)-N-(1-(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)-4-(dimethylamino)but-2-enamide trifluoroacetic acid salt,

**39)** (R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(4-methoxybenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**40)** (R)-(3-aminopiperidin-1-yl)(2-(1-((tetrahydro-2H-pyran-4-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**41)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclobutylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**42)** (R)-2-(2-(7-(3-aminopiperidine-1-carbonyl)-3,4-dihydro-5-ox1,2adiazaacenaphthylen-2-yl)-1H-indol-1-yl)acetic acid,

**43)** (R)- (3-aminopiperidin-1-yl)(2-(1-(piperidin-4-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**44)** (R)-(3-aminopiperidin-1-yl)(2-(1-(oxetan-3-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**45)** (R)-(3-aminopiperidin-1-yl)(2-(1-((1-methylpiperidin-4-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**46)** (*R*)-(3-aminopiperidin-1-yl)(2-(5-fluoro-1-(4-methoxybenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**47)** (R)-(3-aminopiperidin-1-yl)(2-(1-(2,2-difluoroethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**48)** (*R*)-(3-aminopiperidin-1-yl)(2-(5-fluoro-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**49)** (R)-(3-aminopiperidin-1-yl)(2-(6-fluoro-1-(4-fluorobenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**50)** (*R*)-(3-aminopiperidin-1-yl)(2-(6-fluoro-1-(4-methoxybenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**51)** (R)-(3-aminopiperidin-1-yl)(2-(1-(4-fluorobenzyl)-6-methoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**52)** 3-aminopiperidin-1-yl)(2-(6-fluoro-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**53)** (*R*)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(cyclobutylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**54)** (R)-(3-aminopiperidin-1-yl)(2-(5,6-difluoro-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**55)** (R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-isobutyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**56)** (R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(2,2-difluoroethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**57)** (R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**58)** (R,E)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-styryl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**59)** (R)-(3-aminopiperidin-1-yl)(2-(1-((4-methylthiazol-2-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**60)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-methoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**61)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-(hydroxymethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**62)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,3-dimethyl-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**63)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**64)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**65)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**66)** (R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-3-ylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**67)** (R)-(3-aminopiperidin-1-yl)(2-(5-bromo-1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**68)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-(pyridin-3-yl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**69)** (R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-2-ylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**70)** (R)-(3-aminopiperidin-1-yl)(2-(1-(2-fluorobenzyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**71)** (R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-4-ylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**72)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-methyl-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**73)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-methoxy-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone

**74)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-methoxy-1H-indol-2-yl)-6-methyl-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**75)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-6-methyl-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**76)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(methylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**77)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5,6-difluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**78)** (R)-(3-aminopiperidin-1-yl)(6-cyclopropyl-2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**79)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(phenethylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**80)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-4-fluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**81)** (R)-(3-aminopiperidin-1-yl)(6-((4-chlorophenyl)sulfonyl)-2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**82)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(cyclopropylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**83)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-((2-ethoxyethyl)sulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**84)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-methyl-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**85)** (R)-1-(8-(3-aminopiperidine-1-carbonyl)-2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-4,5-dihydro-6H-imidazo[1,5,4-de]quinoxalin-6-yl)ethan-1-one,

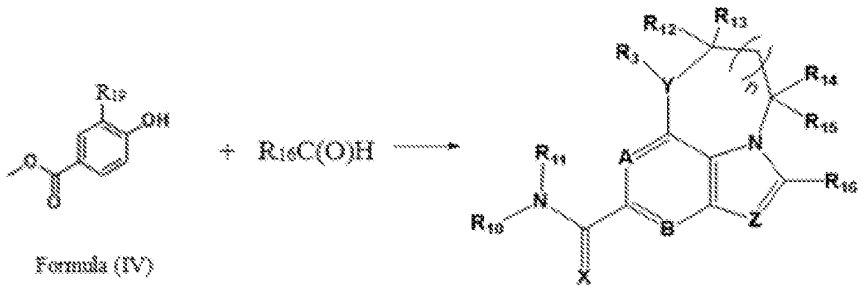
**86)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanethione.

**87)** (R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone, and

**88)** (R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(pyrimidin-5-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone

**[000121]** In an embodiment, the present disclosure relates to a process of preparation of compounds of Formula (I), Formula (II), and Formula (III) or its polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof.

**[000122]** In an embodiment, the disclosure relates to a process of preparation of compounds of Formula (I), or its polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof, the process comprising reacting Formula (IV) and $R_{16}C(O)H$




Formula (IV) Formula (I)

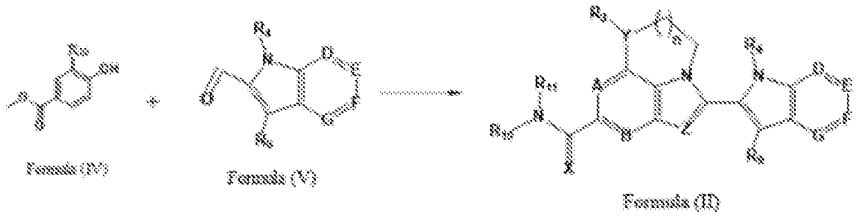
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wherein $R_{19}$ of Formula (IV) is selected from nitro, and $C_{1-6}$ alkoxy; $R_{16}$ of $R_{16}C(O)H$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, -COOH, and cyano; X of Formula (I) is selected from O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one

or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $-NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups

selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000123]** In an embodiment, the present disclosure relates to a process of preparation of compounds of Formula (II), or its polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof, the process comprising reacting Formula (IV) and Formula (V)



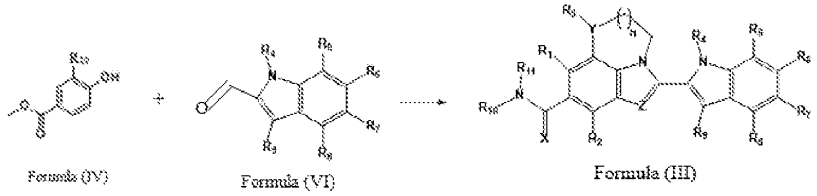
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wherein $R_{19}$ of Formula (IV) is selected from nitro, and $C_{1-6}$ alkoxy; X of Formula (II) is selected from O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; D is selected from N or $CR_5$; E is selected from N or $CR_6$; F is selected from N or $CR_7$; G is selected from N or $CR_8$; n is 0-2; $R_1$, $R_2$, $R_5$, $R_6$, $R_7$, $R_8$, and $R_9$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_4$ is

selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, -COOH, and cyano; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $-NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof; D of Formula (V) is selected from N or $CR_5$; E is selected from N or $CR_6$; F is selected from N or $CR_7$; G is selected from N or $CR_8$, $R_9$ is H; and $R_4$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl,

$C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, -COOH, and cyano.

**[000124]** In an embodiment, the present disclosure relates to a process of preparation of compounds of Formula (III), or its polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof, the process comprising reacting Formula (IV) and Formula (VI)




,

wherein $R_{19}$ of Formula (IV) is selected from nitro, and $C_{1-6}$ alkoxy; X of Formula (III) is selected from O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; n is 0-2; $R_1$, $R_2$, $R_5$, $R_6$, $R_7$, $R_8$, and $R_9$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_4$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl,

wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl,$C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, COOH, and cyano; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $-NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof; and $R_5$, $R_6$, $R_7$, $R_8$, and $R_9$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_4$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$

heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl,$C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, (CO)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, COOH, and cyano; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000125]** In another embodiment, the present disclosure relates to a pharmaceutical composition comprising a compound of Formula (I), Formula (II), and Formula (III) or a pharmaceutically acceptable salt thereof together with a pharmaceutically acceptable carrier, optionally in combination with one or more other pharmaceutical compositions.

**[000126]** In yet another embodiment, the present disclosure relates to the pharmaceutical composition as described herein, wherein the composition is in the form selected from the group consisting of a tablet, capsule, powder, syrup, solution, aerosol, and suspension.

**[000127]** In an embodiment of the present disclosure, there is provided compounds of Formula (I), Formula (II), and Formula (III) or a pharmaceutically acceptable salt thereof as described herein, wherein the pharmaceutically acceptable salt selected derived from inorganic bases such as like Li, Na, K, Ca, Mg, Fe, Cu, Zn and Mn; salts of organic bases such as N, N'-diacetylethylenediamine, glucamine, triethylamine, choline, dicyclohexylamine, benzylamine, trialkylamine, thiamine, guanidine, diethanolamine, α-phenylethylamine, piperidine, morpholine, pyridine, hydroxyethylpyrrolidine, hydroxyethylpiperidine, ammonium, substituted ammonium salts, aluminum salts and the like. Salts also include amino acid salts such as glycine, alanine, cystine, cysteine, lysine, arginine, phenylalanine, and guanidine. Salts may include acid addition salts where appropriate which are sulphates, nitrates, phosphates, perchlorates, borates, hydrohalides, acetates, tartrates, maleates, citrates, succinates, palmoates, methanesulphonates, tosylates, benzoates, salicylates, hydroxynaphthoates, benzenesulfonates, ascorbates, glycerophosphates, ketoglutarates.

**[000128]** In an embodiment of the present disclosure, there is provided compounds of Formula (I), Formula (II), and Formula (III) or a pharmaceutically acceptable salt thereof as described herein, wherein the pharmaceutically acceptable salt thereof for use in the manufacture of a medicament for inhibiting one or more PADs in a cell.

**[000129]** In an embodiment, the present disclosure relates to a method for inhibiting one or more PAD family in a cell with an effective amount of the compounds of Formula (I), Formula (II), and Formula (III) or a pharmaceutically acceptable salt thereof together

with a pharmaceutically acceptable carrier, optionally in combination with one or more other pharmaceutical compositions.

**[000130]** In an embodiment, the present disclosure relates to a method of treating a condition mediated by one or more PADs, comprising administering to a subject suffering from a condition mediated by one or more PAD family, a therapeutically effective amount of the compounds of Formula (I), Formula (II), and Formula (III) or a pharmaceutically acceptable salt thereof together with a pharmaceutically acceptable carrier, optionally in combination with one or more other pharmaceutical compositions.

**[000131]** In an embodiment, the present disclosure relates to a method for the treatment and/or prevention of PAD mediated disorder or disorders associated with PAD activity, comprising administering to a subject suffering from PAD mediated disorder or disorders associated with PAD activity a therapeutically effective amount of the compounds of Formula (I), Formula (II), and Formula (III) or a pharmaceutically acceptable salt thereof together with a pharmaceutically acceptable carrier, optionally in combination with one or more other pharmaceutical compositions.

**[000132]** In an embodiment, the present disclosure relates to a method for the treatment and/or prevention of PAD mediated disorder or disorders associated with PAD, is selected from the group consisting of rheumatoid arthritis, vasculitis, systemic lupus erythematosus, ulcerative colitis, cancer, cystic fibrosis, asthma, cutaneous lupus erythematosis, and psoriasis.

**[000133]** In an embodiment, the present disclosure relates to a method for the treatment of PAD mediated disorder, said method comprising administering a combination of compounds of Formula (I), Formula (II), and Formula (III) or a pharmaceutically acceptable salts thereof together with a pharmaceutically acceptable carrier, optionally in combination with one or more other pharmaceutical compositions, and/or with other clinically relevant agents or biological agents to a subject in need thereof.

**[000134]** In an embodiment, the present disclosure relates to a method for the treatment and/or prevention of PAD mediated disorder or disorders associated with PAD, is selected from the group consisting of acid-induced lung injury, respiratory distress syndrome, allergen induced asthma, allergic bronchopulmonary, aspergillosis, allergic conjunctivitis, alopecia, amyotropic lateral sclerosis, inflammation, arthritis, asthma, atherosclerosis, atopic dermatitis, autoimmune diseases, bone pain, bronchiolitis, chronic lung disease of prematurity, chronic obstructive pulmonary disease, colitis, complex regional pain syndrome, crohn's disease, cystic fibrosis, familial cold urticarial, gout,

gouty arthritis, graftversus- host disease, gut diseases, inflammatory bowel disease, inflammatory lung disease, inflammatory neuropathy, inflammatory pain, insect bite-induced inflammation, irritant-induced inflammation, juvenile rheumatoid arthritis, kidney disease, kidney injury caused by parasitic infections, kidney transplant rejection prophylaxis, lung injury, lupus, lupus nephritis, multiple sclerosis, muscle wasting, muscular dystrophy, non-allergen induced asthma, osterarthritis, periodontitis, peritoneal endometriosis, plant irritant-induced inflammation, psoriasis, pulmonary disease, pulmonary fibrosis, pyogenic sterile arthritis, renal disease, rheumatic carditis, rheumatic disease, rheumatoid arthritis, sepsis, severe pain and ulcerative colitis.

**[000135]** In an embodiment, the present disclosure relates to the use of compounds of Formula (I), Formula (II), and Formula (III) or a pharmaceutically acceptable salts thereof together with a pharmaceutically acceptable carrier, optionally in combination with one or more other pharmaceutical compositions for treatment of a condition mediated by one or more PAD family; or treatment and/or prevention of PAD mediated disorder; or treatment of PAD mediated disorder together with other clinically relevant agents or biological agents.

**[000136]** In an embodiment, the present disclosure relates to a method for the treatment and/or prevention of a condition mediated by one or more PAD family or a proliferative disorder or cancer, comprising administering to a subject suffering from the condition mediated by one or more PAD family or PAD mediated disorder, a therapeutically effective amount of the compound of the present disclosure or the pharmaceutical composition of the present disclosure.

**[000137]** In an embodiment, the present disclosure relates to a method comprising administering a combination of the compounds of Formula (I), Formula (II), and Formula (III) or the pharmaceutical composition with other clinically relevant agents or biologicalagents to a subject in need thereof.

**[000138]** In an embodiment, the present disclosure relates to a method for the treatment of cancer, said method comprising administering a combination of compounds of Formula (I), Formula (II), and Formula (III) or a pharmaceutically acceptable salt thereof together with a pharmaceutically acceptable carrier, optionally in combination with one or more other pharmaceutical compositions, with other clinically relevant immune modulators agents to a subject in need of thereof.

**EXAMPLES**

**[000139]** As used herein the symbols and conventions used in these processes, schemes and examples are consistent with those used in the contemporary scientific literature, for example, the Journal of the American Chemical Society. Unless otherwise noted, all starting materials were obtained from commercial suppliers and used without further purification. Specifically, the following abbreviations may be used in the examples and throughout the specification:

**Abbreviations:**

| | |
|---|---|
| AcOH | Acetic acid |
| $BOC_2O$ | Di-tert-butyl dicarbonate |
| nBuLi | n-Butyllithium |
| BuOH | Butanol |
| Bz | Benzyl |
| Cbz | Carboxybenzyl |
| cHex | Cyclohexane |
| $Cs_2CO_3$ | Caesium carbonate |
| DCM / $CH_2Cl_2$ | Dichloromethane |
| DIAD | Diisopropyl azodicarboxylate |
| Dioxane | 1,4-dioxane |
| DIPEA | N, N-diisopropylethylamine |
| DMSO | Dimethylsulfoxide |
| DMF | N,N-dimethylformamide |
| $Et_3N$ | Tri ethyl amine |
| Ether | Diethyl ether |
| EtOAc | Ethyl acetate |
| HATU | o-(7-Azabenzotriazol- 1 -yl)-N,N,N' ,N' -tetramethyluronium hexafluorophosphate |
| HPLC | High performance liquid chromatography |
| IPA | Isopropyl alcohol |
| $K_2CO_3$ | Potassium carbonate |
| KOH | Potassium hydroxide |
| LiOH | Lithium hydroxide |
| LCMS or LC/MS | Liquid chromatography- mass spectroscopy |
| MeOH | Methanol |
| min | Minutes |

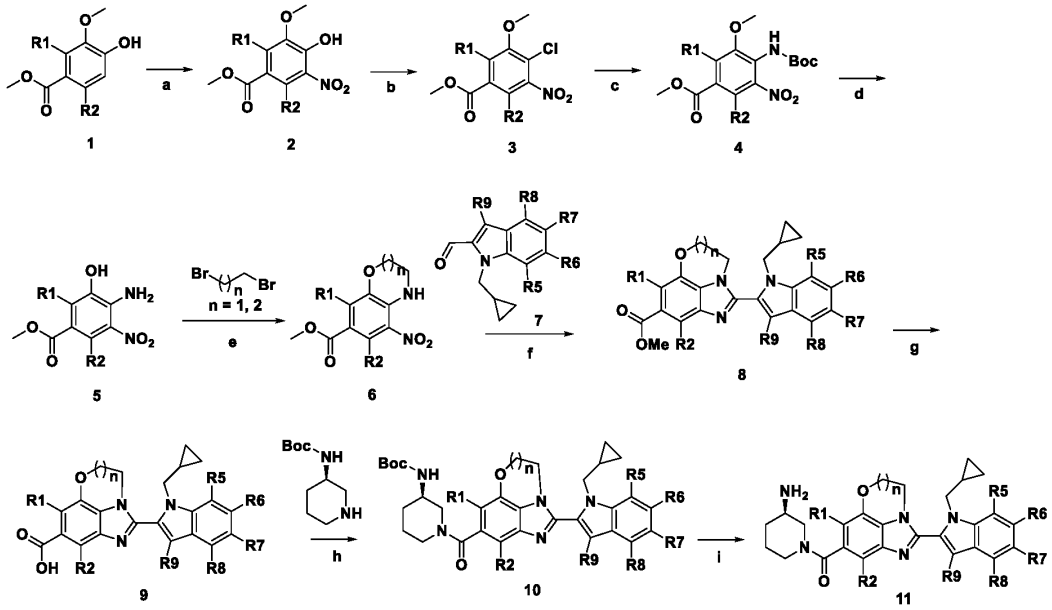
| | |
|---|---|
| $Na_2SO_4$ | Sodium sulfate |
| $NaHCO_3$ | Sodium bicarbonate |
| $NH_4Cl$ | Ammonium chloride |
| Palladium tetrakis | palladium tetrakistriphenylphosphine |
| Pd/C | Palladium on carbon |
| PTSA | p-Toluenesulfonic acid |
| rb | round-bottomed (flask) |
| r.t / rt. | Room temperature |
| Rt | Retention time |
| TFA | Trifluoroacetic acid |
| TFAA | Trifluoroacetic anhydride |
| THF / thf | Tetrahydrofuran |
| TLC / tic | Thin layer chromatography |
| TMEDA | Tetramethyl ethyl enediamine |

**[000140]** The following examples provide the details about the synthesis, activities, and applications of the compounds of the present disclosure. It should be understood the following is representative only, and that the present disclosure is not limited by the details set forth in these examples.

**[000141]** The compounds of the present disclosure may be made by a variety of methods, including standard chemistry. Any previously defined variable will continue to have the previously defined meaning unless otherwise indicated. Illustrative general synthetic methods are set out in the following schemes and can be readily adapted to prepare other compounds of the disclosure.

**[000142]** There is also provided a general process as shown in the following Scheme-1, for the preparation of compounds of the Formula (I, II, and III), wherein all the groups are as defined earlier.

**Scheme 1**




The said process for the preparation of the compounds of Formula (I, II, and III) comprises of the following steps:

**Step 1**: Compound **1** was converted to compound **2** under standard conditions using $CH_3COOH$ and $HNO_3$ (reaction condition **a**).

**Step** 2: Treatment of compound **2** with oxalyl chloride (reaction condition **b**) gave intermediate **3**.

**Step 3**: Intermediate **3** was converted to compound **4** using tert-butyl carbamate, $Cs_2CO_3$ and X-Phos (reaction condition **c**).

**Step 4**: Treatment of compound **4** with $BBr_3$ (reaction condition **d**) gave intermediate **5.**

**Step 5**: Intermediate **5** was converted to compound **6** by reacting with 1, ω-dibromoalkane and $K_2CO_3$ (reaction condition **e**).

**Step 6**: Compound **6** was coupled with substituted indole-2-carbaldehyde **7** (reaction condition **f)** to give compound **8.**

**Step 7**: Compound **8** was hydrolysed (Reaction condition **g**) to give compound **9**.

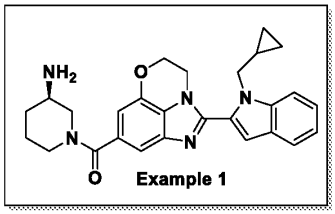
**Step 8**: Coupling of compound **9** with tert-butyl (R)-piperidin-3-ylcarbamate (reaction condition **h**) gave intermediate **10**.

**Step 9**: Compound **10** was converted to final compound **11** by Boc deprotection (reaction condition **i**).

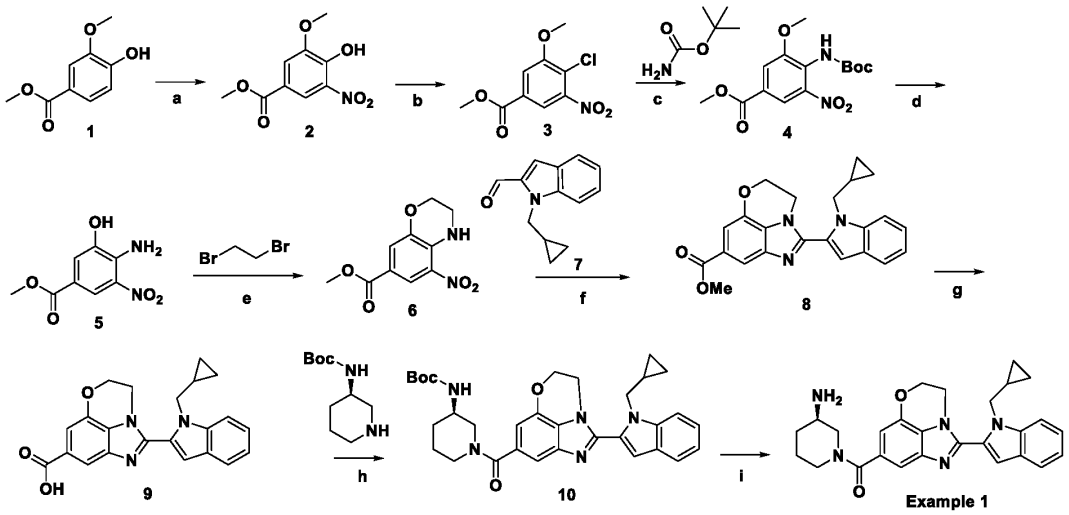
**[000143]** The examples given below are provided by the way of illustration only and therefore should not be construed to limit the scope of the disclosure.

**Example-1:**

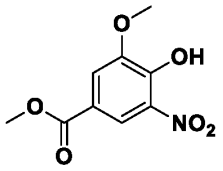
**Synthesis of ((R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone (Example -1)**




Scheme 2




**Step 1: Preparation of methyl 4-hydroxy-3-methoxy-5-nitrobenzoate (2)**

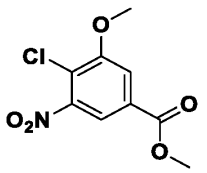


**2**

**[000144]** To a stirred solution of methyl-4-hydroxy-3-methoxybenzoate (**1**, 20 g, 109.7 mmol) in $CH_3COOH$ (100 mL) was added $HNO_3$ (5.9 mL, 94.4 mmol) under 0°C drop wise and then reaction mixture was stirred at room temperature for 4-5 h (reaction

condition **a**). To the reaction mixture ice cold water was added and the reaction mixture was filtered to obtain the precipitate which was dried using high vacuum to get the product as yellow solid (18 g, 75% yield). MS (ESI): mass calcd. for $C_9H_9NO_6$, 227.04; m/z found, 228 $[M+H]^+$.

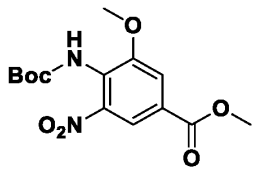
**Step 2: Preparation of methyl 4-chloro-3-methoxy-5-nitrobenzoate (3)**



**3**

**[000145]** To a stirred solution of methyl 4-hydroxy-3-methoxy-5-nitrobenzoate (**2**, 18 g, 79.29 mmol) in DMF (100 mL) was added oxalyl chloride (14.27 mL, 113.28 mmol) under 0°C slowly, then the reaction mixture was refluxed under 80°C for about 12 h (reaction condition **b**). To the reaction mixture ice cold water was added and the resulting solid was filtered. The solid was dried under high vacuum to obtain the product as brown solid (17.5 g, 90% yield). MS (ESI): mass calcd. for $C_9H_8ClNO_5$, 245.01; m/z found, 246 $[M+H]^+$.

**Step 3: Preparation of Methyl 4-((tert-butoxycarbonyl) amino)-3-methoxy-5-nitrobenzoate (4)**

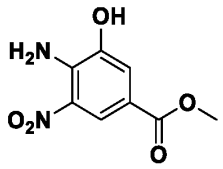


**4**

**[000146]** To a stirred solution of methyl 4-chloro-3-methoxy-5-nitrobenzoate (**3**, 6 g, 24.42 mmol) in t-butanol (50 mL) was added tert-butyl carbamate (2.86 g, 24.42 mmol), $Cs_2CO_3$ (9.5 g, 29.31 mmol) and X-Phos (1.16 g, 2.44 mmol) under $N_2$. $Pd_2(dba)_3$, (,0.44 g, 0.48 mmol) was added and stirred for about 10 min at room temperature and then resulting mixture was heated to 100 °C for 12 h (reaction condition **c**). The reaction mixture was cooled to room temperature and diluted with ethyl acetate (100 mL x 3) and the organic phase was washed with water and brine, dried over sodium sulphate and concentrated under reduced pressure to afford the crude compound which was purified by column chromatography (silica gel, 0-20% EtOAc in hexane) to afford methyl 4-((tert-

butoxycarbonyl) amino)-3-methoxy-5-nitrobenzoate (2.5 g, 75% yield) as colourless liquid. MS (ESI): Mass calcd. for $C_{14}H_{18}N_2O_7$, 325.0; m/z found, 326.3 $[M+H]^+$.

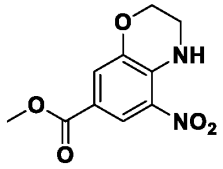
**Step 4: Preparation of Methyl 4-amino-3-hydroxy-5-nitrobenzoate (5)**



**5**

**[000147]** To a stirred solution of methyl 4-((tert-butoxycarbonyl) amino)-3-methoxy-5-nitrobenzoate (**4**, 3.5g, 10.74 mmol) in DCM (30 mL) was added $BBr_3$ (3.5 mL,) at -78°C and the resulting mixture was allowed to stir under room temperature for 3 h (reaction condition **d**). The progress of the reaction was monitored by TLC. The reaction mixture was quenched with ice and sodium bicarbonate solution (30 mL) and extracted with DCM (50 mL x 3). The combined organic extract was washed with brine, dried over sodium sulphate and concentrated under reduced pressure to afford methyl 4-amino-3-hydroxy-5-nitrobenzoate (0.7 g, 35% yield) as brown solid. MS (ESI): Mass calcd. for $C_8H_8N_2O_5$, 212.1; m/z found, 213 $[M+H]^+$.

**Step 5: Preparation of Methyl 5-nitro-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (6)**

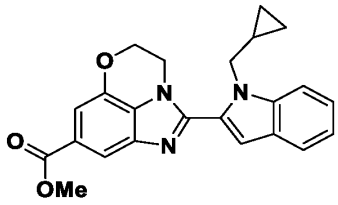


**6**

**[000148]** To a stirred solution of methyl 4-amino-3-hydroxy-5-nitrobenzoate (**5**, 1.1g, 5.12 mmol) in DMF (10 mL) was added 1,2-dibromo ethane (0.44 mL,) and $K_2CO_3$ (0.86 g, 2.38 mmol) the resulting mixture was heated to 80°C for 12 h (reaction condition **e**). The progress of the reaction was monitored by TLC. The reaction mixture was quenched with water and extracted with ethyl acetate (20 mL x 2). The combined organic extract was washed with brine, dried over sodium sulphate and concentrated under reduced pressure to afford the crude compound which was purified by column chromatography (SiO2, 0-20% EtOAc in hexane) to afford methyl 5-nitro-3,4-dihydro-

2H-benzo[b][1,4]oxazine-7-carboxylate (0.45 g, 89% yield) as brown solid. MS (ESI): Mass calcd. for $C_{10}H_{10}N_2O_5$, 238.2; m/z found, 239.1 $[M+H]^+$.

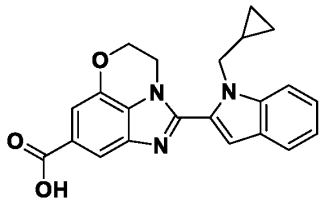
**Step 6: Preparation of Methyl 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2diazaacenaphthylene-7-carboxylate (8)**



**8**

**[000149]** To the stirred solution of mixture of methyl 5-nitro-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (**6**, 0.2 g, 0.84 mmol) and 1-(cyclopropylmethyl)-1H-indole-2-carbaldehyde (**7**, 0.18 g, 0.92 mmol) in EtOH (10 mL), was added $Na_2S_2O_4$ (0.73 g, 4.20 mmol) in water (5 mL) and stirred at 95°C for 16h (Reaction condition **f**). The reaction mixture was cooled to room temperature, water was added and compound was extracted with ethyl acetate (20 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using silica gel with eluent 15-20% ethyl acetate in hexane to afford methyl 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2diazaacenaphthylene-7-carboxylateas yellow solid (0.18 g. 12% yield). MS (ESI): Mass calcd. for $C_{23}H_{21}N_3O_3$, 387.4; m/z found, 388.1 $[M+H]^+$.

**Step 7: Preparation of 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid (9)**

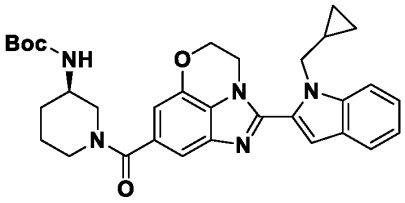


**9**

**[000150]** To the stirred solution of methyl 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2diazaacenaphthylene-7-carboxylate (**8**, 0.18 g, 0.46 mmol) in MeOH (2 mL), was added 5N NaOH solution (0.4 mL) and stirred at 75°C for 1h (reaction condition **g**). The reaction mixture was evaporated completely. The resulting crude was dissolved in water and acidified using citric acid (pH~ 4-6), extracted with DCM (20 mL x 2). Combined organic extracts were washed with brine, dried over sodium

sulfate, filtered and evaporated to get crude product as a yellow solid to afford the2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid as brown solid (0.07 g, 41% yield). MS (ESI): Mass calcd. for $C_{22}H_{19}N_3O_3$, 373.4; m/z found, 374.1 $[M+H]^+$.

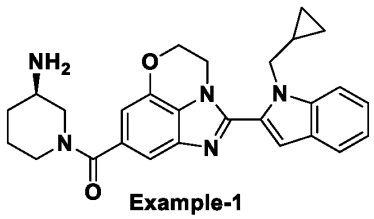
**Step 8: Preparation of tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydrooxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (10)**




**10**

**[000151]** To the stirred solution of 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3-methyl-3H-imidazo[4,5-b]pyridine-6-carboxylic acid (**9**, 0.089 g, 0.24 mmol) in DCM (2 mL), were added tert-butyl (R)-piperidin-3-ylcarbamate (0.05 g, 0.26 mmol), triethylamine (0.1 g, 0.72 mmol) followed by 50% solution of T3P in ethyl acetate (0.2 g, 0.72 mmol) and stirred at room temperature for 12 h (reaction condition **h**). To the reaction mixture was added water and compound was extracted with DCM (20 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using 5% MeOH in DCM to afford the product as yellow solid (0.07 g, 53.8% yield). MS (ESI): Mass calcd. for $C_{32}H_{37}N_5O$, 555.6; m/z found, 556.3 $[M+H]^+$.

**Step 9: Preparation of (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone (Example-1)**




**Example-1**

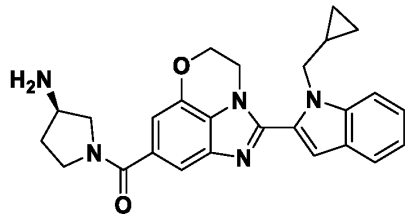
**[000152]** To the stirred solution of tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (**10**, 0.08 g, 0.14 mol) in dichloromethane (10 mL), was added trifluroacetic

acid (0.5 mL) and stirred at room temperature for 2h (reaction condition **i**). The reaction mixture was evaporated completely, dissolved in minimum volume of water (30 mL) and basified by saturated $NaHCO_3$ (20 mL) solution. The compound was extracted with ethyl acetate (50 mL x 2)). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get the product as pale yellow solid (0.044 g, 67.5% yield). $^1$HNMR (400 MHz, DMSO-d6): δ (ppm): 7.68 (t, $J$ = 4.4 Hz, 2H), 7.29 (t, $J$ = 5.2 Hz, 2H), 7.15-7.10 (m, 2H), 6.74 (s, 1H), 4.69-4.68 (m, 4H), 4.55 (s, 2H), 3.56 (m, 2H), 2.92 (s, 1H), 4.13 (s, 2H), 2.69-2.65 (m, 1H), 1.88-1844 (m, 2H), 1.64 (m, 1H), 1.43-1.41 (m, 1H), 1.23-1.22 (m, 2H), 0.32 (d, $J$ = 8 Hz, 2H), 0.28-0.27 (m, 2H). MS (ESI): mass calcd. for $C_{32}H_{37}N_5O_4$, 455.0; m/z found, 456.4 $[M+H]^+$.

**[000153]** Following compounds **(Examples 2-8)** were synthesized using the above procedure as exemplified for **Example-1** above with corresponding reactants.

**Example-2:**

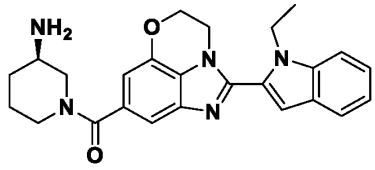
**(R)-(3-aminopyrrolidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000154]** $^1$HNMR (400 MHz, DMSO-d6): δ (ppm): 7.69 (t, $J$ =12 Hz, 2H), 7.43 (s, 1H), 7.29-7.26 (m, 1H), 7.18-7.10 (m, 2H), 6.87 (s, 1H), 4.69 (d, $J$ = 8 Hz, 2H), 4.64 (d, $J$ = 4 Hz, 2H ), 4.56-4.55 (m, 2H), 3.65-3.59 (m, 2H), 3.56-3.45 (m, 2H), 1.97 (m, 2H), 1.64 (m, 2H), 1.31-1.22 (m, 2H), 0.32 (d, $J$ = 8 Hz, 2H), 0.27-0.26 ( m, 2H). MS (ESI): mass calcd. for $C_{26}H_{27}N_5O_2$, 441.22; m/z found, 442.0 $[M+H]^+$.

**Example-3:**

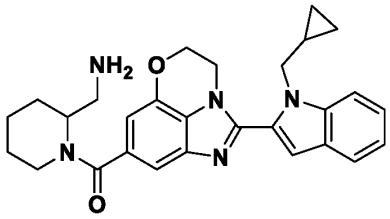
**(R)-(3-aminopiperidin-1-yl)(2-(1-ethyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000155]** $^1$HNMR (400 MHz, DMSO-d6): δ (ppm): 7.67 (d, *J* = 8 Hz, 1H), 7.62 (d, *J* = 8 Hz, 1H), 7.31-7.27 (m, 2H), 7.14-7.11 (m, 2H), 6.70 (s, 1H) , 4.80 (m, 2H), 4.77 (m, 2H), 4.75 (m, 2H) 4.00 (m, 2H), 3.60 (m, 2H), 2.94 (bs, 1H), 2.78 (bs, 2H), 1.89 (m, 1H), 1.73 (m, 1H), 1.42 (m, 1H), 1.35 (m, 3H), 1.31 (m, 1H). MS (ESI): Mass calcd. for $C_{25}H_{27}N_5O_2$, 429.52; m/z found, 430.2 $[M+H]^+$.

**Example-4:**

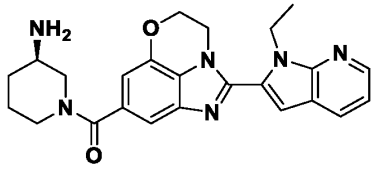
**(2-(aminomethyl)piperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**




**[000156]** $^1$HNMR (400 MHz, DMSO-d6): δ (ppm): 7.68 (t, *J* = 8 Hz, 2H), 7.50 (m, 1H), 7.29-7.26 (m, 2H), 7.14-7.05 (m, 3H), 6.74 (d, *J* = 8 Hz, 1H), 4.68 (d, *J* = 8 Hz, 2H), 4.64 (m, 2H), 4.54 (m, 2H), 3.97-3.96 (m, 2H), 2.87-2.81 (m, 1H), 1.54-1.49 (m, 2H), 1.28 (m, 1H), 1.13 (m, 6H), 0.37-0.27 (m, 4H). MS (ESI): Mass calcd. for $C_{28}H_{31}N_5O_2$, 469.59; m/z found, 470.3 $[M+H]^+$.

**Example-5:**

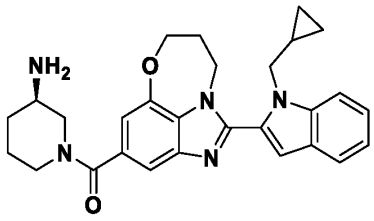
**(R)-(3-aminopiperidin-1-yl)(2-(1-ethyl-1H-pyrrolo[2,3-b]pyridin-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**




**[000157]** $^1$HNMR (400 MHz, DMSO-d6): δ (ppm): 8.42 (d, *J* = 4 Hz, 1H), 8.11 (d, *J* = 4Hz, 1H), 7.31(s, 1H), 7.22-7.19 (m, 2H), 6.75 (s, 1H), 4.89-4.86 (m, 2H), 4.68 (m, 2H), 4.56 (m, 2H), 3.51 (m, 2H), 2.91-2.87 (m,1H), 1.97 (m, 1H), 1.86-1.83 (m, 2H), 1.65 (m, 3H), 1.43-1.33 (m, 5H). MS (ESI): Mass calcd. for $C_{24}H_{26}N_6O_2$, 430.51; m/z found, 431.4 $[M+H]^+$.

**Example-6:**

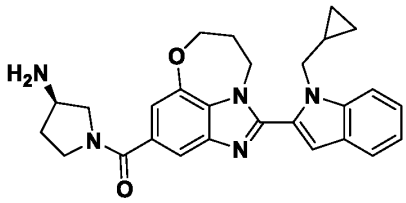
**(R)-(3-aminopiperidin-1-yl)(1-(1-(cyclopropylmethyl)-1H-indol-2-yl)-8,9-dihydro-7H-6-oxa-2,9a-diazabenzo[cd]azulen-4-yl)methanone**



**[000158]** $^1$HNMR (400 MHz, DMSO-d6): δ (ppm): 7.65 (m, 2H), 7.35 (s, 1H), 7.27 (m, 1H), 7.12 (m, 1H), 7.04 (m, 1H), 6.82 (s, 1H), 4.45-4.38 (m, 6H), 2.65 (m, 2H), 1.89 (m, 2H), 1.67 (m, 3H), 1.45-1.31 (m, 2H), 1.22 (m, 4H), 0.83 (s, 1H), 0.30 (m, 2H), 0.06 (m, 2H). MS (ESI): Mass calcd. for $C_{28}H_{31}N_5O_2$, 469.59; m/z found, 470.2 $[M+H]^+$.

**Example-7:**

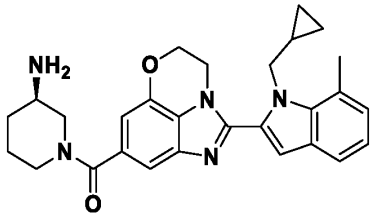
**(R)-(3-aminopyrrolidin-1-yl)(1-(1-(cyclopropylmethyl)-1H-indol-2-yl)-8,9-dihydro-7H-6-oxa-2,9a-diazabenzo[cd]azulen-4-yl)methanone**



**[000159]** $^1$HNMR (400 MHz, DMSO-d6): δ (ppm): 7.68-7.64 (m, 2H), 7.46-7.44 (m, 1H), 7.29 (t, *J* = 16 Hz, 1H), 7.14-7.10 (m, 1H) 7.04 (bs , 1H), 6.92 (s, 1H), 4.44-4.36 (m, 6H), 3.64 (m, 2H), 3.55-3.48 (m, 2H), 2.43 (m, 2H), 1.97 (m, 1H), 1.86 (m, 1H), 1.60 (m, 1H), 1.31 (m, 1H), 1.06 (m, 1H), 0.83 (m, 1H), 0.31 (m, 2H), 0.05 (m, 2H). MS (ESI): Mass calcd. for $C_{27}H_{29}N_5O_2$, 455.56; m/z found, 456.3 $[M+H]^+$.

**Example-8:**

**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-methyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**

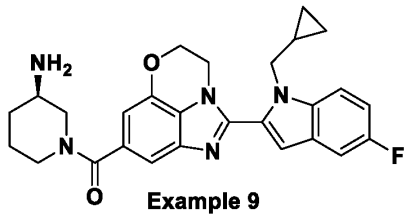


**[000160]** $^1$HNMR (400 MHz, DMSO-d6): δ (ppm): 7.51 (d , *J* = 6.0 Hz, 1H), 7.27 (s, 1H), 7.12 (s, 1H), 7.03-7.00 (m, 2H), 6.75 (s, 1H), 4.89 (d, *J* = 6.0 Hz, 2H), 4.57 (d, *J*

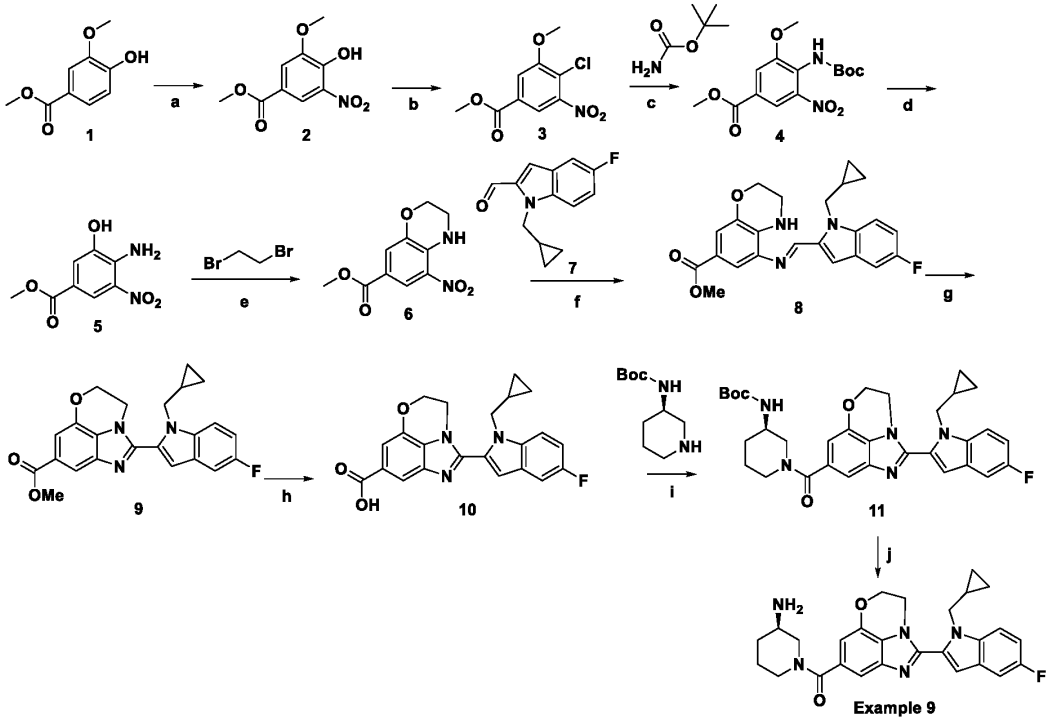
= 7.2 Hz, 4H), 4.30 (s, 1H), 3.65 (s, 1H), 2.90 (s, 1H), 2.78 ( s, 3H), 2.65 (s, 1H), 1.84-1.65 (m, 4H), 1.41 (d, *J* = 10.8 Hz, 1H), 1.22 (m, 2H), 0.94 (bs, 1H), 0.21 (d , *J* = 7.6 Hz, 2H), 0.15 (d, *J* = 4.4 Hz, 2H). MS (ESI): mass calcd. for $C_{28}H_{31}N_5O_2$, 469.5; m/z found, 470 $(M+H)^+$.

**Example-9:**

**Synthesis of (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone (Example-9)**

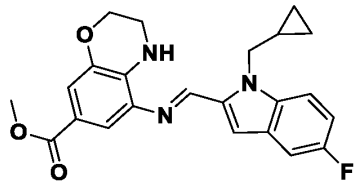



Scheme 3




**[000161]** The reaction procedure followed to obtain intermediate **(6)** was similar to the procedure outlined for the preparation of Example-1 in Scheme-2 above.

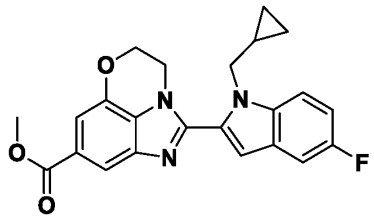
**Step 6: Preparation of methyl (E)-5-(((1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)methylene)amino)-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (8)**



**8**

**[000162]** To a stirred solution methyl 5-nitro-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (**6**, 0.25 g, 1.05 mmol) in ethanol (6 mL), were added 1-(cyclopropylmethyl)-5-fluoro-1H-indole-2-carbaldehyde (**7**, 0.27 g, 1.26 mmol), sodium dithionite (0.91 g, 5.25 mmol) and water (3 mL). Then the reaction mixture was heated to 90°C for 12 h in a sealed tube (reaction condition **f**). The reaction mixture was evaporated, diluted with water and extracted with ethyl acetate (20 mL x 2). Combined organic extracts were washed with water, brine, dried over sodium sulfate, filtered and evaporated to get crude product as a yellow solid (0.25 g, crude). MS (ESI): mass calcd. for $C_{23}H_{22}FN_3O_3$, 407.45; m/z found, 408.1 $[M+H]^+$.

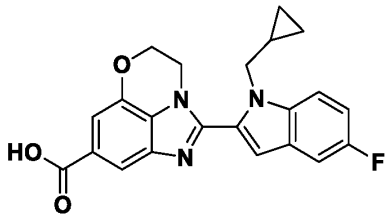
**Step 7: Preparation of methyl 2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylate (9)**



**9**

**[000163]** To a stirred solution methyl (E)-5-(((1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)methylene)amino)-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (**8,** 0.25 g, 0.61 mmol) in toluene (3 mL), was added p-toluene sulfonic acid (0.012 g, 0.0614 mmol) at room temperature. Then the reaction mixture was heated to 90°C for 12 h (reaction condition **g**). The reaction mixture was quenched with sodium bicarbonate, extracted with ethyl acetate (20 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate, filtered and evaporated to get crude product. Crude residue was purified by gradient column chromatography using silica gel and eluent 15-20% ethyl acetate in hexane to get the product as a yellow solid (0.15 g, 35% yield). MS (ESI): mass calcd. for $C_{23}H_{20}FN_3O_3$, 405.43; m/z found, 406.1 $[M+H]^+$.

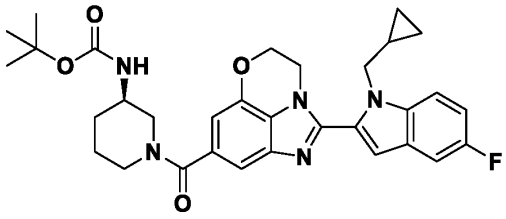
**Step 8: Preparation of 2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid (10)**



**10**

**[000164]** To a stirred solution of methyl 2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylate (**9**, 0.15 g, 0.37 mmol) in methanol (5 mL) was added 5N NaOH (0.37 mL, 1.85 mmol) solution and heated to 80°C for 1 h (reaction condition **h**). The solvent was evaporated completely and dissolved in water (10 mL) and acidified using citric acid, extracted with DCM (20 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate, filtered and evaporated to get crude product as a yellow solid (0.13 g, 90% yield). MS (ESI): mass calcd. for $C_{22}H_{18}FN_3O_3$, 391.40; m/z found, 392.1 $[M+H]^+$.

**Step 9: Preparation of Tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (11)**

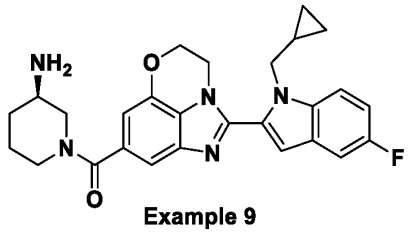


**11**

**[000165]** To a stirred solution of 2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid (**10**, 0.13 g, 0.33 mmol) in DCM (4 mL), were added tert-butyl (R)-piperidin-3-ylcarbamate (0.079 g, 0.398 mmol), triethylamine (0.09 mL, 0.66 mmol), propyl phosphonic anhydride in 50% ethyl acetate (0.316 mL, 0.498 mmol). The reaction mixture was allowed to stir at room temperature for 1h (reaction condition **i**). The reaction mixture was quenched with sodium bicarbonate solution (20 mL), extracted with ethyl acetate (20 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate, filtered and evaporated to get crude product. Crude residue was purified by gradient column

chromatography using silica gel and eluent 5-10% methanol in DCM to get the product as a yellow solid (0.13 g, 68% Yield). MS (ESI): mass calcd. for $C_{32}H_{36}FN_5O_4$, 573.67; m/z found, 574.3 $[M+H]^+$.

**Step 10: Preparation of (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone (Example-9)**



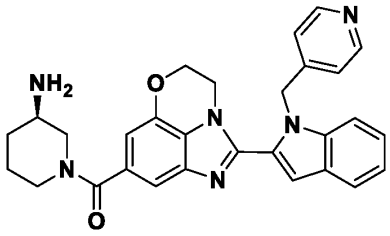

Example 9

**[000166]** To a stirred solution of Tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (**11**, 0.13 g, 0.226 mmol) in DCM (4 mL) was added trifluoro acetic acid (0.5 mL) at 0°C. Then the reaction mixture was allowed to stir at room temperature for 1 h (reaction condition **j**). Reaction mixture was evaporated under reduced pressure, washed with ether and the reaction mixture was basified using saturated sodium bicarbonate solution (20 mL) and extracted with ethyl acetate (20 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate, filtered and evaporated to get crude product. Crude residue was purified by gradient column chromatography using silica gel and eluent 5-10% methanol in DCM to get the product as off white solid (0.06 g, 57% Yield). $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): δ 7.72-7.68 (m, 1H), 7.44 (d, $J$ = 7.2 Hz, 1H), 7.29 (s, 1H), 7.13 (t, $J$ = 7.2 Hz, 2H), 6.75 (s, 1H), 4.69-4.64 (m, 4H), 4.55 (s, 2H), 4.15 (bs, 1H), 3.77 (bs, 1H), 2.91 (bs, 1H), 2.65 (bs, 2H), 1.84 (d, $J$ = 11.6 Hz, 2H), 1.64 (bs, 1H), 1.42 (d, $J$ = 10.8 Hz, 1H), 1.22 (bs, 3H), 0.34 - 0.27 (m, 4H). MS (ESI): mass calcd. for $C_{27}H_{28}FN_5O_2$, 473.55; m/z found, 474.2 $[M+H]^+$.

**[000167]** Following compounds **(Examples 10-60)** were synthesized using the above procedure as exemplified for **Example-9**.

**Example-10:**

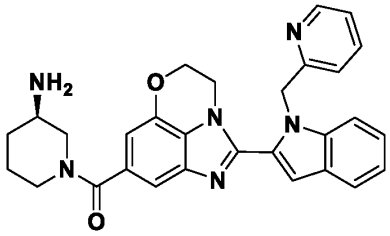
**(R)- (3-aminopiperidin-1-yl)(2-(1-(pyridin-4-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-yl)methanone**



**[000168]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 8.40-8.38 (m, 2H), 7.74-7.72 (m, 1H), 7.44-7.42 (m, 1H), 7.33 (s, 1H), 7.28 (s, 1H), 7.26-7.22 (m, 1H), 7.17-7.13 (m, 1H), 7.01-6.99 (m, 2H), 6.77 (s, 1H), 6.16 (s, 2H), 4.71 (m, 2H), 4.56-4.55 (m, 2H), 4.11(m, 2H) ,3.0 (m, 2H), 2.01-1.8 (m, 3H), 1.67 (m, 1H), 1.44 (bs, 3H). MS (ESI): mass calcd. for $C_{29}H_{28}N_6O_2$, 492.23; m/z found, 493 $[M+H]^+$.

**Example-11:**

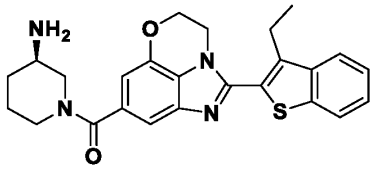
**(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridine-2-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000169]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 8.43 (d, $J$ = 4 Hz, 1H), 7.72-7.70 (m, 1H), 7.61-7.57 (m, 1H), 7.46-7.44 (m, 1H), 7.22 (s, 2H), 7.27 (s, 1H), 7.19-7.09 (m, 3H), 6.72 (s, 1H), 6.17 (s, 2H), 4.68( m, 2H), 4.55( m, 2H), 3.94 ( m, 2H), 2.87 (m, 2H), 1.84-1.81 (m, 2H), 1.62 (m, 3H), 1.40 ( bs, 2H). MS (ESI): mass calcd. for $C_{29}H_{28}N_6O_2$, 492.23; m/z found, 493.2 $[M+H]^+$.

**Example-12:**

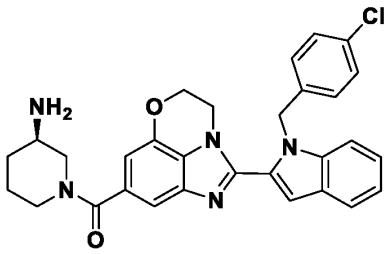
**(R)-(3-aminopiperidin-1-yl)(2-(3-ethylbenzo[b]thiophen-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone:**



**[000170]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 8.08 (m, 1H), 8.06-7.98 (m, 1H), 7.53-7.49 (m, 2H), 7.36 (s, 1H), 6.79 (s, 1H), 4.48 (d, $J$ = 8 Hz, 4H), 4.00 (bs, 2H), 3.28 (m, 2H), 3.22 (m, 3H), 1.95 (m, 1H), 1.70 (m, 1H), 1.48 (m, 2H), 1.31-1.21 (m, 5H). MS (ESI): mass calcd. for $C_{25}H_{26}N_4O_2S$, 446.57; m/z found, 447.2 $[M+H]^+$.

**Example-13:**

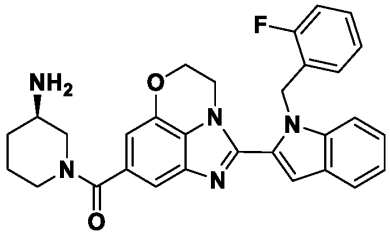
**(R)-(3-aminopiperidin-1-yl)(2-(1-(4-chlorobenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-yl)methanone**




**[000171]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.71 (d, *J* = 8 Hz, 1H), 7.47-7.45 (m, 1H), 7.28-7.21 (m, 4H), 7.15-7.09 (m, 4H), 6.74 (s, 1H), 6.09 (s, 2H), 4.68 (m, 2H), 4.55 (m, 2H), 2.92 (m, 2H), 2.73 (m, 2H), 1.97 (m, 2H), 1.88 (m, 2H), 1.62 (m, 3H). MS (ESI): mass calcd. for $C_{30}H_{28}ClN_5O_2$, 525.19; m/z found, 526.2 $[M+H]^+$.

**Example-14:**

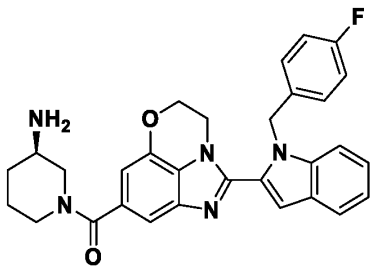
**(R)-(3-aminopiperidin-1-yl)(2-(1-(2-fluorobenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-yl)methanone**




**[000172]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.72 (d, *J* = 8 Hz, 1H), 7.46 (d, *J* = 8 Hz, 1H), 7.29-7.26 (m, 1H), 7.24-7.18 (m, 3H), 7.16-7.12 (m, 2H), 6.96-6.93 (m, 1H), 6.73 (s, 1H), 6.67-6.63 (bs, 1H), 6.17 (s, 2H), 4.66 (m, 2H), 4.55(m, 2H), 4.00 (m, 2H), 2.48 (m, 1H), 2.89 (s, 1H), 2.00 (m, 2H), 1.85 (m, 1H), 1.62 (m, 1H), 1.41-1.39 (m, 1H), 1.22 (m, 2H). MS (ESI): mass calcd. for $C_{30}H_{28}FN_5O_2$, 509.22; m/z found, 510.2$[M+H]^+$.

**Example-15:**

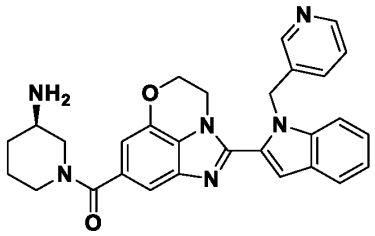
**(R)-(3-aminopiperidin-1-yl)(2-(1-(4-fluorobenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000173]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.71 (d, *J* = 8 Hz, 1H), 7.50-7.48 (d, *J* = 8 Hz, 1H), 7.25 (s, 2H), 7.22 (m, 1H), 7.16-7.10 (m, 3H), 7.05 (t, *J* = 8.8 Hz, 2H), 6.73 (s, 1H), 6.08 (s, 2H), 4.67 (m, 2H), 4.56 (m, 2H), 4.01 (m, 2H), 2.88 (m, 2H), 1.98-1.97 (m, 2H), 1.82 (m, 1H), 1.70 (m, 2H), 1.41-1.31 (m, 2H). MS (ESI): mass calcd. for $C_{30}H_{28}FN_5O_2$, 509.59; m/z found, 510.2 $[M+H]^+$.

**Example-16:**

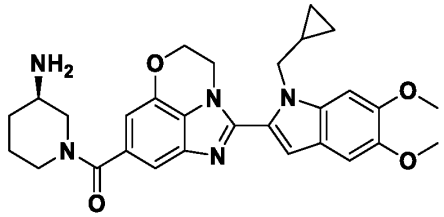
**(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-3-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000174]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 8.40 (s, 1H), 8.36 (d, *J* = 3.6 Hz, 1H), 7.70 (d, *J* = 8 Hz, 1H), 7.54 (d, *J* = 8 Hz, 1H ), 7.46 (d, *J* = 8 Hz, 1H ), 7.29-7.12 (m, 4H), 7.16-7.12 (m, 1H), 6.74 (s, 1H), 6.14 (s, 2H), 4.68-4.55 (m, 4H), 4.12 (m, 2H), 2.90 (m, 1H), 2.71-2.65 (m, 2H), 1.88-1.83 (m, 2H), 1.63 (m, 1H), 1.42-1.12 (m, 3H). MS (ESI): mass calcd. for $C_{29}H_{28}N_6O_2$, 492.58; m/z found, 493.4 $[M+H]^+$.

**Example-17:**

**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5,6-dimethoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**

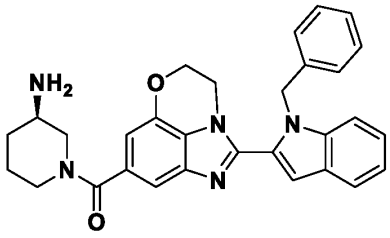


**[000175]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.25 (s, 1H), 7.18 (s, 1H), 7.13 (s, 1H), 6.99 (s, 1H), 6.72 (s, 1H), 4.68 (d, *J* = 6.4 Hz, 2H), 4.61 (s, 2H), 4.54 (s, 2H),

3.85 (s, 3H), 3.78 (s, 3H), 4.30-4.00 (s, 1H), 3.15 (d, $J$ = 4.0 Hz, 1H), 2.92 (bs, 2H), 2.70 (bs, 2H), 1.91 (bs, 1H), 1.81 (bs, 1H), 1.65 (bs, 1H), 1.44 (bs, 2H), 0.84 (s, 1H), 0.33-0.28 (m, 4H). MS (ESI): mass calcd. for $C_{29}H_{33}FN_5O_4$, 515.61; m/z found, 516.3$[M+H]^+$.

**Example-18:**

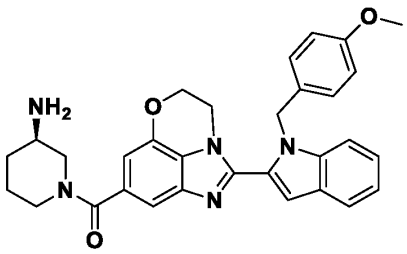
**(R)-(3-aminopiperidin-1-yl)(2-(1-benzyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000176]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.70 (d , $J$ = 8.0 Hz, 1H), 7.47 (d, $J$ = 8.0 Hz, 1H), 7.26-7.10 (m, 7H), 7.06 (d , $J$ = 7.2 Hz, 2H), 6.73 (s, 1H), 6.11 (s, 2H), 4.66 (d , $J$ = 5.0 Hz, 2H), 4.55 (d , $J$ = 5.0 Hz, 2H), 3.65 (bs, 1H), 2.88 (bs, 1H), 2.65 (bs, 1H), 1.98 (d , $J$ = 7.6 Hz, 1H), 1.83 (d, $J$ = 11.6 Hz, 1H), 1.63 (bs, 1H), 1.41-1.22 (m, 4H), 0.84 (s, 1H). MS (ESI): mass calcd. for $C_{30}H_{29}N_5O_2$, 491.6; m/z found, 492.2 $(M+H)^+$.

**Example-19:**

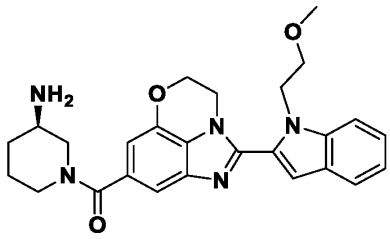
**(R)-(3-aminopiperidin-1-yl)(2-(1-(4-methoxybenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000177]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.68 (d, $J$ = 8 Hz, 1H), 7.45 (d, $J$ = 8 Hz, 1H), 7.25 (s, 1H), 7.23-7.22 (m, 2H), 7.12 (t, $J$ = 7.2 Hz, 1H), 7.03 (d , $J$ =8.4 Hz, 2H), 6.76 (s, 1H), 6.74 (s, 2H), 6.01 (bs, 2H), 4.65-4.55 (m, 2H), 4.55-4.54 (m, 2H), 4.12 (bs, 2H), 3.80 (s, 3H) 2.89 (m, 1H), 2.65 (m, 1H), 1.87 (m,1H), 1.82 (m,1H), 1.63 ( m ,1H), 1.41 (m, 1H), 1.21-1.20 ( m, 3H). MS (ESI): mass calcd. for $C_{31}H_{31}N_5O_3$, 521.62; m/z found, 522.2 $[M+H]^+$.

**Example-20:**

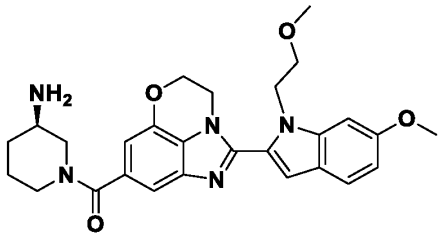
**Synthesis of (R)-(3-aminopiperidin-1-yl)(2-(1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000178]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.69-7.63 (m, 2H), 7.31-7.27 (m, 2H), 7.16-7.12 (m, 2H), 6.76 (s, 1H), 4.91 (t, *J* = 5.7 Hz, 2H), 4.64 (t, *J* = 3.44 Hz, 2H), 4.56 (t, *J* = 4.24 Hz, 2H), 4.16 (bs, 2H), 3.66 (t, *J* = 5.28 Hz, 2H), 3.41 (bs, 1H), 3.09 (s, 3H), 2.91 (bs, 1H), 2.70 (m, 1H), 2.08 (s, 1H), 1.87 (d, *J* = 12.04 Hz, 2H), 1.76-1.68 (m, 1H), 1.50-1.45 (m, 1H), 1.26-1.23 (m, 1H). MS (ESI): mass calcd for. $C_{26}H_{29}N_5O_3$ for 459.23; found *m/z* 460.10 $[M+H]^{+1}$.

**Example-21:**

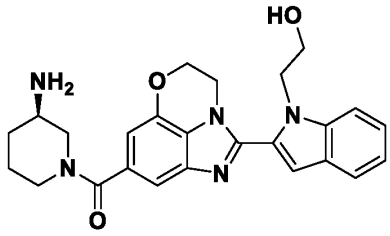
**(R)-(3-aminopiperidin-1-yl)(2-(6-methoxy-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000179]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.54 (d, *J* = 8.64 Hz, 1H), 7.34 (s, 1H), 7.07 (s, 1H), 6.98 (s, 1H), 6.82-6.81 (m, 2H), 4.83 (d, *J* = 11.12 Hz, 2H), 4.57 (s, 4H), 3.89 (s, 3H ), 3.61 (t, *J* = 5.04 Hz, 2H), 3.06 (s, 3H), 2.87 (d, *J* = 10.28 Hz, 2H), 2.04 (d, *J* = 11.80 Hz, 1H), 1.89-1.59 (m, 4H), 1.43-1.37 (m, 2H), 1.33-1.29 (m, 2H). MS (ESI): mass calcd for $C_{27}H_{31}N_5O_4$ 489.19; found m/z 490.27 $[M+1]^+$.

**Example-22:**

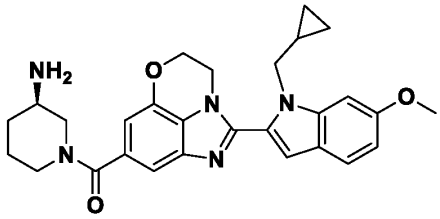
**(R)-(3-aminopiperidin-1-yl)(2-(1-(2-hydroxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000180]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.69 (d, *J* = 7.88 Hz, 1H), 7.65 (d, *J* = 7.91 Hz, 1H), 7.31-7.27 (m, 2H), 7.16-7.12 (m, 2H), 6.76 (s, 1H), 4.99 (bs, 2H), 4.77 (t, *J* = 5.36 Hz, 2H), 4.63 (d, *J* = 3.84 Hz, 2H), 4.56 (s, 2H), 3.74 (t, *J* = 5.52 Hz, 2H), 2.91 (s, 1H), 2.71-2.65 (m, 1H), 1.87 (s, 4H), 1.84 (s, 1H), 1.71-1.65 (m, 1H), 1.44-1.41 (m 1H), 1.24-1.22 (m, 1H). MS (ESI): mass calcd for $C_{25}H_{27}N_5O_3$ 445.21; found m/z 446.24 $[M+H]^{+1}$.

**Example-23:**

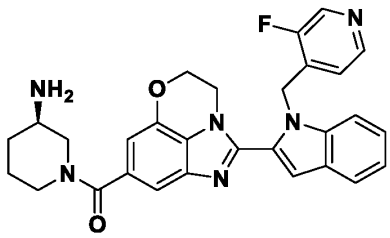
**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-methoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000181]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.56 (d, *J* = 8.64 Hz, 1H), 7.28 (s, 1H), 7.17 (s, 1H), 7.09 (s, 1H), 6.79 (d, *J* = 7.4 Hz, 1H), 6.74 (s, 1H), 4.70 (d, *J* = 6.68 Hz, 2H), 4.64 (s, 2H), 4.55 (s, 2H), 4.15 (bs, 1H), 3.85 (s, 3H), 3.38 (d, *J* = 6.92 Hz, 1H), 2.92 (bs, 2H), 2.07 (m, 2H), 1.86 (d, *J* = 9.28 Hz, 1H), 1.67 (bs, 1H), 1.45 (m, 1H), 1.23 (m, 2H), 1.09 (t, *J* = 7.00 Hz, 1H), 0.35-0.30 (m, 4H). MS (ESI): mass calcd. for $C_{28}H_{31}N_5O_3$ 485.24; found *m/z* 486.20 $[M+H]^{+1}$.

**Example-24:**

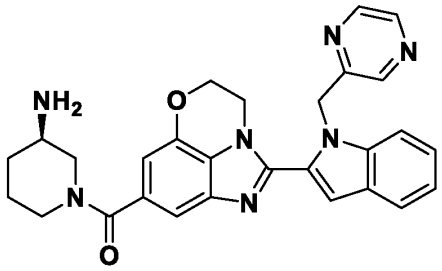
**(*R*)-(3-aminopiperidin-1-yl)(2-(1-((3-fluoropyridin-4-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000182]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 8.53 (s, 1H), 8.18 (d, *J* = 4.72 Hz, 1H), 7.77 (d, *J* = 7.84 Hz, 1H), 7.52 (d, *J* = 8.28 Hz, 1H), 7.36 (s, 1H), 7.31 (t, *J* = 7.32 Hz, 1H), 7.21-7.18 (m, 2H), 6.73 (s, 1H), 6.55 (t, *J* = 5.64 Hz, 1H), 6.25 (s, 2H), 4.71 (t, *J* = 4.16 Hz, 2H), 4.56 (t, *J* = 3.08 Hz, 2H), 2.88 (bs, 1H), 2.63-2.57 (m, 2H), 1.84 (d, *J* = 11.8 Hz, 2H), 1.64 (bs, 2H), 1.41 (m, 2H), 1.23-1.19 (m, 2H). MS (ESI): mass calcd. for $C_{29}H_{27}FN_6O_2$ 511.23; found *m/z* 511.14 $[M+H]^+$.

**Example-25:**

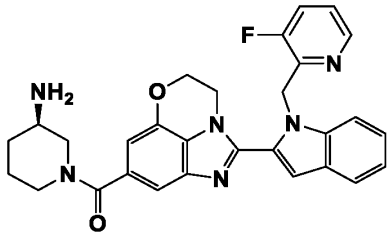
**(R)-(3-aminopiperidin-1-yl)(2-(1-(pyrazin-2-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000183]** $^1$HNMR (400 MHz, DMSO-$d_6$): δ (ppm): 8.49 (d, *J* = 13.1 Hz, 1H), 8.41 (s, 1H), 7.73 (d, *J* = 7.4 Hz, 1H), 7.57 (d, *J* = 7.1 Hz, 1H), 7.30-7.24 (m, 3H), 7.18-7.16 (m, 2H), 6.75 (s, 1H), 6.25 (s, 2H), 4.72 (bs, 2H), 4.56 (bs, 2H), 4.15 (bs, 2H), 2.90 (bs, 2H), 2.69-2.63 (m, 1H), 1.84 (bs, 2H), 1.64 (bs, 2H), 1.42 (bs, 1H), 1.23-1.22 (m, 1H). MS (ESI): mass calcd. for $C_{28}H_{27}N_7O_2$ 493.12; found *m/z* 494.10 $[M+H]^+$.

**Example-26:**

**(R)-(3-aminopiperidin-1-yl)(2-(1-((3-fluoropyridin-2-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**

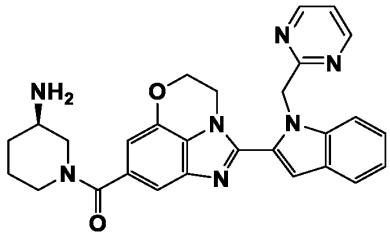


**[000184]** $^1$HNMR (400 MHz, DMSO-d6): δ (ppm): 8.12 (d, *J* = 4.16 Hz, 1H), 7.70 (d, *J* = 7.92 Hz, 1H), 7.62 (t, *J* = 9.2 Hz, 1H), 7.53 (d, *J* = 8.12 Hz, 1H), 7.28-7.20 (m, 4H), 7.13 (t, *J* = 7.16 Hz, 1H), 6.72 (s, 1H), 6.28 (s, 2H), 4.65 (t, *J* = 4.20 Hz, 2H ), 4.55 (t, *J* = 5.52 Hz, 2H ), 4.18 (bs, 2H), 2.87 (bs, 1H), 2.61 (m, 2H), 1.84 (d, *J* = 10.1 Hz,

2H), 1.75-1.66 (m, 1H), 1.45-1.41 (m, 1H), 1.23-1.19 (m, 2H). MS (ESI): mass calcd. for $C_{29}H_{27}FN_6O_2$ 510.22; found *m/z* 511.18 $[M+H]^+$.

**Example-27:**

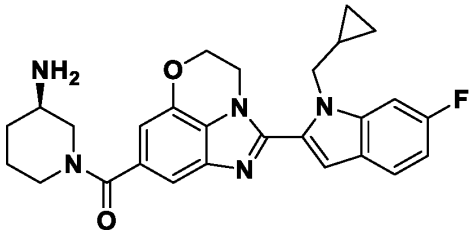
**(R)-(3-aminopiperidin-1-yl)(2-(1-(pyrimidin-2-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000185]** $^1$HNMR (400 MHz, DMSO-d6): δ (ppm): 8.62 (d, *J* = 4.84 Hz, 2H), 7.20 (d, *J* = 7.7 Hz, 1H), 7.43 (d, *J* = 8.2 Hz, 1H), 7.29-7.26 (m, 2H), 7.23-7.20 (t, *J* = 7.28 Hz, 1H), 7.16-7.12 (m, 2H), 6.71 (s, 1H), 6.33 (s, 2H), 4.69 (t, *J* = 6.24 Hz, 2H), 4.55 (t, *J* = 4.88 Hz, 2H), 4.17 (bs, 1H), 3.54 (bs, 1H), 2.87 (bs, 1H), 2.61 (m, 1H), 1.83 (d, *J* = 10.96 Hz, 3H), 1.63 (s, 1H), 1.41-1.38 (m, 1H), 1.23-1.19 (m, 2H). MS (ESI): ): mass calcd. for $C_{28}H_{27}N_7O_2$ 493.22; found *m/z* 494.23 $[M+H]^+$.

**Example-28:**

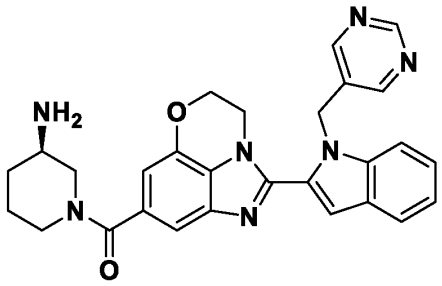
**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000186]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.71-7.68 (m, 1H), 7.58 (d, *J* = 7.9 Hz, 1H), 7.29 (s, 1H), 7.19 (s, 1H), 7.01 (t, *J* = 9.2 Hz, 1H), 6.75 (s, 1H), 4.68-4.65 (m, 4H), 4.51 (s, 2H), 4.21 (bs, 1H), 3.61 (bs, 1H), 2.91 (bs, 1H), 2.63-2.61 (m, 1H), 1.86-1.84 (m, 2H), 1.66 (bs, 1H), 1.64-1.42 (m, 3H), 1.25-1.23 (m, 2H), 0.34-0.28 (m, 4H). MS (ESI): $C_{27}H_{28}FN_5O_2$ 473.12; found *m/z* 474.20 $[M+H]^+$.

**Example-29:**

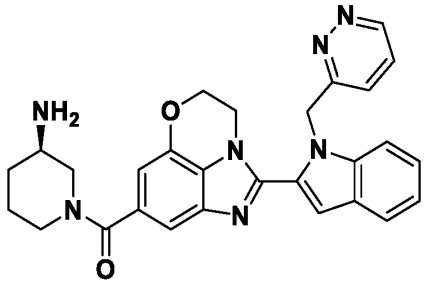
**(R)-(3-aminopiperidin-1-yl)(2-(1-(pyrimidin-5-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000187]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 9.03 (s, 1H), 8.65 (s, 2H), 7.75 (d, *J* = 7.8 Hz, 1H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.33-7.26 (m, 3H), 7.18 (t, *J* = 7.7 Hz, 1H), 6.76 (s, 1H), 6.17 (s, 2H), 4.72 (bs, 2H), 4.57 (bs, 2H), 4.18 (bs, 2H), 3.60 (bs, 2H), 3.17 (d, *J* = 4.8 Hz, 1H), 2.88 (bs, 1H), 2.66-2.62 (m, 1H), 1.83 (bs, 1H), 1.65 (bs, 1H), 1.39-1.33 (bs, 1H), 1.23-1.22 (m, 1H). MS (ESI): mass calcd. for $C_{28}H_{27}N_7O_2$ 493.12; found *m/z* 494.27 $[M+H]^+$.

**Example-30:**

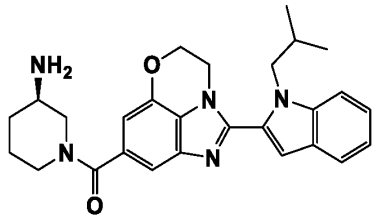
**(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridazin-3-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000188]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 9.07 (d, *J* = 3.9 Hz, 1H), 7.74 (d, *J* = 7.9 Hz, 1H), 7.58-7.52 (m, 2H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.32 (s, 1H), 7.27 (d, *J* = 7.1 Hz, 1H), 7.23 (s, 1H), 7.16 (t, *J* = 7.7 Hz, 1H), 6.77 (s, 1H), 6.37 (s, 2H), 4.71 (bs, 2H), 4.57 (bs, 2H), 4.15 (bs, 1H), 3.54 (bs, 1H), 2.88 (bs, 1H), 2.66-2.62 (m, 2H), 1.96 (bs, 2H), 1.85-1.82 (m, 1H), 1.64 (bs, 1H), 1.41-1.39 (m, 1H), 1.25-1.20 (m, 1H). MS (ESI): mass calcd. for $C_{28}H_{27}N_7O_2$ 493.12; found *m/z* 494.24 $[M+H]^+$.

**Example-31:**

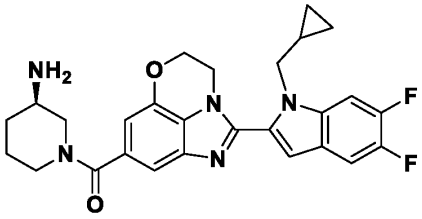
**(R)-(3-aminopiperidin-1-yl)(2-(1-isobutyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000189]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.68 (d, *J* = 8.1 Hz, 1H), 7.64 (d, *J* = 7.9 Hz, 1H), 7.30-7.26 (m, 2H), 7.16-7.11 (m, 2H), 6.75 (s, 1H), 4.64 (m, 4H), 4.56 (s, 2H), 4.17 (bs, 1H), 3.62 (bs, 1H), 2.90 (bs, 1H), 2.66 (m, 1H), 2.1-2.04 (m, 1H), 1.86 (d, *J* = 9.84 Hz, 3H), 1.65 (bs, 1H), 1.43 (d, *J* = 9.68 Hz, 1H), 1.23 (m, 2H), 0.73 (d, *J* = 6.6 Hz, 6H). MS (ESI): mass calcd. for $C_{27}H_{31}N_5O_2$ 457.25; found *m/z* 458.28 $[M+H]^+$.

**Example-32:**

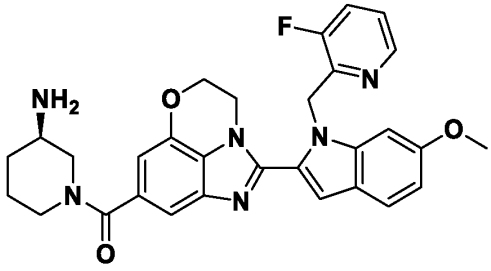
**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5,6-difluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000190]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.90-7.86 (m, 1H), 7.70 (t, *J* = 7.7 Hz, 1H), 7.30 (s, 1H), 7.17 (s, 1H), 6.76 (s, 1H), 4.68-4.62 (m, 4H), 4.56 (s, 2H), 4.24 (bs, 1H), 3.66 (bs, 1H), 2.98-2.89 (m, 2H), 2.67-2.63 (m, 1H), 1.86-1.84 (d, *J* = 9.7 Hz, 1H), 1.67 (m, 2H), 1.23 (m, 3H), 1.44 (m, 1H), 0.34 (d, *J* = 7.2 Hz, 2H), 0.29 (m, 2H). MS (ESI): mass calcd. for $C_{27}H_{27}F_2N_5O_2$ 491.12; found *m/z* 492.25 $[M+H]^+$.

**Example-33:**

**(R)-(3-aminopiperidin-1-yl)(2-(1-((3-fluoropyridin-2-yl)methyl)-6-methoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**

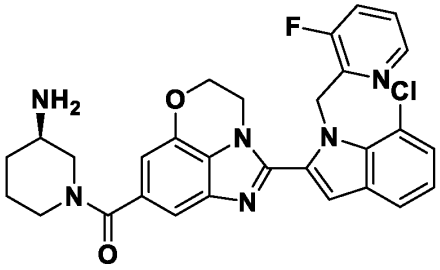


**[000191]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 8.14 (d, *J* = 4.52 Hz, 1H), 7.62 (t, *J* =9.0 Hz, 1H), 7.57 (d, *J* = 9.6 Hz, 1H), 7.30-7.28 (m, 1H), 7.17 (s, 1H), 7.08 (s, 1H),

6.81 (d, *J* = 1.9 Hz, 2H), 6.78 (s, 1H), 6.27 (s, 2H), 4.64 (d, *J* = 4.32 Hz, 2H), 4.54 (d, *J* = 4.0 Hz, 2H), 4.08 (bs, 2H), 3.76 (s, 3H), 3.20-3.10 (m, 4H), 2.00-1.97 (m, 2H), 1.72-1.71 (m, 1H), 1.55-1.53 (m, 2H). MS (ESI): mass calcd. for $C_{30}H_{29}FN_6O_3$ 540.60; found *m/z* 541.29 $[M+H]^+$.

**Example-34:**

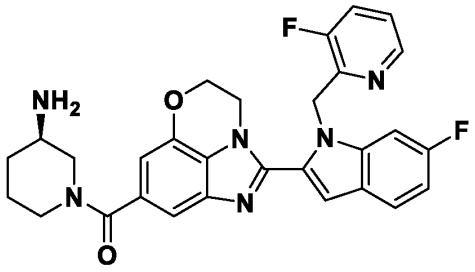
**(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-((3-fluoropyridin-2-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**




**[000192]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 8.06 (d, *J* = 4.3 Hz, 1H), 7.22-7.63 (m, 2H), 7.34 (s, 1H), 7.28-7.22 (m, 3H), 7.12 (t, *J* = 7.6 Hz, 1H), 6.74 (m, 1H), 6.62 (s, 2H), 4.63 (s, 2H), 4.53 (s, 2H), 4.01 (bs, 1H), 3.75 (bs, 1H), 2.88 (bs, 1H), 2.66 (bs, 1H), 1.83 (d, *J* = 10.2 Hz, 2H), 1.68 (m, 2H), 1.42 (s, 1H ), 1.26-1.23 (m, 2H). MS (ESI): mass calcd. for $C_{29}H_{26}ClFN_6O_2$ 544.18; found *m/z* 545.27 $[M+H]^+$.

**Example-35:**

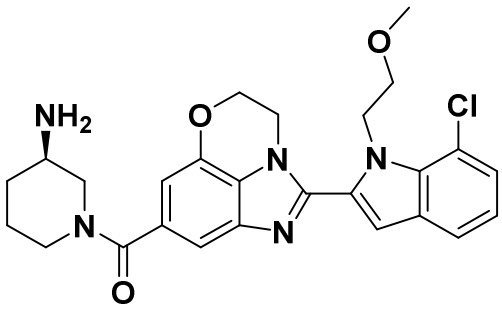
**(R)-(3-aminopiperidin-1-yl)(2-(6-fluoro-1-((3-fluoropyridin-2-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**




**[000193]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 8.12 (d, *J* = 7.7 Hz, 1H), 7.73-7.70 (m, 1H), 7.63 (t, *J* = 8.1 Hz, 1H), 7.45 (d, *J* = 9.7 Hz, 1H), 7.29-7.26 (m, 2H),7.18 (s, 1H), 7.04 (t, *J* = 9.6 Hz, 1H), 6.71 (s, 1H), 6.25 (s, 2H), 4.63 (s, 2H), 4.53 (s, 2H), 4.28 (bs, 1H), 2.88 (m, 1H), 2.72-2.62 (m, 2H), 1.85 (d, *J* = 11.1 Hz, 2H), 1.65 (bs, 2H), 1.39 (m, 1H), 1.23-1.17 (m, 2H) MS (ESI): mass calcd. for $C_{29}H_{26}F_2N_6O_2$ 528.18; found *m/z* 529.26 $[M+H]^+$.

**Example-36:**

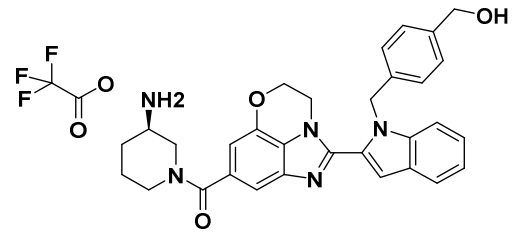
**(*R*)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000194]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.68 (d, *J* = 7.8 Hz, 1H), 7.34 (d, *J* = 7.9 Hz, 1H), 7.31 (s, 1H), 7.22 (s, 1H), 7.15 (t, *J* = 7.7 Hz, 1H), 6.77 (s, 1H), 5.23 (t, *J* = 5.4 Hz, 2H), 4.57 (s, 4H), 3.58 (t, *J* = 5.48 Hz, 2H), 2.97 (s, 3H), 2.92 (bs, 2H), 2.66 (m, 2H), 1.85 (d, *J* = 10.2 Hz, 2H), 1.66 (bs, 2H), 1.43 (m, 1H), 1.23-1.15 (m, 2H). MS (ESI): mass calcd. for $C_{26}H_{28}ClN_5O_3$ 493.1; found *m/z* 494.5 $[M+H]^+$.

**Example-37:**

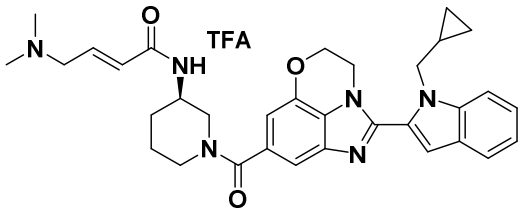
**(R)-(3-aminopiperidin-1-yl)(2-(1-(4-(hydroxymethyl)benzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone trifluoroacetic acid salt**



**[000195]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.71 (d, *J* = 7.7 Hz, 1H), 7.47 (d, *J* = 8.3 Hz, 1H), 7.27 (s, 2H), 7.23 (t, *J* = 7.5 Hz, 1H), 7.15-7.11 (m, 3H), 7.02 (d, *J* = 8.0 Hz, 2H), 6.75 (s, 1H), 6.10 (s, 2H), 5.04 (bs, 1H), 4.69 (s, 2H), 4.56 (s, 2H), 4.36 (s, 2H), 2.91 (bs, 2H), 2.69 (m, 2H), 1.90-1.83 (m, 2H), 1.64 (m, 2H) 1.39 (m, 1H), 1.25-1.23 (m, 2H). MS (ESI): mass calcd. for $C_{31}H_{31}N_5O_3$ 521.2; found *m/z* 522.2 $[M+H]^+$.

**Example-38:**

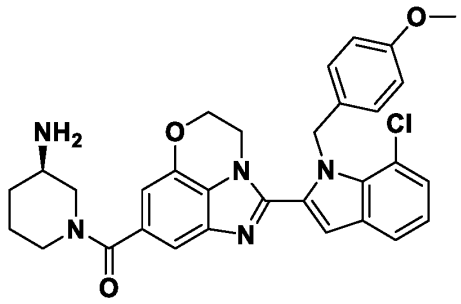
**(R,E)-N-(1-(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)-4-(dimethylamino)but-2-enamide trifluoroacetic acid salt**



**[000196]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 9.62 (bs, 1H), 8.29 (bs, 1H), 7.68 (t, *J* = 6.92 Hz, 2H), 7.33-7.28 (m, 2H), 7.17-7.12 (m, 2H), 6.77 (s, 1H), 6.28 (d, *J* = 15.1 Hz, 1H), 4.71-4.66 (m, 4H), 4.56 (s, 2H), 3.86 (m, 4H), 3.24-3.06 (m, 2H), 2.76 (s, 6H), 1.90 (bs, 1H), 1.76 (m, 2H), 1.56-1.50 (m, 2H ), 1.27-1.21 (m, 2H ), 0.35-0.28 (m, 4H). MS (ESI) ): mass calcd. for $C_{35}H_{39}N_6F_3O_4$ 566.30; *m/z* found 567.42.

**Example-39:**

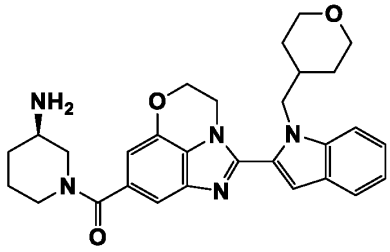
**(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(4-methoxybenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**




**[000197]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.71 (d, *J* = 7.7 Hz, 1H), 7.36 (s, 1H), 7.29 (d, *J* = 5.4 Hz, 2H), 7.14 (t, *J* = 7.7 Hz, 1H), 6.76 (s, 1H), 6.73-6.67 (m, 4H), 6.34 (s, 2H), 4.59 (t, *J* = 3.9 Hz, 2H), 4.53 (t, *J* = 3.3 Hz, 2H), 4.16 (bs, 2H), 3.61 (s, 3H), 2.89 (bs, 1H), 2.66 (bs, 2H), 1.88-1.82 (m, 2H), 1.64 (bs, 1H), 1.41-1.39 (m, 1H ), 1.25-1.20 (m, 2H). MS (ESI): mass calcd. for $C_{31}H_{30}ClN_5O_3$ 555.18; found *m/z* 556.36 $[M+H]^+$.

**Example-40:**

**(R)-(3-aminopiperidin-1-yl)(2-(1-((tetrahydro-2H-pyran-4-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**

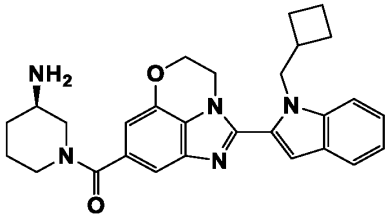



**[000198]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.69 (d, *J* = 8.32 Hz, 2H), 7.33-7.28 (m, 2H), 7.17-7.12 (m, 2H), 6.76 (s, 1H), 4.74 (d, *J* = 6.68 Hz, 2H), 4.65 (s, 2H), 4.56 (s, 2H), 4.18 (bs, 1H), 3.70 (d, *J* = 9.4 Hz, 2H), 3.40-3.39 (m, 1H), 3.09 (t, *J* = 10.88 Hz, 2H), 2.92 (bs, 1H), 2.66 (m, 1H), 2.08-2.05 (m, 1H), 1.85 (d, *J* = 10.28 Hz, 2H), 1.69

(bs, 2H), 1.44-1.41 (m, 2H), 1.28-1.17 (m, 5H). MS (ESI): mass calcd. for $C_{29}H_{33}N_5O_3$ 499.26; found *m/z* 500.30 $[M+H]^+$.

**Example-41:**

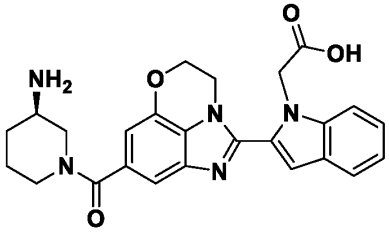
**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclobutylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000199]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.67(d, *J* = 8.1 Hz, 2H), 7.34 (s, 1H), 7.29 (t, *J* = 8.3 Hz, 1H), 7.14-7.11 (m, 2H), 6.78 (s, 1H), 4.87 (d, *J* = 7.0 Hz, 2H), 4.65 (s, 2H), 4.56 (s, 2H), 4.14 (bs, 2H), 2.97 (bs, 1H), 2.81(m, 2H), 2.72-2.65 (m, 1H), 1.88 (m, 1H), 1.77-1.66 (m, 6H), 1.63-1.57 (m, 3H), 1.51-1.45 (m, 1H), 1.23 (s, 1H). MS (ESI): mass calcd. for $C_{28}H_{31}N_5O_2$ 469.25; found *m/z* 470.31 $[M+H]^+$.

**Example-42:**

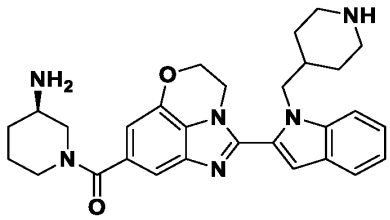
**(R)-2-(2-(7-(3-aminopiperidine-1-carbonyl)-3,4-dihydro-5-oxa1,2adiazaacenaphthylen-2-yl)-1H-indol-1-yl)acetic acid**



**[000200]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.67 (d, *J* = 7.7 Hz, 1H), 7.48 (d, *J* = 8.2 Hz, 1H), 7.31 (s, 1H), 7.24 (t, *J* = 7.4 Hz, 1H), 7.13-7.10 (m, 2H), 6.74 (s, 1H), 5.32 (s, 2H), 4.64 (s, 2H), 4.55 (s, 2H), 4.17 (bs, 2H), 2.95-2.88 (m, 4H), 1.79 (bs, 3H), 1.25-1.08 (m, 3H). MS (ESI): mass calcd. for $C_{25}H_{25}N_5O_4$ 459.18; found *m/z* 460.21 $[M+H]^+$.

**Example-43:**

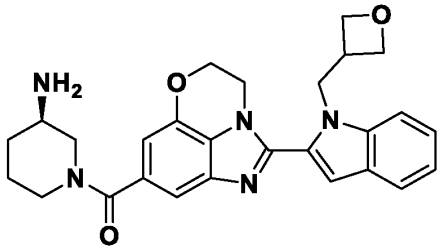
**(R)- (3-aminopiperidin-1-yl)(2-(1-(piperidin-4-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000201]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.69 (d, $J$ = 7.7 Hz, 1H), 7.64 (d, $J$ = 8.32 Hz, 1H), 7.30-7.27 (m, 2H), 7.14-7.11 (m, 2H) 6.75 (s, 1H), 4.71 (d, $J$ = 6.68 Hz, 2H), 4.64 (s, 2H), 4.56 (s, 2H ), 4.10 (bs, 1H ), 2.91 (bs, 1H ), 2.73 (d, $J$ = 11.8 Hz, 2H), 2.66-2.64 (m, 3H), 2.19 (t, $J$ = 11.3 Hz, 2H), 1.83 (bs, 2H), 1.66 (bs, 2H), 1.44-1.41 (m, 2H), 1.25-1.23 (m, 3H), 0.97-0.89 (m, 3H). MS (ESI): mass calcd. for $C_{29}H_{34}N_6O_2$ 498.1; found *m/z* 499.29 $[M+H]^+$.

**Example-44:**

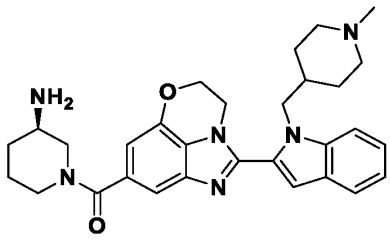
**(R)-(3-aminopiperidin-1-yl)(2-(1-(oxetan-3-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000202]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.71 (d, $J$ = 7.9 Hz, 1H), 7.51 (d, $J$ = 8.4 Hz, 1H), 7.32 (s, 1H), 7.28 (t, $J$ = 7.7 Hz, 1H), 7.22 (s, 1H), 7.15 (t, $J$ = 7.9 Hz, 1H), 6.78 (s, 1H), 5.47 (s, 2H), 5.01-5.05 (m, 1H), 4.91 (s, 1H), 4.66 (s, 2H), 4.56 (s, 2H), 4.36 (s, 1H), 3.80 (s, 2H), 2.98-2.87 (m, 4H), 1.90 (m, 2H), 1.69 (m, 1H), 1.46-1.37 (m, 2H). MS (ESI): mass calcd. for $C_{27}H_{29}N_5O_3$ 471.23; found *m/z* 472.27 $[M+H]^+$.

**Example-45:**

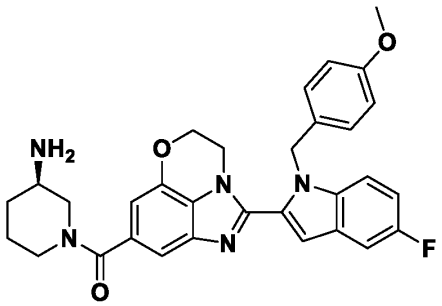
**(R)-(3-aminopiperidin-1-yl)(2-(1-((1-methylpiperidin-4-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000203]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.69-7.64 (m, 2H), 7.30-7.27 (m, 2H), 7.15-7.12 (m, 2H), 6.70 (s, 1H), 4.73 (d, *J* = 6.72 Hz, 2H), 4.65 (s, 2H), 4.56 (s, 2H ), 4.15 (bs, 1H ), 3.63 (bs, 1H ), 2.90 (bs, 1H), 2.66-2.56 (m, 4H), 2.00 (s, 3H), 1.87-1.84 (m, 2H), 1.73-1.72 (m, 2H), 1.60 (t, *J* = 11.3 Hz, 2H), 1.44-1.41 (m, 1H), 1.31-1.28 (m, 2H), 1.23-1.13 (m, 2H), 1.11-0.92 (m, 2H). MS (ESI): mass calcd. for $C_{30}H_{36}N_6O_2$ 512; found *m/z* 513.34 $[M+H]^+$.

**Example-46:**

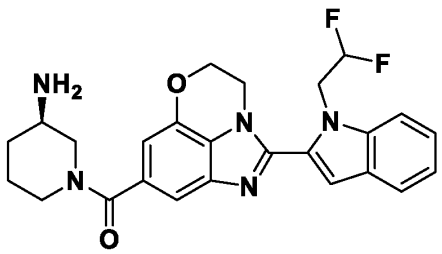
**(*R*)-(3-aminopiperidin-1-yl)(2-(5-fluoro-1-(4-methoxybenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000204]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.56-7.53 (m, 1H), 7.47 (d, *J* = 9.36 Hz, 1H), 7.28 (s, 1H), 7.22 (s, 1H), 7.10 (t, *J* = 7.81 Hz, 1H), 7.05 (d, *J* = 8.11 Hz, 2H), 6.77 (d, *J* = 8.96 Hz, 3H), 6.02 (s, 2H), 4.66 (s, 2H), 4.56 (s, 2H), 4.18 (bs, 2H), 3.64 (s, 3H), 2.89 (bs, 1H), 2.62 (m, 1H), 1.83 (d, *J* = 9.92 Hz, 2H), 1.63-1.42 (m, 3H), 1.21 (m, 2H). MS (ESI): mass calcd. for $C_{31}H_{30}FN_5O_3$ 539.23; found *m/z* 540.33 $[M+H]^+$.

**Example-47:**

**(R)-(3-aminopiperidin-1-yl)(2-(1-(2,2-difluoroethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**

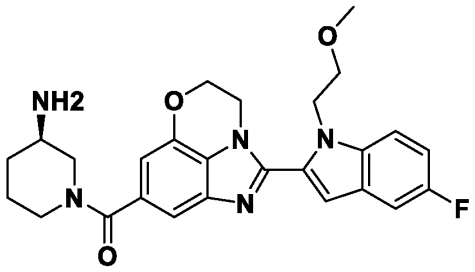


**[000205]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.71 (t, *J* = 7.2 Hz, 2H), 7.34 (t, *J* = 7.1 Hz, 1H), 7.29-7.21 (m, 2H), 7.19 (t, *J* = 7.1 Hz, 1H), 6.76 (s, 1H), 6.50 (t, *J* = 55.4 Hz, 1H), 5.27 (t, *J* = 13.1 Hz, 2H), 4.68 (s, 2H), 4.57 (s, 2H), 4.10 (bs, 1H), 3.70 (bs, 1H), 2.90 (m, 1H), 2.66 (m, 2H), 1.86 (t, *J* = 10.5 Hz, 2H), 1.66 (bs, 2H), 1.44-1.41 (m, 1H),

1.24-1.21 (m, 1H). MS (ESI): mass calcd. for $C_{25}H_{25}F_2N_5O_2$ 465.12; found *m/z* 466.26 $[M+H]^+$.

**Example-48:**

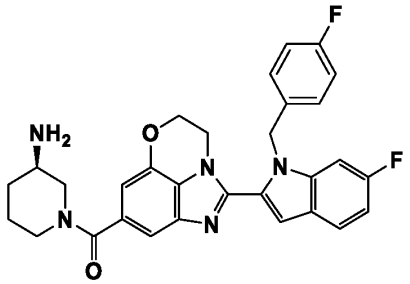
**(*R*)-(3-aminopiperidin-1-yl)(2-(5-fluoro-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**




**[000206]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.69-7.66 (m, 1H), 7.45 (d, *J* = 7.6 Hz, 1H), 7.29 (s, 1H), 7.17-7.14 (m, 2H), 6.76 (s, 1H), 4.90 (t, *J* = 5.8 Hz, 2H), 4.63 (s, 2H), 4.56 (s, 2H), 4.20 (bs, 2H), 3.66 (t, *J* = 5.1 Hz, 2H), 3.08 (s, 3H), 2.92 (bs, 1H), 2.65 (m, 2H), 1.85 (d, *J* = 10.28 Hz, 1H), 1.69 (bs, 2H), 1.43 (m, 1H), 1.23 (m, 2H). MS (ESI): $C_{26}H_{28}FN_5O_3$ 477.23; found *m/z* 478.39 $[M+H]^+$.

**Example-49:**

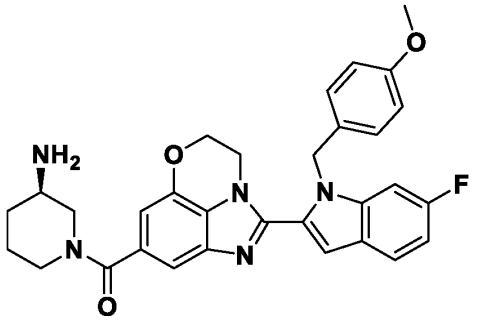
**(R)-(3-aminopiperidin-1-yl)(2-(6-fluoro-1-(4-fluorobenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**




**[000207]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.75-7.71(m, 1H), 7.41 (d, *J* = 9.76 Hz, 1H), 7.28 (d, *J* = 10.24 Hz, 2H), 7.18-7.14 (m, 2H), 7.08-7.00 (m, 3H), 6.75 (s, 1H), 6.07 (s, 2H), 4.66 (s, 2H), 4.56 (s, 2H), 4.18 (bs, 1H ), 3.60 (bs, 1H ), 2.90 (bs, 1H), 2.66 (bs, 2H ), 1.96 (bs, 1H), 1.84 (d, *J* = 9.68 Hz, 1H), 1.64 (bs, 1H), 1.42-1.39 (m, 1H), 1.23 (bs, 2H). MS (ESI): mass calcd. for $C_{30}H_{27}F_2N_5O_2$ 527.21; found *m/z* 528.36 $[M+H]^+$.

**Example-50:**

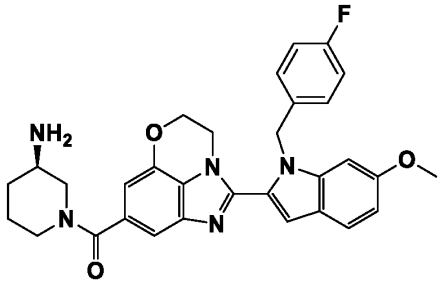
**(*R*)-(3-aminopiperidin-1-yl)(2-(6-fluoro-1-(4-methoxybenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000208]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.73-7.70 (m, 1H), 7.41 (d, *J* = 10.08 Hz, 1H), 7.27 (d, *J* = 6.76 Hz, 2H), 7.02 (d, *J* = 7.76 Hz, 2H), 6.99 (d, *J* = 6.96 Hz, 1H), 6.78-6.72 (m, 3H), 6.01 (s, 2H), 4.65 (s, 2H), 4.56 (s, 2H), 4.11 (bs, 2H), 3.64 (s, 3H), 2.89 (bs, 1H), 2.66-2.62 (m, 1H), 1.84 (d, J = 10.48 Hz, 1H), 1.64 (bs, 2H), 1.42 (m, 2H), 1.22-1.19 (m, 2H). MS (ESI): mass calcd. for $C_{31}H_{30}FN_5O_3$ 539.23; found *m/z* 540.27 $[M+H]^+$.

**Example-51:**

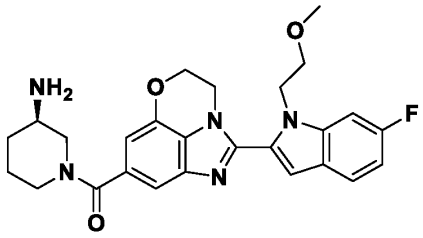
**(R)-(3-aminopiperidin-1-yl)(2-(1-(4-fluorobenzyl)-6-methoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000209]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.59 (d, *J* = 8.64 Hz, 1H), 7.24 (s, 1H), 7.19 (s, 1H), 7.18-7.14 (m, 2H), 7.07-7.04 (m, 3H), 6.80 (d, *J* = 8.52 Hz, 1H), 6.73 (s, 1H), 6.09 (s, 2H), 4.65 (s, 2H), 4.54 (s, 2H), 4.16 (bs, 1H), 3.76 (s, 3H), 3.60-3.45 (m, 1H), 2.88 (bs, 1H), 2.62 (bs, 2H), 1.83-1.65 (m, 3H), 1.39-1.33 (m, 1H), 1.23 (bs, 1H), 1.19-1.10 (m, 1H). MS (ESI): mass calcd. for $C_{31}H_{30}FN_5O_3$ 539.23; found *m/z* 540.42 $[M+H]^+$.

**Example-52**

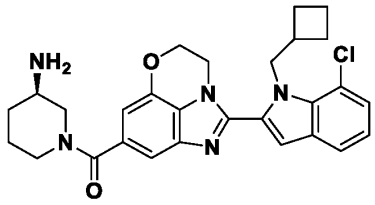
**3-aminopiperidin-1-yl)(2-(6-fluoro-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000210]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.71-7.67 (m, 1H), 7.51 (d, *J* = 9.8 Hz, 1H), 7.28 (s, 1H), 7.18 (s, 1H), 7.01 (t, *J* = 8.2 Hz, 1H), 6.75 (s, 1H), 4.88 (t, *J* = 5.16 Hz, 2H), 4.63 (s, 2H), 4.56 (s, 2H), 4.13 (bs, 2H), 3.65 (t, *J* = 4.9 Hz, 2H), 3.09 (s, 3H), 2.91-2.90 (m, 1H), 2.66 (m, 2H), 1.85 (d, *J* = 11.2 Hz, 2H), 1.66 (bs, 2H), 1.42 (d, *J* = 11.5 Hz, 1H), 1.27-1.17 (m, 1H). MS (ESI): mass calcd. for $C_{26}H_{28}FN_5O_3$ 477.12; found *m/z* 478.26 $[M+H]^+$.

**Example-53**

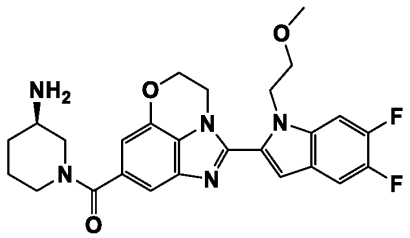
**(*R*)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(cyclobutylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000211]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.68 (d, *J* = 7.8 Hz, 1H), 7.35-7.33 (m, 2H), 7.23 (s, 1H), 7.13 (t, *J* = 7.7 Hz, 1H), 6.78 (s, 1H), 5.21 (d, *J* = 6.9 Hz, 2H), 4.60-4.56 (m, 4H), 4.18 (bs, 1H), 3.64 (bs, 1H), 2.92 (bs, 1H), 2.68 (m, 1H), 2.62-2.55 (m, 1H), 1.86 (d, *J* = 10.6 Hz, 2H), 1.69-1.52 (m, 6H), 1.42-1.38 (m, 4H), 1.23 (bs, 1H). MS (ESI): mass calcd. for $C_{28}H_{30}ClN_5O_2$ 503.26; found *m/z* 504.44 $[M+H]^+$.

**Example-54**

**(R)-(3-aminopiperidin-1-yl)(2-(5,6-difluoro-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**

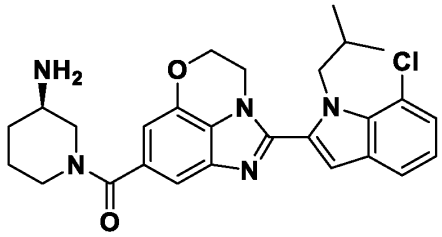


**[000212]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.81-7.76 (m, 1H), 7.71-7.66 (m, 1H), 7.28 (s, 1H), 7.16 (s, 1H), 6.75 (s, 1H), 4.88 (t, *J* = 5.08 Hz, 2H), 4.61 (d, *J* = 4.44

Hz, 2H), 4.56 (d, *J* = 4.16 Hz, 2H), 4.16 (bs, 1H), 3.65 (t, *J* = 5.28 Hz, 2H), 3.07 (s, 3H), 2.90 (bs, 1H), 2.67-2.64 (m, 3H), 1.85 (d, *J* = 11.04 Hz, 1H), 1.66 (bs, 2H), 1.42 (d, *J* = 9.44 Hz, 1H), 1.26-1.20 (m, 2H). MS (ESI): $C_{26}H_{27}F_2N_5O_3$ 495.21; found *m/z* 496.15 $[M+H]^+$.

**Example-55**

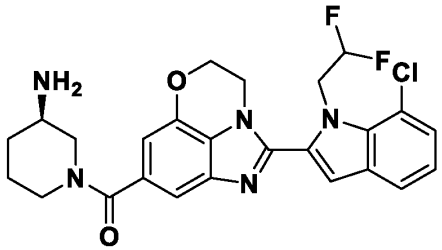
**(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-isobutyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**




**[000213]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.69 (d, *J* = 8.9 Hz, 1H), 7.35-7.33 (m, 2H), 7.24 (s, 1H), 7.14 (t, *J* = 7.8 Hz, 1H), 6.78 (s, 1H), 4.95 (d, *J* = 7.24 Hz, 2H), 4.60 (s, 2H), 4.56 (s, 2H), 4.16 (bs, 1H), 3.68 (bs, 1H), 2.92 (bs, 1H), 2.67-2.62 (m, 1H), 2.08-1.91(m, 1H), 1.87-1.71 (m, 4H), 1.44-1.41 (m, 1H), 1.23 (s, 2H), 0.60 (s, 6H) MS (ESI): mass calcd. for $C_{27}H_{30}ClN_5O_2$ 492.02; found *m/z* 492.41 $[M+H]^+$.

**Example-56**

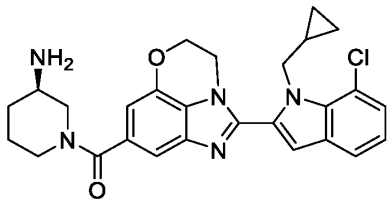
**(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(2,2-difluoroethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**




**[000214]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.70 (d, *J* = 7.5 Hz, 1H), 7.39 (s, 2H), 7.32 (s, 1H), 7.21-7.19 (m, 1H), 6.78 (s, 1H), 6.39 (t, *J* = 55.2 Hz, 1H), 5.71 (t, *J* = 12.2 Hz, 2H), 4.64 (s, 2H), 4.57 (s, 2H), 4.13 (bs, 1H), 3.71 (bs, 1H), 2.92 (m, 1H), 2.66 (m, 1H), 1.84 (m, 1H), 1.65 (bs, 2H), 1.44 (m, 2H), 1.23 (m, 2H) MS (ESI): mass calcd. for $C_{25}H_{24}ClF_2N_5O_2$ 499.16; found *m/z* 500.35 $[M+H]^+$.

**Example-57**

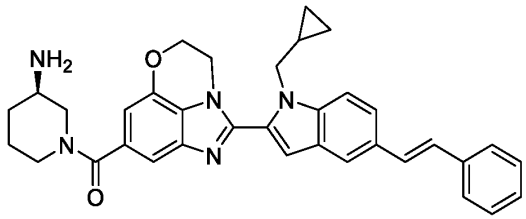
**(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000215]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.69 (d , *J* = 8.0 Hz, 1H), 7.36-7.33 (m, 2H), 7.26 (s, 1H), 7.16-7.12 (t, *J* = 8.0Hz, 1H), 6.81 (s, 1H), 6.0-5.9 (bs, 2H), 5.05 (d , *J* = 7.2 Hz, 2H), 4.61-4.56 (m, 4H), 4.11 (d , *J* = 4.0 Hz, 1H), 2.96-2.94 (m, 2H), 1.94-1.46 (m, 4H), 1.11 (s, 1H), 0.88-0.84 (m, 2H),0.27-0.25 (m, 2H), 0.04-0.03 (m, 2H). MS (ESI): mass calcd. For $C_{27}H_{28}ClN_5O_2$, 490.0 m/z found, 490.2 (M+H).

**Example-58**

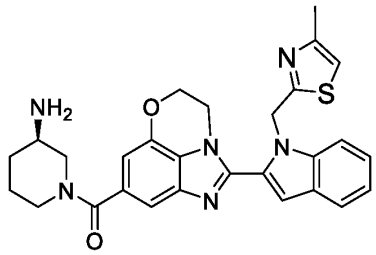
**(R,E)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-styryl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000216]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.84 (s, 1H), 7.70-7.59 (m, 4H), 7.39-7.35(m, 3H), 7.31 (s, 1H), 7.25-7.17 (m, 3H), 6.77 (s, 1H), 4.71-4.66 (m, 4H), 4.57 (s, 2H), 4.0-3.9 (bs, 2H), 2.95 (s, 2H), 2.77 (s, 2H), 1.89-1.22 (m, 5H), 0.88-0.84 (m, 1H). 0.33-0.26 (m,4H). MS (ESI): mass calcd. For $C_{35}H_{35}N_5O_2$, 557.0 m/z found, 558.6 $(M+H)^+$.

**Example-59**

**(R)-(3-aminopiperidin-1-yl)(2-(1-((4-methylthiazol-2-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**

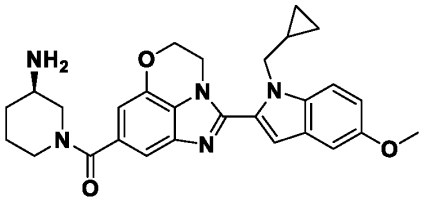


**[000217]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.77-7.64 (m, 2H), 7.31-7.30 (m, 2H), 7.19 (s, 1H), 7.023 (s, 2H), 6.78 (s, 1H), 6.34 (s, 1H), 4.68 (m, 2H), 4.56 (m, 2H), 3.05-2.9 (m, 3H), 2.25 (s, 3H), 1.90-1.87 (m, 2H), 1.70-1.67 (m, 2H), 1.49-1.45 (m, 1H),

1.37-1.33 (m, 2H), 1.26-1.21 (m, 2H). MS (ESI): mass calcd.for $C_{27}H_{28}N_6OS$ , 484.20; *m/z* found 485.1 $(M+H)^+$.

**Example-60**

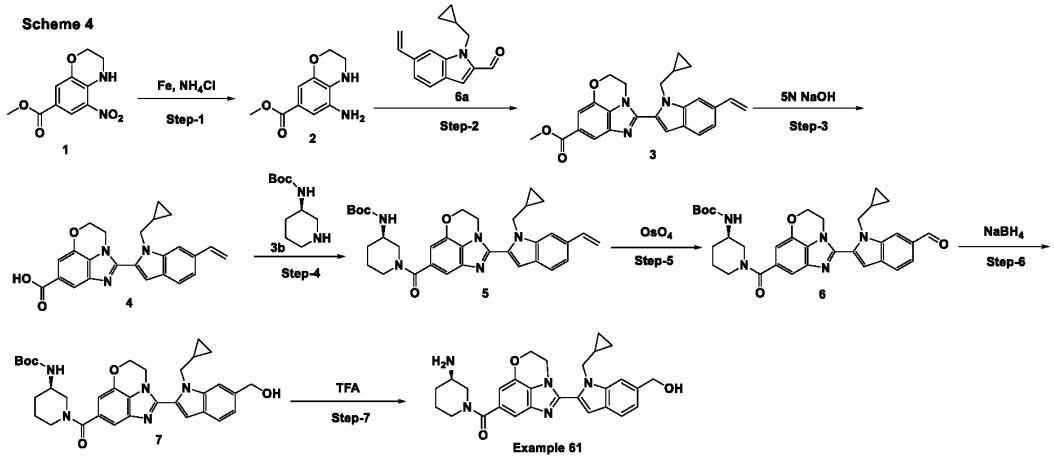
**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-methoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000218]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.56 (d , *J* = 9.2 Hz, 1H), 7.30 (s, 1H), 7.14 (s, 1H), 7.04 (s, 1H), 6.94-6.91 (m, 1H), 6.75 (s, 1H), 4.65-4.63 (m, 4H), 4.55 (s, 2H), 3.96-3.9 (bs, 2H), 3.79 (s, 3H), 2.95 (s, 1H), 2.79 (d , *J* = 7.2 Hz, 2H), 1.89-1.26 (m, 6H), 0.88-0.84 (m, 1H), 0.33-0.26 (m, 4H). MS (ESI): mass calcd. For $C_{28}H_{31}N_5O_3$, 485.5 m/z found, 486.5 $(M+H)^+$.

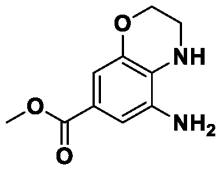
**Example-61**

**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-(hydroxymethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**




**[000219]** Intermediate 1 was synthesized using the procedure described in Scheme-3.

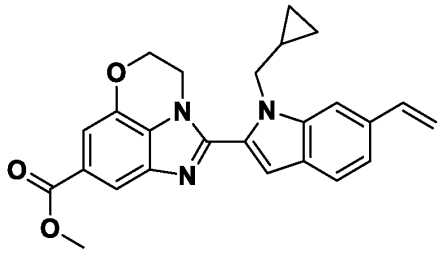
**Step 1: Synthesis of methyl 5-amino-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (2).**



**[000220]** To a stirred solution of methyl 5-nitro-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (**1**, 11.0 g, 46.18 mmol) in mixture of ethanol (110 mL, 10 vol) and water (33 mL, 3 vol) were added ammonium chloride (37.0 g, 692.0 mmol) and iron powder (38.6 g, 692.0 mmol) at room temperature and the resulting mixture was stirred at 80 °C for 3 h. The progress of the reaction was monitored by TLC. After completion of reaction, the reaction mixture was evaporated, filtered through celite and celite bed washed with ethyl acetate (200 mL × 3). The combined ethyl acetate layer was washed with water and brine. Obtained organic layer was dried over anhydrous sodium sulphate and concentrated under reduced pressure to afford methyl 5-amino-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (**2**) as brown solid. Yield: 9.0 g (93%).

**[000221]** $^1$HNMR (400 MHz, DMSO-$d_6$), δ (ppm): 6.86 (d, $J$ = 1.6 Hz, 1H), 6.67 (d, $J$ = 1.6 Hz, 1H), 5.39 (s, 2H), 4.73 (s, 1H), 4.06 (s, 2H), 3.70 (s, 3H), 3.35 (s, 2H). MS (ESI): 208.12, *m/z* found 209.20 $[M+H]^{+1}$.

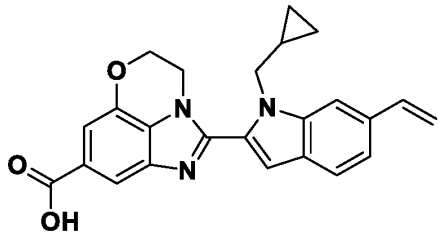
**Step-2: Synthesis of methyl-2-(1-(cyclopropylmethyl)-6-vinyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylate (3)**



**[000222]** To a stirred solution of methyl-5-amino-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (**2**, 1.0 g, 4.80 mmol) and 1-(cyclopropylmethyl)-6-vinyl-1H-indole-2-carbaldehyde (**6a**, 1.2 g, 5.70 mmol) in *N, N*-dimethylformamide (10.0 mL) and water (3.0 mL), potassium peroxomonosulfate (0.88 g, 5.76 mmol) was added at room temperature. The reaction mixture was stirred at room temperature for 16 h. After completion of reaction, the reaction mixture was cooled to room temperature and water was added. Precipitated solid was filtered and washed with water (20 mL × 2) and methanol (10 mL × 2). The compound obtained was dried under vacuum to afford methyl 2-(1-(cyclopropylmethyl)-6-vinyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-

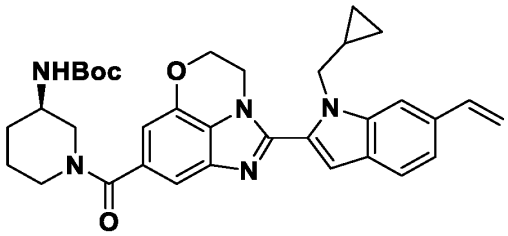
diazaacenaphthylene-7-carboxylate (**3**) as yellow solid. Yield: 0.550 g (crude). MS (ESI) 413.17; *m/z* found 414.26 $[M+H]^{+1}$.

**Step-3: Synthesis of 2-(1-(cyclopropylmethyl)-6-vinyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid (4)**



**[000223]** To a stirred solution of afford methyl 2-(1-(cyclopropylmethyl)-6-vinyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylate (**3**, 0.55 g, 1.3 mmol) in tetrahydrofuran (5.0 mL) and methanol (3.0 mL) 5N sodium hydroxide solution (3.0 mL) was added and reaction mixture was stirred at 60 °C for 2 h. After completion of reaction, the reaction mixture was concentrated under reduced pressure. The resulting crude was dissolved in minimum volume of water and acidified with saturated citric acid solution at 0 °C up to pH 2~3. The precipitated solid was filtered, washed with water (10 mL × 2). The compound obtained was dried under vacuum to afford 2-(1-(cyclopropylmethyl)-6-vinyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid (**4**) as white solid. Yield: 0.440 g (Crude). MS (ESI) 399.16; *m/z* found 400.16 $[M+H]^{+1}$.

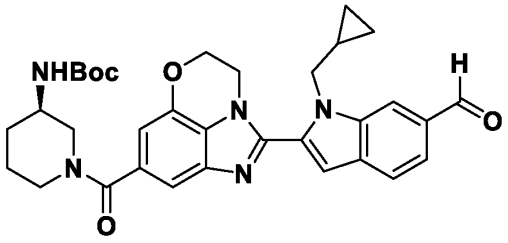
**Step-4: Synthesis of tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-6-vinyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (5)**



**[000224]** To a stirred solution of 2-(1-(cyclopropylmethyl)-6-vinyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid (**4**, 0.44 g, 1.10 mmol) in dichloromethane (10.0 mL), *tert*-butyl-(*R*)-piperidin-3-ylcarbamate (**3b**, 0.26 g, 1.29 mmol) and triethylamine (0.4 mL, 3.31 mmol) were added, followed by addition of propylphosphonic anhydride (50% solution in ethyl acetate, 0.8 mL, 3.37 mmol). The reaction mixture was stirred at room temperature for 2 h. After completion of reaction,

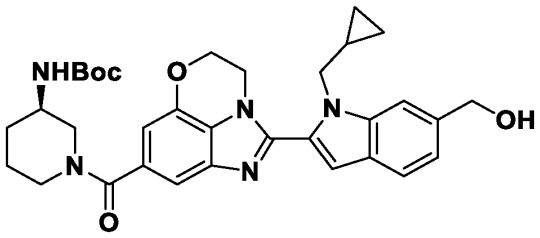
the reaction mixture was diluted with water and extracted with dichloromethane (10 mL × 2). The combined organic layers were washed with water and brine solution, further dried over anhydrous sodium sulfate, filtered and concentrated to get crude product. The crude was purified by CombiFlash using 12.0 g, RediSep and 70% ethyl acetate in hexane as eluent to afford tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-6-vinyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (**5**) as brown solid. Yield: 0.250 g (44%). MS (ESI) 581.30; *m/z* found 582.41 $[M+1]^+$.

**Step-5: preparation of tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-6-formyl-1H-indol-2-yl)-3, 4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (6)**



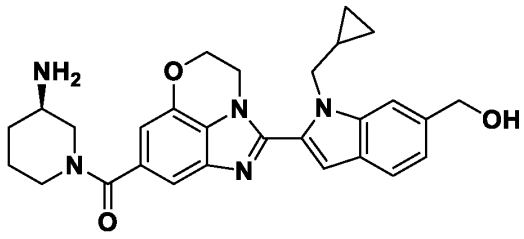

**[000225]** To a stirred solution of tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-6-vinyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl) piperidin-3-yl)carbamate (**5**, 0.25 g, 0.43 mmol) in tetrahydrofuran (10.0 mL) and water (3.0 mL), osmium tetroxide ( 0.6 ml , 0.08 mmol) and sodium per iodate (0.29 g, 1.37 mmol) were added at 0 °C . The reaction mixture was stirred at room temperature for 20 min. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (10 mL × 2). The combined organic layers were washed with water and brine solution, further dried over anhydrous sodium sulfate, filtered and concentrated to get crude product. The crude was purified by CombiFlash using 12.0 g, RediSep and 70% ethyl acetate in hexane as eluent to afford tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-6-formyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (**6**) as white solid. Yield: 0.200 g (80%). MS (ESI) 583.28; *m/z* found 584.30 $[M+1]^+$.

**Step-6: preparation of tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-6-(hydroxymethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl) carbamate (7)**




**[000226]** To a stirred solution of tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-6-formyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl) piperidin-3-yl)carbamate (**6**, 0.2 g, 0.34 mmol) in methanol (10.0 mL), sodium borohydride ( 0.014 g, 0.34 mmol) was added at 0 °C. The reaction mixture was stirred at room temperature for 1 h. After completion of reaction, the reaction mixture was diluted with water and extracted with dichloromethane (10 mL × 2). The combined organic layers were washed with water and brine solution, further dried over anhydrous sodium sulfate, filtered and concentrated to get crude product. The crude was purified by CombiFlash using 12.0 g, RediSep and 70% ethyl acetate in hexane as eluent to afford tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-6-(hydroxymethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (**7**) as yellow solid. Yield: 0.100 g (51%). MS (ESI) 585.30; *m/z* found 586.30 $[M+1]^+$.

**Step-7: prepararion of (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-(hydroxymethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl) methanone (Example-61)**



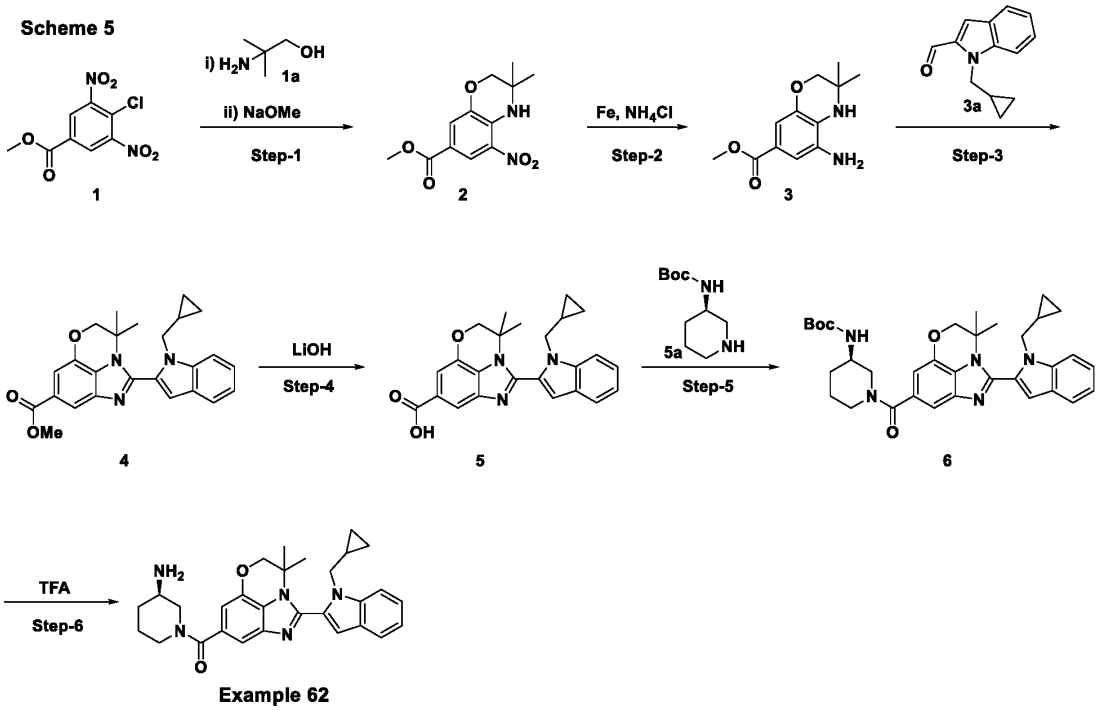

**[000227]** To a stirred solution tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-6-(hydroxymethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (**6**, 0.1 g, 0.17 mmol) in dichloromethane (10.0 mL), trifluoroacetic acid (1.0 mL) was added at 0 °C and stirred at room temperature for 2 h. After completion of reaction, the reaction mixture was concentrated completely, basified by saturated sodium bicarbonate solution (10 mL). The compound was extracted with dichloromethane (10 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated to get crude product. The crude was purified by reverse prep HPLC to afford ((R)-(3-aminopiperidin-1-yl)(2-(1-

(cyclopropylmethyl)-6-(hydroxymethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone as off white solid. Yield: 0.0023 g (0.02%).

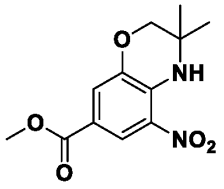
**[000228]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.63 (d, *J* = 8.1 Hz, 1H), 7.59 (s, 1H), 7.29 (s, 1H), 7.13 (s, 1H), 7.11 (d, *J* = 8.2 Hz, 1H), 6.75 (s, 1H), 5.22 (s, 2H), 4.70-4.65 (m, 6H), 4.56 (s, 2H), 4.15 (s, 1H), 2.92 (s, 1H), 2.66 (m, 2H), 1.88-1.84 (m, 3H), 1.66 (s, 1H), 1.43 (m, 1H), 1.24 (m, 2H), 0.35-0.29-(m, 4H). MS (ESI): mass calcd. for $C_{28}H_{31}N_5O_3$ 485.24; found *m/z* 486.32 $[M+H]^+$.

**Example-62**

**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,3-dimethyl-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**

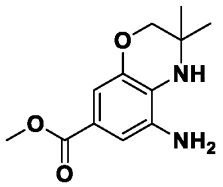



**Step-1: Synthesis of methyl 3,3-dimethyl-5-nitro-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (2)**



**[000229]** To the stirred solution of methyl-4-chloro-3,5-dinitrobenzoate (**1**, 5.0 g, 19.19 mmol) in methanol (30.0 mL), 2-amino-2-methylpropan-1-ol (**1a**, 2.6 g, 28.7 mmol) was added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After 3 h, 25% sodium methoxide solution in methanol (12.5 mL, 57.6 mmol) was added in the reaction mixture at 0 °C. The reaction mixture subjected to 80 °C for 3 h. After completion of reaction, the reaction mixture was diluted with water. Precipitated solid was filtered and washed with water. The crude was dried under reduced pressure to afford methyl 3,3-dimethyl-5-nitro-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (**2**) as yellow solid. Yield: 1.8 g (35%). MS (ESI): 266.0, *m/z* found 267.1 $[M+H]^{+1}$.

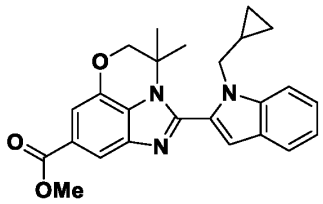
**Step-2: Synthesis of methyl 5-amino-3,3-dimethyl-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (3)**



**[000230]** To a stirred solution of methyl 3,3-dimethyl-5-nitro-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (**2**, 1.8 g, 6.76 mmol) in ethanol (20 mL) - water (10 mL) were added ammonium chloride (5.4 g, 101.4 mmol) and iron powder (5.6 g, 101.4 mmol) at room temperature and the resulting mixture was stirred at 60 °C for 3 h. The progress of the reaction was monitored by TLC. After completion of reaction, the reaction mixture was evaporated, filtered through celite and washed with ethyl acetate (50 mL × 3). The combined ethyl acetate layer was washed with water and brine. The organic layer was dried over anhydrous sodium sulphate and concentrated under reduced pressure to afford methyl 5-amino-3,3-dimethyl-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (**3**) as yellow solid.

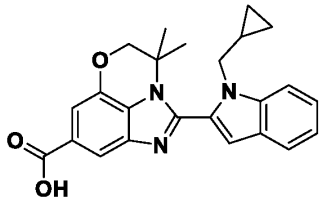
**[000231]** Yield: 1.0 g (55%). MS (ESI): 236.11, *m/z* found 237.20 $[M+H]^{+1}$.

**Step-3: Synthesis of methyl 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,3-dimethyl-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylate (4)**



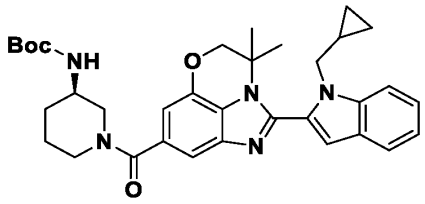
**[000232]** To a stirred solution of methyl-5-amino-3,3-dimethyl-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (**3**, 0.5 g, 2.12 mmol) and 1-(cyclopropylmethyl)-1H-indole-2-carbaldehyde (**3a**, 0.46 g, 2.33 mmol) in *N, N*-dimethylformamide (5.0 mL) and water (0.5 mL), potassium peroxomonosulfate (Oxone, 0.39 g, 2.54 mmol) was added at room temperature. The reaction mixture was stirred at room temperature for 16 h. After completion of reaction, the reaction mixture was cooled to room temperature and water was added. The precipitated solid was filtered and washed with water (10 mL × 2) and methanol (5 mL × 2). The compound obtained was dried under vacuum to afford methyl 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,3-dimethyl-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylate (**4**) as yellow solid. Yield: 0.50 g, crude, MS (ESI) 415.19; *m/z* found 416.27 $[M+H]^{+1}$.

**Step-4: Synthesis of 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,3-dimethyl-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid (5)**



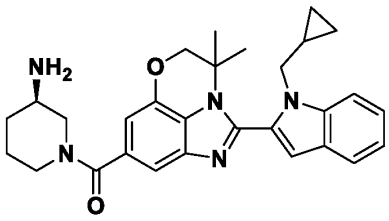
**[000233]** To a stirred solution of afford methyl 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,3-dimethyl-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylate (**4**, 0.5 g, 1.2 mmol) in tetrahydrofuran (10.0 mL) and methanol (5.0 mL) 5N sodium hydroxide solution (5.0 mL) was added and reaction mixture was stirred at 60 °C for 3 h. After completion of reaction, the reaction mixture was concentrated under reduced pressure completely. The resulting crude was dissolved in minimum volume of water and acidified with saturated citric acid solution at 0 °C up to pH 2~3. The precipitated solid was filtered, washed with water (10 mL × 2). The compound obtained was dried under vacuum to afford 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,3-dimethyl-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid (**5**) as orange solid. Yield: 0.50 g (Crude). MS (ESI) 401.17; *m/z* found 402.27 $[M+H]^{+1}$.

**Step-5: Synthesis of tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,3-dimethyl-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (6)**




**[000234]** To a stirred solution of 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,3-dimethyl-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid (**5**, 0.5 g, 1.25 mmol) in dichloromethane (20.0 mL), *tert*-butyl-(*R*)-piperidin-3-ylcarbamate (**5a**, 0.3 g, 1.49 mmol) and triethylamine (0.6 mL, 3.99 mmol) were added, followed by addition of propylphosphonic anhydride (50% solution in ethyl acetate, 2.5 mL, 3.99 mmol). The reaction mixture was stirred at room temperature for 12 h. After completion of reaction, the reaction mixture was diluted with water and extracted with dichloromethane (40 mL × 2). The combined organic layers were washed with water and brine solution, further dried over anhydrous sodium sulfate, filtered and concentrated to get crude product. The crude was purified by CombiFlash using 12.0 g, RediSep and 70% ethyl acetate in hexane as eluent to afford tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,3-dimethyl-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl) carbamate (**6**) as yellow solid. Yield: 0.25 g (34%). MS (ESI) 583.32; *m/z* found 584.37 $[M+1]^+$.

**Step-6: preparation of (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,3-dimethyl-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone (Example 62)**

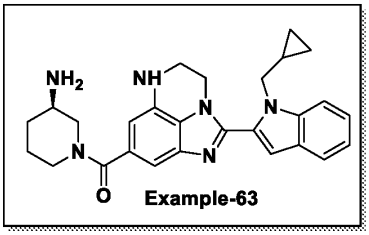


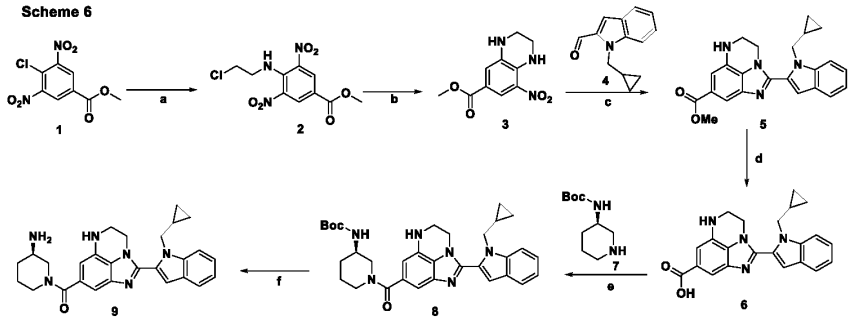

**[000235]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.71-7.65 (m, 2H), 7.32 (s, 1H), 7.28 (t, *J* = 7.7 Hz, 2H), 7.14 (t, *J* = 7.8 Hz, 1H), 7.00 (s, 1H), 6.82 (s, 1H), 4.21 (s, 2H), 4.18 (d, *J* = 6.8 Hz, 2H), 3.67 (bs, 2H), 2.92 (bs, 1H), 2.66-2.64 (m, 2H), 1.87-1.84 (m, 1H), 1.64-1.55 (m, 3H), 1.43 (s, 6H), 1.25-1.21 (m, 1H), 1.10-1.07 (m, 1H), 0.32 (d, *J* =

5.0 Hz, 2H), 0.31 (d, $J$ = 4.3 Hz, 2H). MS (ESI): mass calcd. for $C_{29}H_{33}N_5O_2$ 483.2; found $m/z$ 484.37 $[M+H]^+$.

**Example-63:**

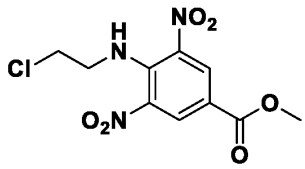
**Synthesis of (R)-(3-aminopiperidin-1-yl) (2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5, 6-dihydro-4H-imidazo [1, 5, 4-de]quinoxalin-8-yl) methanone (Example-63)**




**[000236]** The intermediate **(1)** used for the preparation of **Example-61** was purchased commercially (from Reddy N Reddy Pharmaceuticals). The intermediate **(1)** mentioned in Scheme-4 is equivalent to intermediate **(3)** of Scheme-2 above.

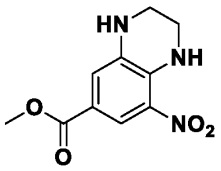
**Step 3: Preparation of methyl 4-((2-chloroethyl) amino)-3, 5-dinitrobenzoate (2)**




**2**

**[000237]** To a stirred solution of (**1**, 0.5g 1.92 mmol) in MeOH (50 mL) was added 2-Chloro-ethylamine hydrochloride (0.46 g, 4.03 mmol), followed by triethylamine (0.7 ml, 4.031 mmol) then resulting mixture was heated to 80 °C for 1h (Reaction condition **a**). The reaction mixture was cooled to room temperature and diluted with ethyl acetate (100 mL x 2) and the organic phase was evaporated through vacuum and crude carried to next step without purification to give yellow color solid (0.9g, 100% yield). MS (ESI): mass calcd. for $C_{10}H_{10}ClN_3O_6$, 303.66; m/z found, 304.0 $[M+H]^+$.

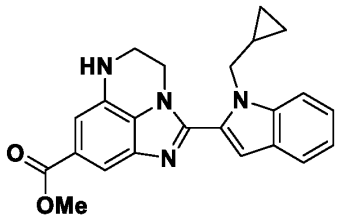
**Step 4: Preparation of methyl 8-nitro-1, 2, 3, 4-tetrahydroquinoxaline-6-carboxylate (3)**



3

**[000238]** To a stirred solution of methyl 4-((2-chloroethyl)amino)-3,5-dinitrobenzoate (**2**, 0.3g, 0.99 mmol) in AcOH (30 mL) was added iron powder (0.27 g, 4.95 mmol) at room temperature and the resulting mixture was allowed to stir under room temperature for 12 h (Reaction condition **b**). The progress of the reaction was monitored by TLC. Then reaction mixture was evaporated, filtered through celite and extracted with ethyl acetate (50 mL x 3). The combined organic extract was washed $NaHCO_3$ solution with brine, dried over sodium sulphate and concentrated under reduced pressure to afford crude compound which was purified by column chromatography (silica gel, 0-20% EtOAc in hexane) to give dark brown solid (0.23 g, 99% yield). MS (ESI): mass calcd. for $C_{10}H_{11}N_3O_4$ 237.22; m/z found, 238.1 $[M+H]^+$.

**Step 5: Preparation of methyl 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylate (5)**

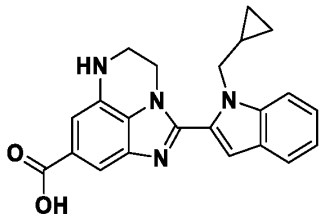


5

**[000239]** To the stirred solution of mixture of methyl 5-nitro-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (**3**, 0.1g, 0.42mmol) and 1-(cyclopropylmethyl)-1H-indole-2-carbaldehyde (**4**, 0.09 g, 0.46 mmol) in EtOH (10 mL), was added $Na_2S_2O_4$ (0.4 g, 2.32 mmol) in water (5 mL) and the reaction mixture was stirred at 80°C for 16h (reaction condition **c**). The reaction mixture was cooled to room temperature, water was added and the compound was extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using silica

gel and eluent 15-20% ethyl acetate in hexane to afford yellow solid (0.08 g, 62% Yield). MS (ESI): mass calcd. for, $C_{23}H_{22}N_4O_2$ 386.46; m/z found, 387.2 $[M+H]^+$.

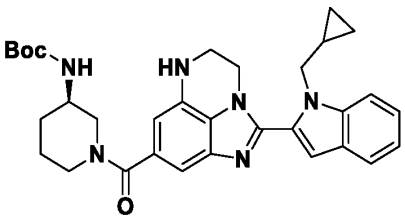
**Step 6: Preparation of 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylic acid (6)**




**6**

**[000240]** To the stirred solution of methyl 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylat**e** (**5**, 0.1 g, 0.25 mmol) in MeOH (2 mL), was added 5N NaOH solution (0.4 mL) and stirred at 75°C for 1h (reaction condition **d**). The reaction mixture was evaporated completely. The resulting crude was dissolved in minimum volume of water and acidified with saturated citric acid solution. Compound was extracted with DCM (50 mL x 2), washed with brine, dried over sodium sulfate and evaporated to get crude product as pale yellow color solid (0.07g, 72% Yield). MS (ESI): mass calcd. for, $C_{22}H_{20}N_4O_2$ 372.43; m/z found, 373 $[M+H]^+$.

**Step 7: Preparation of tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carbonyl)piperidin-3-yl)carbamate (8)**

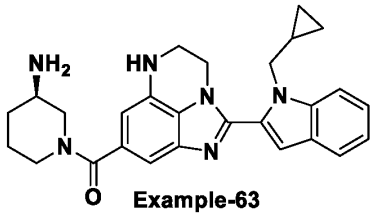



**8**

**[000241]** To the stirred solution of 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylic acid (**6**, 0.07 g, 0.18 mmol) in DCM (5 mL), were added tert-butyl-(R)-piperidin-3-ylcarbamate (**7**, 0.041 g, 0.206 mmol), triethylamine (0.07 mL, 0.56 mmol) followed by 50% solution of T3P in ethyl acetate (0.17 g, 0.565 mmol) and stirred at room temperature for 12 h (reaction condition **e**). To the reaction mixture was added water and compound was extracted with DCM (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate

and evaporated to get crude product. The crude residue was purified by gradient column chromatography using silica gel and eluent 5% MeOH in DCM to afford the product as yellow solid (0.1g.71% Yield). MS (ESI): mass calcd. for $C_{32}H_{38}N_6O_3$, 554.7; m/z found, 555.3 $[M+H]^+$.

**Step 8: Preparation of (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone (Example-63)**



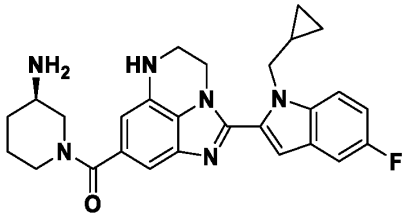
Example-63

**[000242]** To the stirred solution Tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H- imidazo[1,5,4-de]quinoxaline-8-carbonyl)piperidin-3-yl)carbamate) (**8**, 0.05 g, 0.09 mmol) in dichloromethane (10 mL), was added trifluroacetic acid (0.5 mL) stirred at room temperature for 2 h (reaction condition **f**). The reaction mixture was evaporated completely, dissolved in minimum volume of water and basified by saturated $NaHCO_3$ solution (20 mL). The compound was extracted with DCM (20 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get the product as pale yellow solid (0.025g, 62.5% yield). $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.67 (t , $J$ = 8 Hz, 2H), 7.28 (t, $J$ = 8 Hz, 1H), 7.13-7.07 (m, 2H), 6.94 ( s, 1H), 6.40 (s, 1H) 6.37 (s, 1H), 4.65 (d, $J$ = 8 Hz, 2H), 4.48 (t , $J$ = 4 Hz, 2H ), 3.93-3.88 (m, 2H), 3.53 (m, 2H), 2.87 (m, 1H), 2.66-2.65 (m, 2H), 1.88-1.85 (m, 2H), 1.64 (m, 1H), 1.42-1.17 (m, 4H), 0.33-0.199 (m, 4H). MS (ESI): mass calcd. for, $C_{27}H_{30}N_6O$ 455.58; m/z found, 456.2 $[M+H]^+$.

**[000243]** Following compounds **(Examples 64-80)** were synthesized using procedure as exemplified for **Example-63**.

**Example-64**

**R-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**

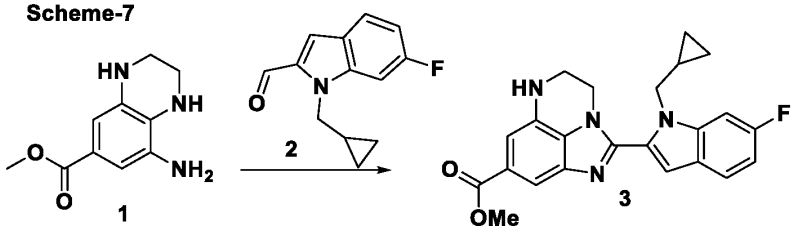


**[000244]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.70-7.66 (m ,1H), 7.43-7.40 (m, 1H), 7.13-7.09 (m, 1H), 7.05 ( s, 1H), 6.94 (s, 1H), 6.41 (s, 1H), 6.38 (s, 1H), 4.63 (d , *J* = 6.8 Hz, 2H ), 4.46 (m, 2H), 4.00 (s, 2H), 3.52 (m, 2H), 2.88 (m, 2H), 2.68 (m, 2H), 1.64 (m, 1H), 1.89-1.85 (m, 1H), 1.64 (m, 1H), 1.42-1.39 (m , 1H), 1.26-1.22 (m, 2H), 0.32 (d, *J* = 7.6 Hz, 2H), 0.21 (m, 2H). MS (ESI): mass calcd. for $C_{27}H_{29}FN_6O$, 472.57; m/z found, 473.58 $[M+H]^+$.

**Example-65**

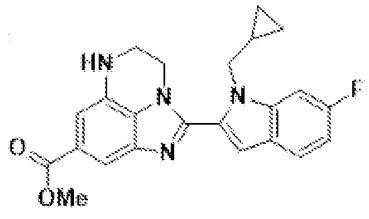
**Synthesis of (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone (Example-65)**

**Scheme-7**



**[000245]** Intermediate **(1)** was synthesized from intermediate **(3)** of Scheme-6 under reduction conditions.

**Step 5: Preparation of methyl 2-(1-(cyclopropylmethyl)-6-fluro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylate (3)**



3

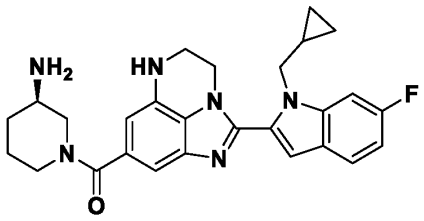
**[000246]** To the stirred solution of methyl 8-amino-1, 2, 3, 4-tetrahydroquinoxaline-6-carboxylate (**1**, 0.1 g, 0.48 mmol) and 1-(cyclopropylmethyl)-6-fluoro-1H-indole-2-carbaldehyde (**2**, 0.11 g, 0.53 mmol) in DMF (3 mL), was added water (0.1 mL) and finally added oxone (0.09 g, 0.31 mmol). Then reaction mixture was allowed to stir under

room temperature for about 1 h. The reaction mixture was quenched with potassium carbonate (0.005g), extracted with ethyl acetate (20 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate, filtered and evaporated to get crude product. Crude residue was purified by gradient column chromatography using silica gel and eluent 20-30% ethyl acetate in hexane to get the product as a yellow solid (0.15 g, 65.2% yield). MS (ESI): mass calcd. for $C_{23}H_{21}FN_4O_2$, 404.16; m/z found, 405.2 $[M+H]^+$.

**[000247]** Following compounds **(Examples 65-71)** were synthesized using the above intermediate **(3)**, and the procedure as exemplified for **Example-63**.

**Example-65:**

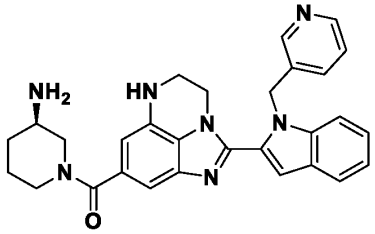
**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**




**[000248]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.68-7.64 (m, 1H), 7.54 (d, *J* = 8 Hz, 1H), 7.09 (s, 1H), 7.0 (s, 1H), 6.96 (d, *J* = 12 Hz, 1H), 6.4-6.38 (m, 2H), 4.63-4.61 (m, 2H), 4.46 (m, 2H), 4.0 (m, 2H), 3.52 (m, 2H), 2.91 (m, 1H), 2.76 (m, 2H), 1.89 (m, 2H), 1.65 (m, 1H), 1.43 (m, 1H), 1.41 (m, 1H), 1.17 (m, 2H), 0.31-0.24 (m, 2H), 0.24-0.20 (m, 2H). MS (ESI): mass calcd. for $C_{27}H_{29}FN_6O$, 472.24; m/z found, 473.3 $[M+H]^+$.

**Example-66**

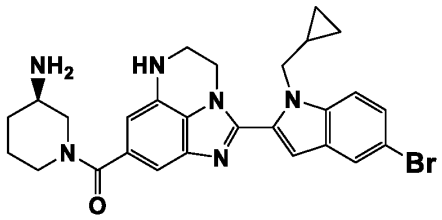
**(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-3-ylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**




**[000249]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 8.36 (bs, 2H), 7.70-7.69 (m, 1H), 7.54-7.52 (m, 1H), 7.44-7.52 (m, 1H), 7.24-7.23 (m, 3H), 7.15-7.11 (m, 1H), 6.99 (bs, 1H), 6.77 (s, 1H), 6.39-6.37 (m, 1H), 6.10 (bs, 2H), 4.50 (m, 2H), 4.00 (m, 2H), 3.51 (m, 2H), 2.65-2.55 (m, 2H), 1.88-1.82 (m, 2H), 1.56 (m, 1H), 1.44 (m, 2H), 1.22 ( m, 2H). MS (ESI): mass calcd. for $C_{29}H_{29}N_7O$, 491.60; m/z found, 492.4 $[M+H]^+$.

**Example-67**

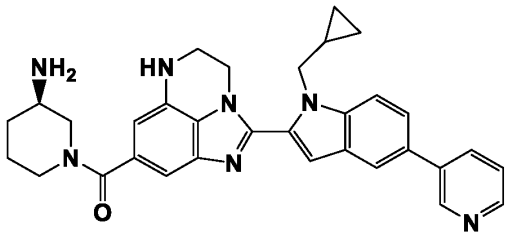
**(R)-(3-aminopiperidin-1-yl)(2-(5-bromo-1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**



**[000250]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.85 (s, 1H), 7.65 (d, *J* = 8.8 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.06 (s, 1H), 6.98 (s, 1H), 6.42-6.40 (m, 2H), 5.40-5.30 (bs. 2H), 4.64 (d, *J* = 7.2 Hz, 2H), 4.46 (s, 2H), 3.53 (s, 2H), 2.87-2.84 (m, 3H), 1.93-1.88 (m, 1H), 1.67 (s, 1H), 1.45-1.17 (m, 4H), 0.88-0.84 (m, 1H), 0.32-0.20 (m,4H). MS (ESI): mass calcd. For, $C_{27}H_{29}BrN_6O$ 533.47; m/z found, 497 [M+H]+.

**Example-68**

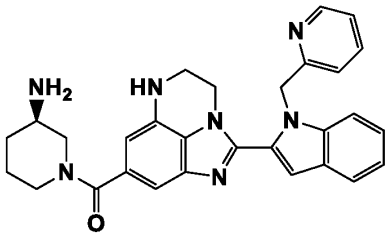
**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-(pyridin-3-yl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**



**[000251]** $^1$HNMR (400 MHz, DMSO-$d_6$ δ(ppm): 8.93 (s, 1H), 8.52 (d , *J* = 4.8 Hz, 1H), 8.09 (d , *J* = 8.4 Hz, 1H), 7.99 (s, 1H), 7.78 (d, *J* = 8.8 Hz, 1H), 7.61 (d, *J* = 8.8 Hz, 1H), 7.48-7.45 (m, 1H), 7.14 (s, 1H), 6.96 (s, 1H), 6.41-6.39 (m, 2H), 4.68 (d, *J* = 7.2 Hz, 2H), 4.49 (s, 2H), 4.12-3.80 (bs, 2H), 3.54 (s, 2H), 2.95 (s, 1H), 2.75 (s, 2H), 1.96-1.31 (m, 6H), 0.87-0.81 (m, 1H). 0.33-0.22 (m,4H). MS (ESI): mass calcd. For, $C_{32}H_{33}N_7O$ 531.6; m/z found, 533.2 [M+H]+.

**Example-69**

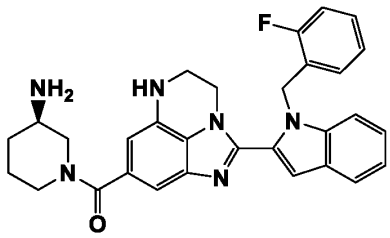
**(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-2-ylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**



**[000252]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 8.43 (d , *J* = 4.6 Hz, 1H), 7.70 (d, *J* = 7.7 Hz, 1H), 7.62-7.58 (m, 1H), 7.44 (d, *J* = 7.7 Hz, 1H), 7.23-7.11 (m, 4H) 6.91 (s, 1H), 6.84 (d, *J* = 7.68 Hz, 1H), 6.40 (s, 2H), 6.15 (s, 1H), 4.53 (bs, 2H ), 3.53 (bs, 2H), 3.53 (m, 2H), 2.89 (m, 1H), 2.73-2.66 (m, 2H), 1.90-1.86 (m, 2H), 1.64 (bs, 1H), 1.44-1.08 (m, 4H). MS (ESI): mass calcd. For, $C_{29}H_{29}N_7O$ 491.02; m/z found, 492.09 $[M+H]^+$.

**Example-70**

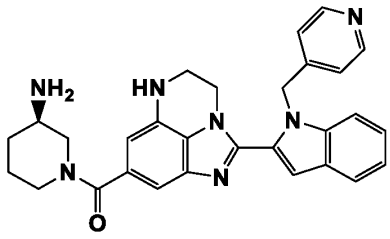
**(R)-(3-aminopiperidin-1-yl)(2-(1-(2-fluorobenzyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**



**[000253]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.71 (d, *J* = 7.3 Hz, 1H), 7.47 (t, *J* = 7.8 Hz, 1H), 7.26-7.12 (m, 4H), 7.01-6.86 (m, 3H), 6.40 (s, 2H), 6.10 (s, 2H), 4.52 (d, *J* = 3.36 Hz, 2H), 4.17 (bs, 2H), 3.53 (s, 2H), 2.83 (bs, 2H), 2.67 (bs, 2H ), 1.84 (d, *J* = 9.24 Hz, 2H), 1.64 (bs, 2H), 1.39 (bs,2H). MS (ESI): mass calcd. for $C_{30}H_{29}FN_6O$ 508.2; found *m/z* 509.16 $[M+H]^+$.

**Example-71**

**(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-4-ylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**



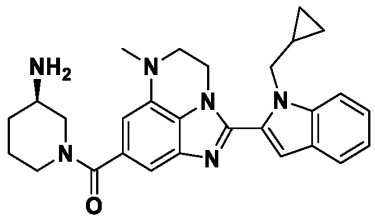
**[000254]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 8.39 (d, J = 5.7 Hz, 1H), 7.73 (d, J = 7.9 Hz, 1H), 7.43 (d, J =7.5 Hz, 1H), 7.25-7.21 (m, 2H), 7.15 (t, J = 7.5 Hz, 1H), 6.98

(d, J = 5.3 Hz, 2H), 6.87 (s, 2H), 6.39 (s, 2H), 6.15 (s, 2H), 4.54 (s, 2H), 4.34 (m, 2H), 3.53 (s, 2H), 2.89 (bs, 1H), 2.66 (m, 1H), 1.85 (d, J =12.8 Hz, 2H), 1.63-1.62 (m, 2H), 1.38-1.33 (m, 1H), 1.23-1.17 (m, 2H). MS (ESI): mass calcd. for $C_{29}H_{29}N_7O$ 491.12; found m/z 492.22 $[M+H]^+$.

**[000255]** Following compound was synthesized using the above intermediate **3**, and the procedure as exemplified for Example 63.

**Example-72**

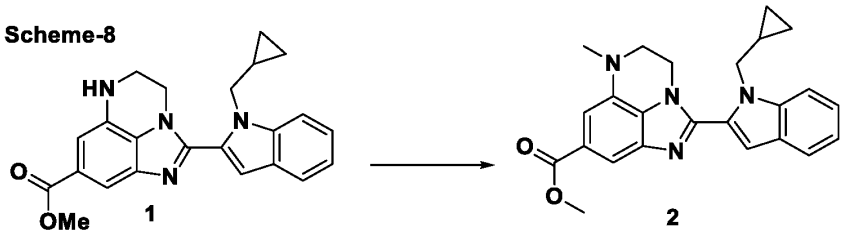
**R-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-methyl-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone (Example-72)**



**Preparation of methyl2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-methyl-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylate (2)**

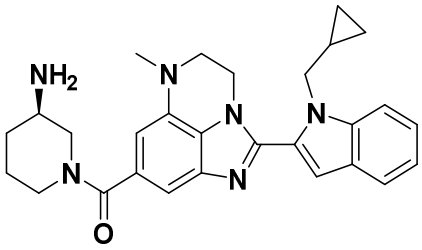
**[000256]** The intermediate **(3)** obtained from the Scheme-6 above was methylated to obtain intermediate **(2)** as given below. Rest of the reaction steps were the same as exemplified for **Example-63**.

**Scheme-8**



**[000257]** To a stirred solution of methyl 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylate (**1** 0.1 g, 0.25 mmol) in DMF(10 mL) was added potassium carbonate (0.07g, 0.51mmol) followed by methyl iodide (0.01 mL, 0.28 mmol) at room temperature and the resulting mixture was allowed to stir under room temperature for 12 h. The progress of the reaction was monitored by TLC. Then reaction mixture was evaporated, and extracted with ethyl acetate (50 mL x 3), dried over sodium sulphate and concentrated under reduced pressure to afford crude compound which was purified by column chromatography (silica gel, 0-20% EtOAc in hexane) to give pale yellow solid (0.05g, 50% yield). MS (ESI): mass calcd. for $C_{24}H_{24}N_4O_2$, 400.48; m/z found, 401.2 $[M+H]^+$.

**R-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-methyl-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone (Example-72)**

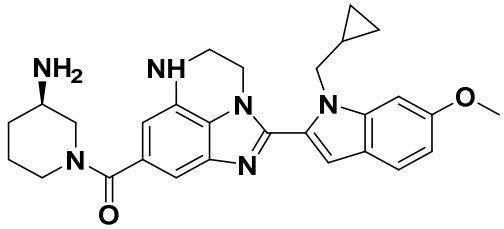


**[000258]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.67 (t , *J* = 8 Hz, 2H), 7.28 (t, *J* = 8 Hz, 1H), 7.13-7.05 (m, 3H), 6.45 ( s, 1H), 4.65 (d, *J* = 8 Hz, 2H), 4.47 ( m, 2H ), 4.12 (m, 2H), 3.46 (m, 2H) 2.96 (s, 4H), 2.80 (m, 2H), 1.99 (m, 2H), 1.66 (m, 1H), 1.46-1.44 (m, 1H) ,1.33-1.18 (m, 3H), 0.31-133 (m, 4H). MS (ESI): mass calcd. for $C_{28}H_{32}N_6O$, 468.61; m/z found, 469.3 $[M+H]^+$.

**[000259]** Following compounds **(Examples 73, 77 and 80)** were synthesized using the procedure as exemplified for **Example-63**.

**Example-73**

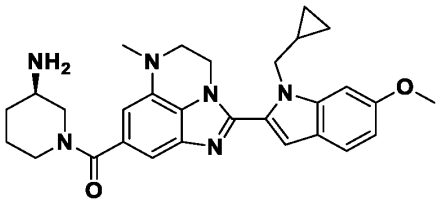
**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-methoxy-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**



**[000260]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.60 (m, 1H), 7.14 (bs, 1H), 6.98 (s, 1H), 6.91 (m, 1H), 6.74 (m, 1H), 6.38 (m, 2H), 4.65 (d, *J* = 8 Hz, 2H), 4.45 (m, 2H), 3.83 (bs, 4H), 2.91 (bs, 1H), 2.53 (m, 3H), 1.88 (m, 2H), 1.64 (m,2H), 1.41 (m, 2H), 1.22-1.17 (m, 3H), 0.21-0.20 (m, 2H), 0.01 (m, 2H). MS (ESI): mass calcd. for $C_{28}H_{32}N_6O_2$, 484.26; m/z found, 485.3 $[M+H]^+$.

**Example-74**

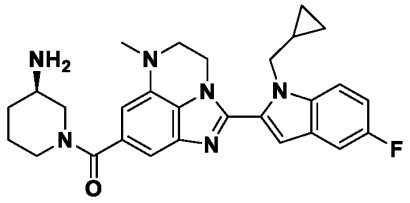
**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-methoxy-1H-indol-2-yl)-6-methyl-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**



**[000261]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.56 (d , *J* = 9.2 Hz, 1H), 7.30 (s, 1H), 7.14 (s, 1H), 7.04 (s, 1H), 6.94-6.91 (m, 1H), 6.75 (s, 1H), 4.65-4.63 (m , 4H), 4.55 (s, 2H), 3.96-3.9 (bs, 2H), 3.79 (s, 3H), 2.95 (s, 3H), 2.79 (d , *J* = 7.2 Hz, 2H), 1.89-1.26 (m, 4H), 0.88-0.84 (m, 1H). 0.33-0.26 (m,4H). MS (ESI): mass calcd. For $C_{28}H_{31}N_5O_3$, 485.5 m/z found, 486.5 $(M+H)^+$.

**Example-75**

**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-6-methyl-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**

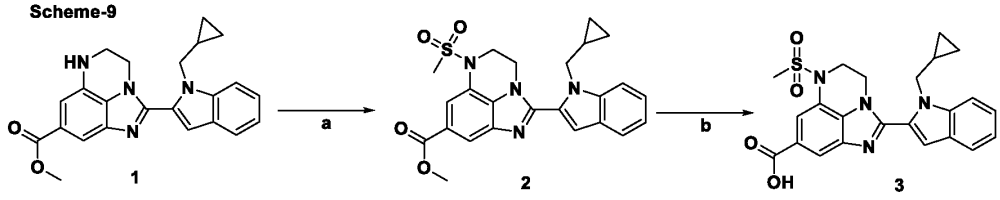


**[000262]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.70 – 7.63 (m, 1H), 7.43 - 7.40 (m, 1H), 7.14 – 7.02 (m, 3H), 6.44 (s, 1H), 4.64 (d, *J* = 6.8 Hz, 2H), 4.58 - 4.56 (m, 2H), 3.45 – 3.44 (m, 2H), 2.96 (s, 3H), 2.89 - 2.79 (bs, 1H), 2.65 (bs, 2H), 2.01 – 1.97 (m, 2H),1.88 - 1.84 (m, 2H), 1.43 -1.37 (m, 2H), 1.35 – 1.26 (m, 2H), 0.87 – 0.84 (bs, 1H), 0.33 – 0.29 (m, 2H), 0.25 - 0.20 (m, 2H). MS (ESI) calculated for $C_{28}H_{31}FN_6O$ *m/z* 486.25 found $(M+H)^+$. 487.3.

**Example-76**

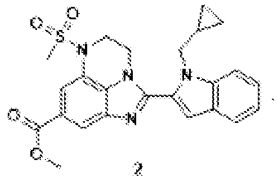
**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(methylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**

Scheme-9




**[000263]** Intermediate **(1)** of the above Scheme-9 was obtained by a similar procedure as exemplified for **Example-63** (Scheme 6).

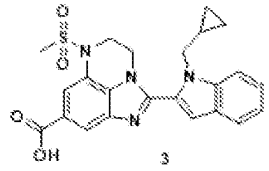
**Step 6: Preparation of methyl 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(methylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylate (2)**



2

**[000264]** To a stirred solution of methyl 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylate (**1,** 0.15 g, 0.39 mmol) in DCM (10 mL) was added pyridine (0.061 g, 0.77 mmol) followed by methanesulfonyl chloride (0.03 ml, 0.39 mmol) at 0° C and the resulting mixture was allowed to stir under room temperature for 1 h. The progress of the reaction was monitored by TLC. Then reaction mixture was evaporated, and extracted with DCM (50 mL x 3), dried over sodium sulphate and concentrated under reduced pressure to give brown solid (0.18 g, crude ). LC-MS m/z calcd for $C_{24}H_{24}N_4O_4S$, 464.5; m/z found, 465.1 $[M+H]^+$.

**Step 7: Preparation of 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(methylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylic acid-(3)**

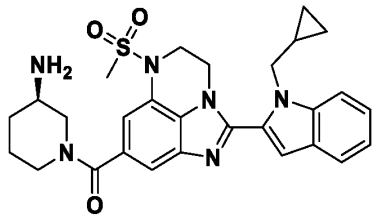


3

**[000265]** To the stirred solution of methyl 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(methylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylate (**2**, 0.18 g, 0.39 mmol) in MeOH (5 mL) and Water (0.5 mL) was added $LiOH.H_2O$ (0.027 g, 0.12 mmol) and stirred at 60°C for 2 h. The reaction mixture was evaporated completely. The resulting crude was dissolved in minimum volume of water and acidified with saturated citric acid solution. Compound was extracted with DCM (30 mL x 2), washed with brine, dried over sodium sulfate and evaporated to give crude product as a pale yellow solid (0.15 g, crude). MS (ESI): Mass calcd. for, $C_{23}H_{22}N_4O_4S$, 450.51; m/z found, 451.1 $[M+H]^+$. Further steps for **Example-76** were carried using the similar procedure as exemplified for **Example-63**.

**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(methylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**

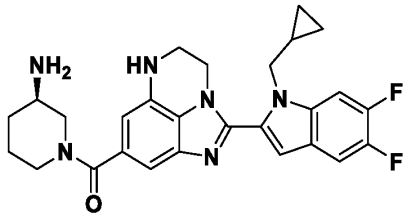
**(Example-76)**



**[000266]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.68 (d , *J* = 6.4 Hz, 2H), 7.52 (s, 1H), 7.31 (d, *J* = 18 Hz, 2H), 7.15 (s, 2H), 4.66 (bs, 4H), 4.12 (s, 2H), 3.60 (bs, 1H), 3.21 (s, 3H), 2.95 (s, 1H), 2.68 (s, 2H), 1.86-1.68 (m, 4H), 1.44 (s, 1H), 1.23 (s, 3H), 0.33-0.27 (m ,4H). MS (ESI): mass calcd. For $C_{28}H_{32}N_6O_3S$ 532.6; m/z found 533 $[M+H]^+$.

**Example-77**

**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5,6-difluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**

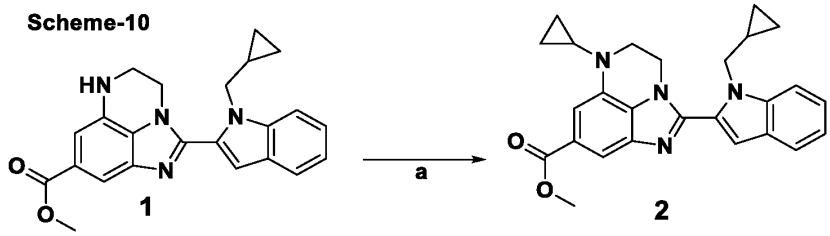


**[000267]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.84 (m, 1H), 7.68-7.63 (m, 1H), 7.08 (s, 1H), 6.97 (s, 1H), 6.42-6.40 (m, 2H), 4.63-4.62 (m, 2H), 4.46 (m, 2H), 3.97 (m, 2H), 3.52 (m, 3H), 2.94 (m, 3H), 1.89 (m, 1H), 1.67 (m, 1H), 1.42-1.34 (m, 2H), 1.22-1.16 (m, 2H), 0.31 (m, 2H), 0.20 (m, 2H). MS (ESI): Mass calcd. for $C_{27}H_{28}F_2N_6O$, 490.23; m/z found, 491.2 $[M+H]^+$.

**Example-78**

**<u>(R)-(3-aminopiperidin-1-yl)(6-cyclopropyl-2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone</u> (Example-78)**

**Scheme-10**

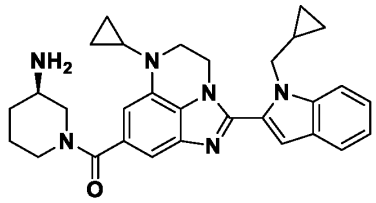



**<u>Step 6: Preparation of methyl 6-cyclopropyl-2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylate (2)</u>**

**[000268]** To a stirred solution of methyl 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylate (**1,** 0.2 g, 0.52 mmol) and cyclopropyl boronic acid (0.088 g, 1.04 mmol) in DCM (10 mL) was added copper (II) acetate (0.164 g, 1.036 mmol) followed by pyridine (0.1 mL, 1.04 mmol) at room temperature and the resulting mixture was allowed to stir under room temperature in the presence of air for 24 h. The progress of the reaction was monitored by TLC. Then reaction mixture was quenched with dilute HCl, extracted with DCM (50 mL x 3), dried over sodium sulphate and concentrated under reduced pressure to afford crude compound. This was purified by column chromatography (silica gel, 0-20% EtOAc in hexane) to give pale yellow solid (0.11g, 50% yield). MS (ESI): Mass calcd. for $C_{26}H_{26}N_4O_2$, 426.2; m/z found, 427 $[M+H]^+$.

**[000269]** Further steps for **Example-78** were carried using the similar procedure as exemplified for **Example-63**.

**(R)-(3-aminopiperidin-1-yl)(6-cyclopropyl-2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone (Example-78)**

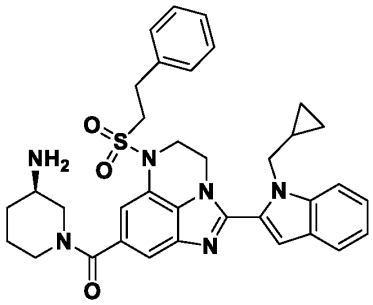



**[000270]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.65 (t , *J* = 6.8 Hz, 2H), 7.26 (t, *J* = 7.6 Hz, 1H), 7.13-7.09 (m, 2H), 7.054 (s, 1H), 6.74 (s, 1H), 4.65 - 4.64 (m, 2H), 4.52 ( m, 2H ), 4.00 (m, 2H), 3.54 (bs, 2H), 2.74 (m, 1H), 2.65 (bs, 2H), 1.88 (m, 2H), 1.69 (bs, 2H), 1.46-1.44 (m, 2H), 1.17 (m, 3H), 0.87- 0.86 (m, 2H), 0.66 (s, 1H), 0.31 - 0.29 (m, 2H), 0.20 - 0.19 (m, 2H). MS (ESI): Mass calcd. for $C_{30}H_{34}N_6O$, 494.64; m/z found, 495.5 $[M+H]^+$.

**[000271]** **Example 79** was synthesized using the above procedure as exemplified for **Example-76**.

**Example 79**

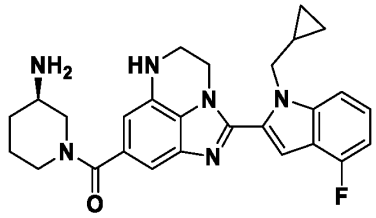
**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(phenethylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**



**[000272]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.67 (d, *J* = 7.2 Hz, 2H), 7.49 (s, 1H), 7.35 (s, 1H), 7.28 (d, *J* = 7.6 Hz, 1H), 7.23-7.20 (m, 4H), 7.17-7.13 (m, 3H), 4.65-4.64 (m, 2H), 4.59-4.57 (m, 2H), 4.14-4.11 (m, 3H), 3.72-3.36 (m, 3H), 3.05 (t, *J* = 8.0 Hz, 2H), 2.95-2.93 (m, 2H), 2.71-2.69 (m, 2H), 1.88-1.85 (m, 1H), 1.66-1.64 (m, 1H), 1.45-1.43 (m, 1H), 1.27-1.22 (m, 3H), 0.31 (d, *J* = 8.0 Hz, 2H), 0.25 (d, *J* = 3.6 Hz, 2H). MS (ESI): Mass calcd. for $C_{35}H_{38}N_6O_3S$ , 622.27; m/z found 623.2 $(M+H)^+$.

**Example-80**

**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-4-fluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**

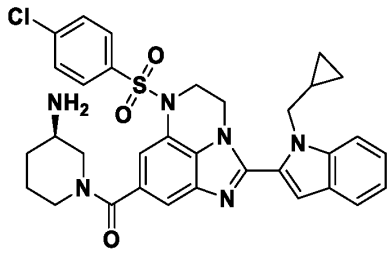


**[000273]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.52 (d , *J* = 8.4 Hz, 1H), 7.27-7.21 (m, 1H), 7.13 (s, 1H), 6.95 (s, 1H), 6.92-6.88 (m, 1H), 6.41-6.38 (m, 2H), 4.66 (d, *J* = 6.8 Hz, 2H), 4.49 (bs, 2H), 4.00 (m, 2H), 3.93 (m, 3H), 2.88 (m, 1H), 2.69 (m, 1H), 1.88 (m, 2H), 1.64 (m, 1H), 1.39 (m, 1H), 1.24-1.17 (m, 3H), 0.32 (d, *J* =7.6 Hz, 2H), 0.21 (m, 2H). MS (ESI): Mass calcd. for $C_{27}H_{29}FN6O$, 472.57; m/z found, 473.2 $[M+H]^+$.

**[000274]** **Examples 81-83** were synthesized using the above procedure as exemplified for **Example-76. Example 84** was synthesized using the above procedure as exemplified for **Example-63.**

**Example-81**

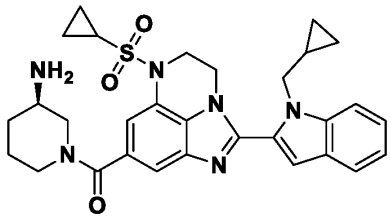
**(R)-(3-aminopiperidin-1-yl)(6-((4-chlorophenyl)sulfonyl)-2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**



**[000275]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.82 (d, *J* = 8.4 Hz, 2H), 7.67 - 7.63 (m, 4H), 7.51 (s, 1H), 7.42 (s, 1H), 7.27 (t , *J* = 7.2 Hz, 1H), 7.12 (t, *J* = 7.6 Hz, 1H), 7.03 (s, 1H), 4.57 (d, *J* = 6.4 Hz, 2H), 4.30 – 4.24 (m, 4H), 3.09 – 2.97 (bs, 2H), 2.74 – 2.65 (m, 1H), 1.88 – 1.86 (m, 2H), 1.70 (bs, 1H), 1.43 - 1.31 (m, 2H), 1.28 – 1.21 (m, 3H), 1.10 (bs, 2H), 0.25 - 0.23 (m, 2H), 0.13 – 0.12 (m, 2H). MS (ESI): mass calcd. for $C_{30}H_{34}N_6O_3S$, 629.18; m/z found, 629.2 $[M+H]^+$ .

**Example-82**

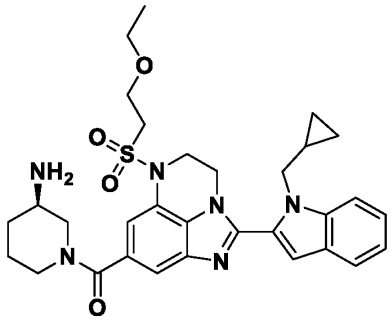
**(R)- (3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(cyclopropylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**



**[000276]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.68 (t , *J* = 7.2 Hz, 2H), 7.53 (s, 1H), 7.35 (s, 1H), 7.29 (t, *J* = 7.2 Hz, 1H), 7.16 - 7.12 (m, 2H), 4.67 - 4.63 (m, 4H), 4.12 (bs, 2H), 2.96 – 2.87 (bs, 2H), 2.73 – 2.65 (m, 3H), 1.89 (m, 2H), 1.67 (bs, 1H), 1.43 - 1.31 (m, 1H), 1.28 – 1.22 (m, 4H), 1.03 – 1.01 (m, 4H), 0.33 - 0.31 (m, 2H), 0.26 (bs, 2H). MS (ESI): mass calcd. for $C_{30}H_{34}N_6O_3S$, 558.7; m/z found, 559.2 $[M+H]^+$.

**Example-83**

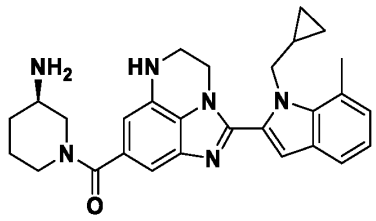
**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-((2-ethoxyethyl)sulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**



**[000277]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.68 (d, *J* = 7.2 Hz, 2H), 7.49 (s, 1H), 7.33-7.27 (m, 2H), 7.15-7.10 (m, 2H), 4.68-4.65 (m, 2H), 4.60-4.58 (m, 2H), 4.14-4.11 (m, 3H), 3.67-3.65 (m, 3H), 3.62-3.60 (m, 2H), 3.12-3.10 (m, 1H), 2.91-2.89 (m, 3H), 2.71-2.69 (m, 2H), 1.88-1.85 (m, 2H), 1.66-1.64 (m, 2H), 1.45-1.43 (m, 1H), 1.27-1.22 (m, 3H), 0.70-0.67 (m, 1H), 0.32(d, *J* = 6.8 Hz, 2H), 0.23 (d, *J* = 3.6 Hz, 2H). MS (ESI): mass calcd. for $C_{31}H_{38}N_6O_4S$, 590.27; *m/z* found, 591.3 $(M+H)^+$.

**Example-84**

**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-methyl-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**

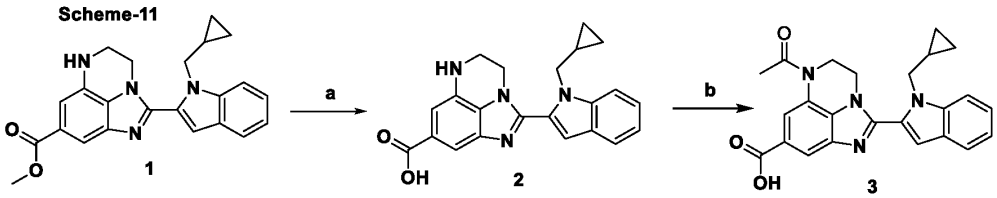


**[000278]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.56 (m, 1H), 7.08 (m, 3H), 6.97 (s, 1H), 6.45 (m, 2H), 4.89 (d, *J* = 8 Hz, 2H), 4.46 (m, 2H), 4.00 (m, 2H), 3.57 (bs, 2H), 2.83 (s, 3H), 2.70 (m, 2H), 1.93 (m, 2H), 1.80 (m, 2H), 1.30 (m,1H), 1.26 (m,1H), 0.98 (m, 2H), 0.24 (d, *J* =12 Hz, 2H), 0.19 (m, 2H). MS (ESI): mass calcd. for $C_{28}H_{32}N_6O$, 468.61; m/z found, 469.1 $[M+H]^+$.

**Example-85**

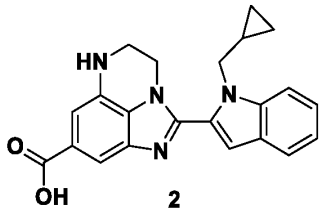
**(R)-1-(8-(3-aminopiperidine-1-carbonyl)-2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-4,5-dihydro-6H-imidazo[1,5,4-de]quinoxalin-6-yl)ethan-1-one**

Scheme-11



**[000279]** Intermediate **(1)** of the above Scheme-11 was obtained by a similar procedure as exemplified for **Example-63** (Scheme 6).

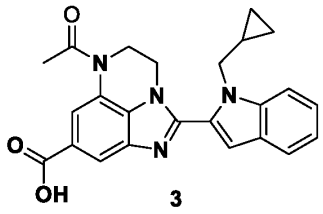
**Step 6: Preparation of 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylic acid-(2)**




2

**[000280]** To the stirred solution of methyl methyl 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylate (**1**, 0.09 g, 0.21 mmol) in MeOH (5 mL) and water (0.5 mL) was added LiOH.$H_2O$ (0.044 g, 1.05 mmol) and stirred at room temperature for 12 h. The reaction mixture was evaporated completely. The resulting crude was dissolved in minimum volume of water and acidified with saturated citric acid solution. Compound was extracted with DCM (30 mL x 2), washed with brine, dried over sodium sulfate and evaporated to give the crude product as a pale yellow solid (0.07 g, crude). MS (ESI): Mass calcd. for $C_{22}H_{20}N_4O_2$, 372.43; m/z found, 373.0 $[M+H]^+$.

**Step 7: Preparation of 6-acetyl-2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylic acid (3)**



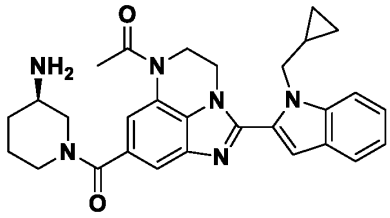

3

**[000281]** To a stirred solution of 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylic acid (0.07 g, 0.19 mmol) in DCM (10 mL) was added pyridine (0.03 mL, 0.37 mmol) followed by acetyl chloride (0.02 mL, 0.28 mmol) at 0°C and the resulting mixture was stirred at room temperature for 1 h. The progress of the reaction was monitored by TLC. The reaction mixture was evaporated, extracted with DCM (50 mL x 3), dried over sodium sulphate and concentrated under reduced pressure to give the brown solid (0.059 g, 76 % ). LC-MS m/z calcd for $C_{24}H_{22}N_4O_3$, 414.4, found 415.1 $[M+H]^+$.

**[000282]** The remaining steps for preparing **Example-85** were carried using the similar procedure as exemplified for **Example-63**.

**Example-85**

**(R)-1-(8-(3-aminopiperidine-1-carbonyl)-2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-4,5-dihydro-6H-imidazo[1,5,4-de]quinoxalin-6-yl)ethan-1-one**

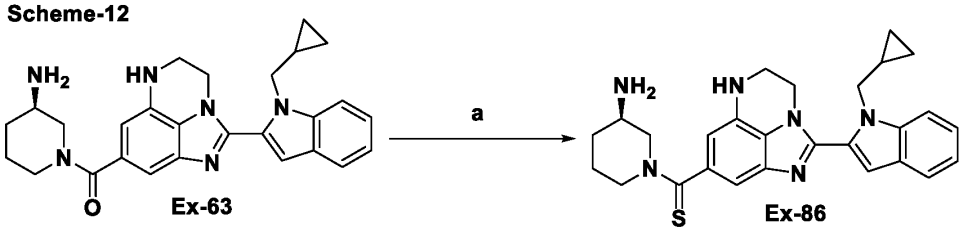


**[000283]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.90 (s,1H), 7.68 (t, *J* = 7.6 Hz, 2H), 7.53 (s, 1H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.13 (t, *J* = 6.8 Hz, 2H), 6.00 (bs, 2H), 4.67-4.58 (m, 4H), 4.17 (s, 3H), 3.00 (bs, 3H), 2.40 (s, 3H), 1.96 (s, 1H), 1.70 (s, 1H), 1.46 (s, 2H), 1.22 (s, 2H), 0.34-0.26 (m,4H). MS (ESI): Mass calcd. for $C_{29}H_{32}N_6O_2$, 496.6; m/z found, 497.3 $[M+H]^+$.

**Example-86**

**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanethione**

**Scheme-12**

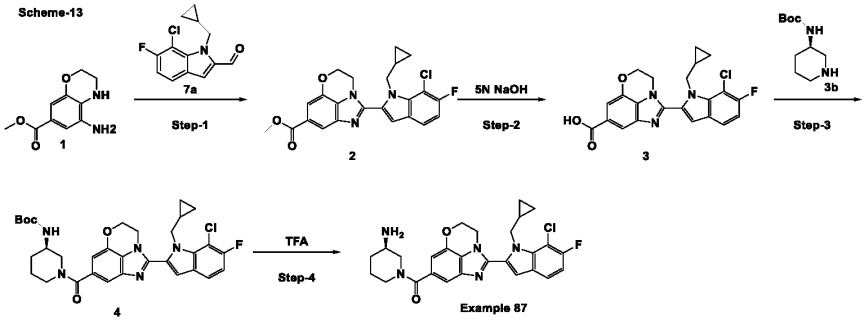



**[000284]** To the stirred solution (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone (**Example-63**, 0.07g, 0.15 mmol) in Toluene (50 mL), was added Lawessons reagent (0.12 g, 0.39 mmol) at room temperature. The reaction mixture was reflux at bath temperature of 100°C for 12 h. The reaction mixture was diluted with $NaHCO_3$ (50 mL x 2) and extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using 15-100% ethyl acetate in hexane to afford (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-

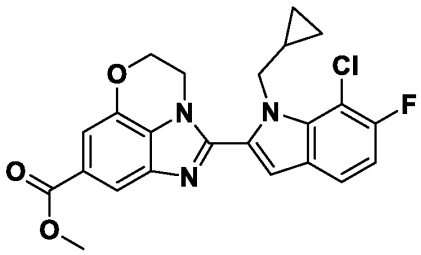
yl)methanethionen as yellow colour solid (0.007 g, 10% Yield). $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 8.06 (m, 1H), 7.79 (m, 1H), 7.67 (t, *J* = 8 Hz, 2H), 7.28 (t, *J* = 12 Hz, 1H), 7.28-7.03 (m, 2H), 6.39 (m, 1H), 5.12 (m, 1H), 4.63 (m, 2H), 4.47 (bs, 2H), 3.79 (bs, 1H), 3.48 (bs, 2H), 2.04-1.97 (m, 3H), 1.72-1.61 (m, 4H), 1.44 (m, 2H), 0.83 (s, 1H), 0.32-0.31 (d. *J* = 4 Hz, 2H), 0.21 (m, 2H). MS (ESI): Mass calcd. for $C_{27}H_{30}N_6S$, 470.64; m/z found 471.2$[M+H]^+$.

**Example-87**

**Synthesis of (R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



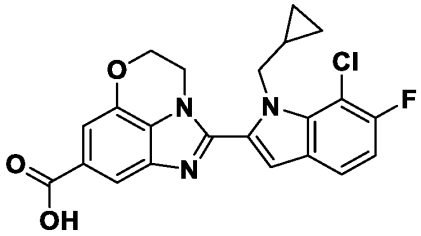

**Step-1: Synthesis of methyl-2-(7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylate (2)**



**[000285]** To a stirred solution of methyl-5-amino-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (**1**, 0.33 g, 1.31 mmol) and 7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indole-2-carbaldehyde (**7a**, 0.27 g, 1.31 mmol) in *N*, *N*-dimethylformamide (10.0 mL) and water (3.0 mL), potassium peroxomonosulfate (Oxone, 0.484 g, 1.57 mmol) was added at room temperature. The reaction mixture was stirred at room temperature for 16 h. After completion of reaction, the reaction mixture was cooled to room temperature, water was added. Precipitated solid was filtered and washed with water (20 mL × 2) and methanol (10 mL × 2). The compound obtained was dried under vacuum to afford methyl-2-(7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-

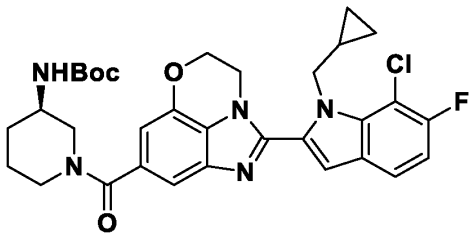
indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylate (**2**) as yellow solid. Yield: 0.12 g (22%). MS (ESI) 439.11; *m/z* found 440.28 $[M+H]^{+1}$.

**Step-2: Synthesis of 2-(7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid (3)**




**[000286]** To a stirred solution of methyl-2-(7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylate (**2**, 0.12 g, 0.29 mmol) in tetrahydrofuran (5.0 mL) and methanol (3.0 mL), 5N sodium hydroxide solution (3.0 mL) was added and reaction mixture was stirred at 60 °C for 2 h. After completion of reaction, the reaction mixture was concentrated under reduced pressure. The resulting crude was dissolved in minimum volume of water and acidified with saturated citric acid solution at 0 °C up to pH 2~3. The precipitated solid was filtered, washed with water (10 mL × 2). The compound obtained was dried under vacuum to afford 2-(7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid (**3**) as white solid. Yield: 0.11 g (89%). MS (ESI) 425.09; *m/z* found 424.13 $[M-H]^{-1}$.

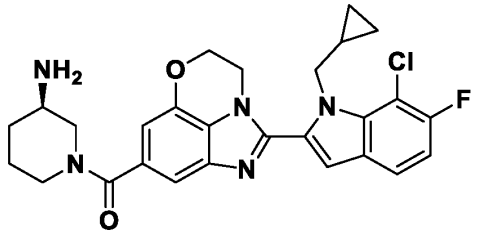
**Step-3: Synthesis of tert-butyl (R)-(1-(2-(7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (4)**




**[000287]** To a stirred solution of 2-(7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid (**3**, 0.11 g, 0.25 mmol) in dichloromethane (10.0 mL), *tert*-butyl-(*R*)-piperidin-3-ylcarbamate (**3b**, 0.06 g, 0.31 mmol) and triethylamine (0.11 mL, 0.83 mmol) were added, followed by

addition of propylphosphonic anhydride (50% solution in ethyl acetate, 0.25 mL, 0.86 mmol). The reaction mixture was stirred at room temperature for 2 h. After completion of reaction, the reaction mixture was diluted with water and extracted with dichloromethane (10 mL × 2). The combined organic layers were washed with water and brine solution, further dried over anhydrous sodium sulfate, filtered and concentrated to get crude product. The crude was purified by CombiFlash using 4.0 g, RediSep column and 70% ethyl acetate in hexane as eluent to afford tert-butyl (R)-(1-(2-(7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (**4**) as yellow solid. Yield: 0.07 g (45%). MS (ESI) 607.24; *m/z* found 608.32 $[M+1]^{+1}$.

**Step-4: Synthesis of (R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone (Example-87)**

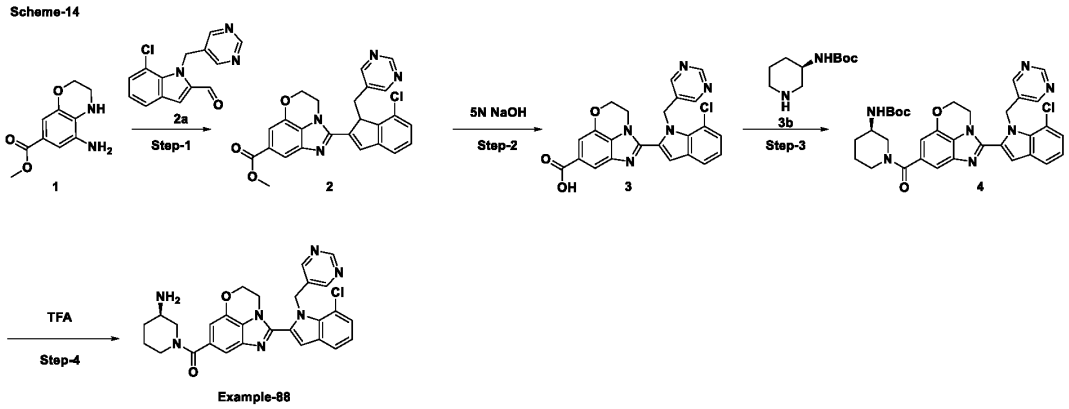



**[000288]** To a stirred solution of tert-butyl (R)-(1-(2-(7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (**4**, 0.07 g, 0.11 mmol) in dichloromethane (5.0 mL), trifluoroacetic acid (1.0 mL) was added at 0 °C and stirred at room temperature for 2 h. After completion of reaction, the reaction mixture was concentrated completely, basified by saturated sodium bicarbonate solution (10 mL). The compound was extracted with dichloromethane (10 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated to afford (R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone, as white solid. Yield: 0.042 g (72%).

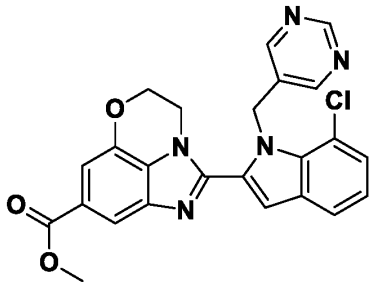
**[000289]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.74-7.70 (m, 1H), 7.31 (s, 1H), 7.28 (s, 1H), 7.24 (t, *J* = 9.16 Hz, 1H), 6.78 (s, 1H), 5.06 (d, *J* = 6.8 Hz, 2H), 4.60-4.58 (m, 4H), 4.17(bs, 1H), 3.60 (bs, 1H), 2.90 (bs, 2H), 2.64 (m, 1H), 1.86-1.83 (m, 1H), 1.64 (bs, 2H), 1.43 (m, 1H), 1.23-1.12 (m, 3H), 0.28 (d, *J* = 7.68 Hz, 2H), 0.06 (d, *J* = 4.36 Hz, 2H). MS (ESI): 507.18; found *m/z* 508.36 $[M+H]^+$.

**Example-88**

**Synthesis of (R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(pyrimidin-5-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**

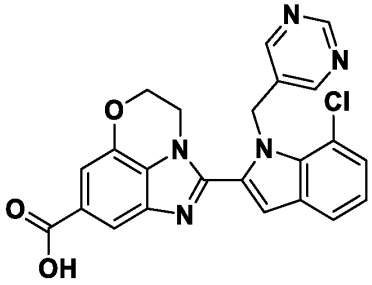



**Step-1: Synthesis of methyl-2-(7-chloro-1-(pyrimidin-5-ylmethyl)-1H-inden-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylate (2)**



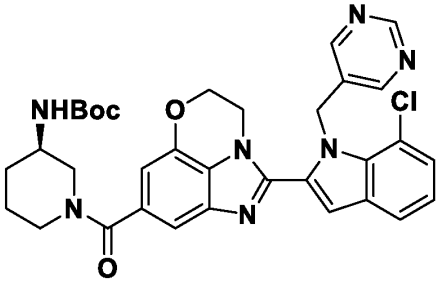
**[000290]** To a stirred solution of methyl-5-amino-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (**1**, 0.200 g, 0.96 mmol) and 7-chloro-1-(pyrimidin-5-ylmethyl)-1H-indole-2-carbaldehyde (**2a**, 0.260 g, 1.05 mmol) in *N,N*-dimethylformamide (5.0 mL) and water (1.5 mL), potassium peroxomonosulfate (Oxone, 0.175g, 1.15 mmol) was added at room temperature. The reaction mixture was stirred at room temperature for 16 h. After completion of reaction, the reaction mixture was cooled to room temperature, water was added. Precipitated solid was filtered and washed with water (10 mL × 2) and methanol (5 mL × 2). The compound obtained was dried under vacuum to afford methyl 2-(7-chloro-1-(pyrimidin-5-ylmethyl)-1H-inden-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylate (**2**) as yellow solid. Yield: 0.30 g (crude). MS (ESI) 458.90; *m/z* found 459.80 $[M+H]^{+1}$.

**Step-2: Synthesis of 2-(7-chloro-1-(pyrimidin-5-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid (3)**



**[000291]** To a stirred solution of methyl-2-(7-chloro-1-(pyrimidin-5-ylmethyl)-1H-inden-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylate (**2**, 0.30 g, 0.65 mmol) in tetrahydrofuran (5.0 mL) and methanol (3.0 mL), 5N sodium hydroxide solution 3.0 mL) was added and reaction mixture was stirred at 60 °C for 2 h. After completion of reaction, the reaction mixture was concentrated under reduced pressure completely. The resulting crude was dissolved in minimum volume of water and acidified with saturated citric acid solution at 0 °C up to pH 2~3. The precipitated solid was filtered, washed with water (10 mL × 2). The compound obtained was dried under vacuum to afford 2-(7-chloro-1-(pyrimidin-5-ylmethyl)-1H-indol-2-yl)-3, 4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid (**3**) as white solid. Yield: 0.250 g (Crude). MS (ESI) 445.86; *m/z* found 446.89 $[M+H]^{+1}$.

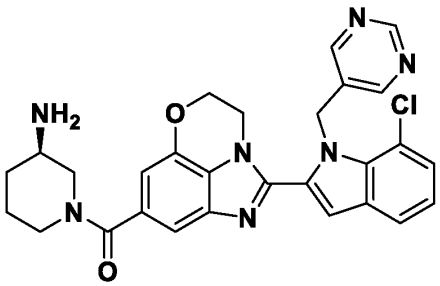
**Step-3: Synthesis of tert-butyl (R)-(1-(2-(7-chloro-1-(pyrimidin-5-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (4)**



**[000292]** To a stirred solution of 2-(7-chloro-1-(pyrimidin-5-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid (**3**, 0.25 g, 0.56 mmol) in dichloromethane (10.0 mL), *tert*-butyl-(*R*)-piperidin-3-ylcarbamate (**3b**, 0.134 g, 0.67 mmol) and triethylamine (0.2 mL, 1.74 mmol) were added, followed by addition of propylphosphonic anhydride (50% solution in ethyl acetate, 0.5 mL, 1.96 mmol). The

reaction mixture was stirred at room temperature for 2 h. After completion of reaction, the reaction mixture was diluted with water and extracted with dichloromethane (10 mL × 2). The combined organic layers were washed with water, brine solution and dried over anhydrous sodium sulfate. The organic layer was filtered and concentrated to get crude product. The crude was purified by CombiFlash using 12.0 g, RediSep column and 70% ethyl acetate in hexane as eluent to afford tert-butyl (R)-(1-(2-(7-chloro-1-(pyrimidin-5-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (**4**) as white solid. Yield: 0.10 g (30%). MS (ESI) 628.13; *m/z* found 629.35 $[M+1]^+$.

**Step-4: Synthesis of (R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(pyrimidin-5-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone (Example-88)**



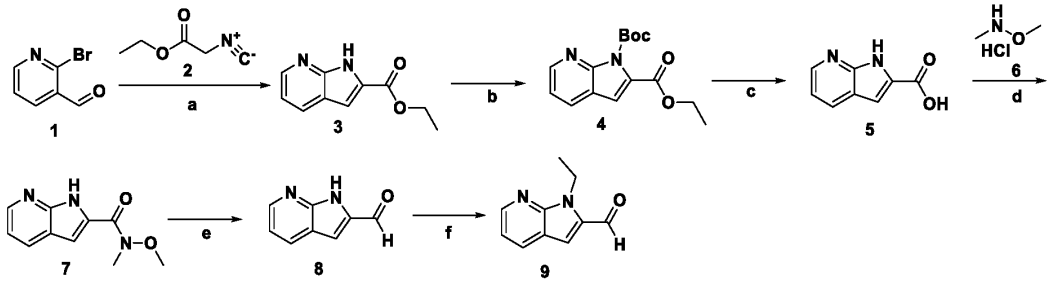

**[000293]** To a stirred solution tert-butyl (R)-(1-(2-(7-chloro-1-(pyrimidin-5-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (**4**, 0.1 g, 0.15 mmol) in dichloromethane (5.0 mL), trifluoroacetic acid (1.0 mL) was added at 0 °C and stirred at room temperature for 2 h. After completion of reaction, the reaction mixture was concentrated. The reaction mixture was basified by saturated sodium bicarbonate solution (5.0 mL). The compound was extracted with dichloromethane (10 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under vacuum to afford (R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(pyrimidin-5-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone, as off white solid. Yield: 0.025 g (30%).

**[000294]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 9.03 (s, 1H), 8.40 (s, 2H), 7.76 (d, *J* = 7.84 Hz, 1H), 7.45 (s, 1H), 7.31 (d, *J* = 7.52 Hz, 1H), 7.23 (s, 1H), 7.16 (t, *J* = 7.76 Hz, 1H), 6.76 (s, 1H), 6.44 (s, 2H), 4.70 (d, *J* = 4.28 Hz, 2H), 4.57 (d, *J* = 4.24 Hz, 2H), 4.14 (s, 1H), 3.58 (s, 1H), 2.89 (bs, 1H), 2.69-2.66 (m, 1H), 2.17-1.89 (m, 2H), 1.84

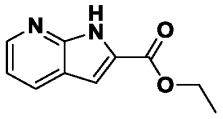
(d, *J* = 11.6 Hz, 1H), 1.63 (bs, 1H), 1.41 (m, 1H), 1.22 (m, 2H). MS (ESI): 528.01; found *m/z* 528.42 $[M+H]^+$.

## SYNTHESIS OF INTERMEDIATES

**Synthesis of 1-ethyl-1H-pyrrolo[2,3-b]pyridine-2-carbaldehyde (Intermediate for Example-5):**



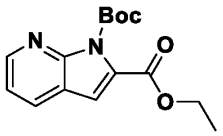

**Step-1: Ethyl 1H-pyrrolo[2,3-b]pyridine-2-carboxylate (3)**



**3**

**[000295]** To the stirred solution of 2-bromonicotinaldehyde (**1**, 10.0 g, 53.7 mmol) in DMSO (100 mL), was added $Cs_2CO_3$ (35.0 g, 107 mmol), CuI (1.05 g, 5.37 mmol) followed by ethyl-2- isocyanoacetate (**2**, 7.9 mL, 69.8 mmol) and stirred at 80°C for 16h (reaction condition **a**). The reaction mixture was cooled to room temperature and filtered through celite. To this added water (100 mL) and compound was extracted with EtOAc (200 mL). Organic layer was dried over anhydrous $Na_2SO_4$ and evaporated under vacuum. Crude was purified by column chromatography using 30-50% EtOAc in Hexane to afford the product as brown gum. (Yield: 45%, 4.5 g). MS (ESI): mass calcd. for $C_{10}H_{10}N_2O_2$, 190.20; *m/z* found 191.0 $(M+H)^+$.

**Step-2: 1-(Tert-butyl) 2-ethyl 1H-pyrrolo[2,3-b]pyridine-1,2-dicarboxylate (4)**

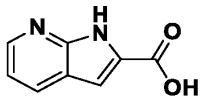


**4**

**[000296]** To the stirred solution of ethyl 1H-pyrrolo[2,3-b]pyridine-2-carboxylate (**3**, 34.5 g, 23.6 mmol) in THF (50 mL), was added triethylamine (6.5 mL, 47.3 mmol)

followed by Boc anhydride (3.6 g, 35.5 mmol) and stirred at room temperature for 16 h (reaction condition **b**). To the reaction mixture was added water (100 mL) and extracted with EtOAc (200 mL). Organic layer was dried over anhydrous $Na_2SO_4$ and evaporated under vacuum. Crude was purified by column chromatography using silica gel and eluent 20-30% EtOAc in hexane to afford the product as brown gum. (Yield: 81%, 5.5 g). MS (ESI): mass calcd. for $C_{15}H_{18}N_2O_4$ , 290.32; *m/z* found, 291.1 $(M+H)^+$.

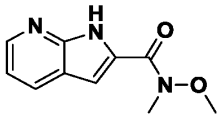
**Step-3: 1H-pyrrolo[2,3-b]pyridine-2-carboxylic acid (5)**



**5**

**[000297]** To a stirred solution 1-(tert-butyl) 2-ethyl 1H-pyrrolo[2,3-b]pyridine-1,2-dicarboxylate (**4**, 5.5 g, 18.9 mmol) in THF (40 mL), LiOH (3.9 g, 94.8 mmol) in water (10 mL) and stirred at room temperature for 4h. The reaction mixture was evaporated and dissolved in minimum amount of water. To this, added saturated citric acid solution till acidic and precipitate formed was collected by filtration, dried to afford the product as white solid. (Yield: 81%, 2.5 g). MS (ESI): mass calcd. for $C_8H_6N_2O_2$, 162.04; *m/z* found, 163.1 $(M+H)^+$.

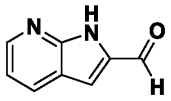
**Step-4: N-methoxy-N-methyl-1H-pyrrolo[2,3-b]pyridine-2-carboxamide (7)**



**7**

**[000298]** To the stirred solution of 1H-pyrrolo[2,3-b]pyridine-2-carboxylic acid (**5**, 2.5 g, 15.4 mmol) and N,O-dimethylhydroxylamine hydrochloride (**6**, 1.8 g, 18.5 mmol in DCM (50 mL), was added triethylamine (10.6 mL, 77.1 mmol), HOBt (3.54 g, 23.14 mmol) followed by EDC.HCl (4.42 g, 23.18 mmol) at 0°C and the reaction mixture was stirred at room temperature for 16h. The reaction mixture was cooled to room temperature, filtered through celite and evaporated the filtrate. To the crude, added water (10 mL) and compound was extracted with DCM (30mL). Organic layer was dried over sodium sulfate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using silica gel and eluent 2-4% MeOH in DCM to afford the product as off white solid. (Yield: 82%, 2.6 g). MS (ESI): mass calcd. for $C_{10}H_{11}N_3O_2$, 205.09; *m/z* found, 206.1 $(M+H)^+$.

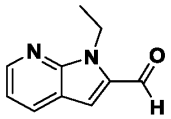
**Step-5: 1H-pyrrolo[2,3-b]pyridine-2-carbaldehyde (8)**



8

**[000299]** To a stirred solution N-methoxy-N-methyl-1H-pyrrolo[2,3-b]pyridine-2-carboxamide (**7**, 0.5 g, 2.43 mmol) in THF (10 mL), was added 1M LAH in THF (3.6 mL, 3.65 mmol) at -78°C and the reaction mixture was stirred at same temperature for 3 h. The reaction mixture was basified using saturated $Na_2CO_3$ solution and extracted with DCM (2 X 25mL). The reaction was quenched with saturated $NH_4Cl$ (10 mL) solution and compound was extracted with EtOAc (50 mL). The organic layer was dried over anhydrous $Na_2SO_4$. Crude was purified by flash column chromatography using 25-30% EtOAc in hexane to get the compound as white solid. (Yield: 85%, 0.3g). MS (ESI): mass calcd. for $C_8H_6N_2O$, 146.15; *m/z* found, 147.1 $(M+H)^+$.

**Step-6: 1-ethyl-1H-pyrrolo[2,3-b]pyridine-2-carbaldehyde (9)**

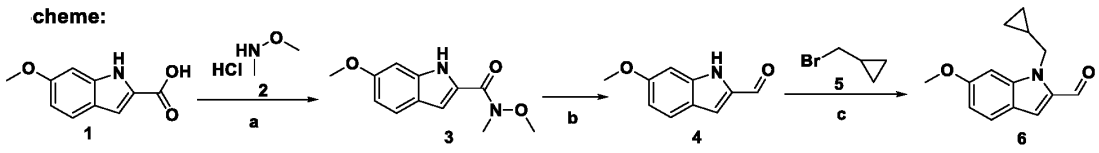


9

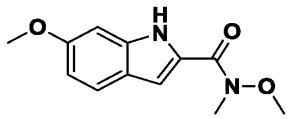
**[000300]** To a stirred solution 1H-pyrrolo[2,3-b]pyridine-2-carbaldehyde (**8**, 0.3 g, 2.19 mmol) in DMF (10 mL), was added $K_2CO_3$ (0.91 g, 6.57 mmol) followed by ethyl iodide (0.5 g, 3.28 mmol) and the reaction mixture was stirred at same temperature for 16 h. To the reaction mixture was added water (15 mL) and extracted with EtOAc (50 mL). The organic layer was dried over anhydrous $Na_2SO_4$. Crude was purified by flash column chromatography using 15-20% EtOAc in hexane to get the compound as colourless oil. (Yield: 95%, 0.34 g). $^1$HNMR (400 MHz, DMSO-$d_6$) δ, ppm: 9.94 (s, 1H), 8.52 (d, $J$ = 4.0 Hz, 1H), 8.23 (d, $J$ = 8.0 Hz, 1H), 7.49 (s, 1H), 7.23 (t, $J$ = 5.2 Hz, 1H), 4.65-4.60 (m, 2H), 1.27 (t, $J$ = 6.4 Hz, 3H). MS (ESI): mass calcd. for $C_{10}H_{10}N_2O$, 174.08; *m/z* found, 175.2 $(M+H)^+$.

**Synthesis of 1-(cyclopropylmethyl)-6-methoxy-1H-indole-2-carbaldehyde (Intermediate for Example-74):**

cheme:



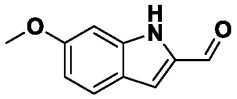
**Step-1: Preparation of N,6-dimethoxy-N-methyl-1H-indole-2-carboxamide (3)**



**3**

**[000301]** To a stirred solution 6-methoxy-1H-indole-2-carboxylic acid (**1**, 3 g, 15.69 mmol) in DCM (20 mL), was added N,O-dimethylhydroxylamine hydrochloride (**2**, 3 g, 31.38 mmol), followed by hydroxybenzotriazole (3.6 g, 23.5 mmol), *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (4.5 g, 23.5 mmol) and TEA (11.3 mL, 120.7 mmol), and the reaction mixture was stirred at same temperature for 5 h. The reaction mixture was quenched with water, extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate, filtered and evaporated to get crude product. Crude residue was purified by gradient column chromatography using 25-30% ethyl acetate in hexane to get the product as beige colour solid. (Yield: 75%, 0.86 g). MS (ESI): mass calcd. for $C_{12}H_{14}N_2O_3$, 234.10; *m/z* found, 235 $(M+H)^+$.

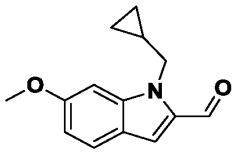
**Step-2: Preparation of 6-methoxy-1H-indole-2-carbaldehyde (4)**



**4**

**[000302]** To a stirred solution of N,6-dimethoxy-N-methyl-1H-indole-2-carboxamide (**3**, 2 g, 8.54 mmol) in THF (20 mL), was added LAH 1M soln. in THF (12.8 mL, 12.75 mmol) slowly under cooling condition, and then the reaction mixture was allowed to stir at room temperature for 1h. The reaction mixture was quenched with ammonium chloride, extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate, filtered and evaporated to get crude product. Crude residue was purified by gradient column chromatography using 5-10% ethyl acetate in hexane to get the product as white solid. (Yield: 60%, 0.9 g). MS (ESI): mass calcd. for $C_{10}H_9NO_2$, 175.06; *m/z* found, 176.1 $(M+H)^+$.

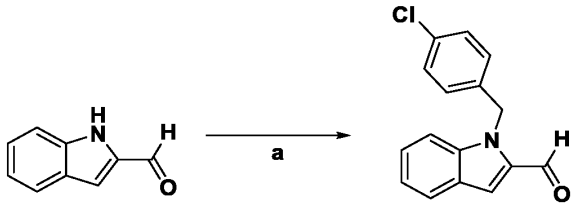
**Step-3:Preparation of 1-(cyclopropylmethyl)-6-methoxy-1H-indole-2-carbaldehyde (6)**



6

**[000303]** To a stirred solution of 6-methoxy-1H-indole-2-carbaldehyde (**4**, 0.28 g, 1.6 mmol) in DMF (5 mL), was added potassium carbonate (1.1 g, 8 mmol) followed by (bromomethyl)cyclopropane (**5**, 0.23 mL, 1.72 mmol) and the reaction mixture was stirred at same temperature for 4h. The reaction mixture was quenched with water, extracted with ethyl acetate (20 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate, filtered and evaporated to get crude product. Crude residue was purified by gradient column chromatography using 5-10% ethyl acetate in hexane to get the product as brown liquid. (Yield: 63%, 0.23 g). $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 9.72 (s, 1H), 7.62 (d, *J* = 8 Hz, 1H), 7.3 (s, 1H), 7.07 (s, 1H), 6.78 (d, *J* = 8 Hz, 1H), 4.43 (d, *J* = 8 Hz, 2H), 3.84 (s, 3H), 1.26-1.21 (m, 1H), 0.40-0.38 (m, 4H). MS (ESI): mass calcd. for $C_{14}H_{15}NO_2$, 229.1; *m/z* found, 230.2 $(M+H)^+$.

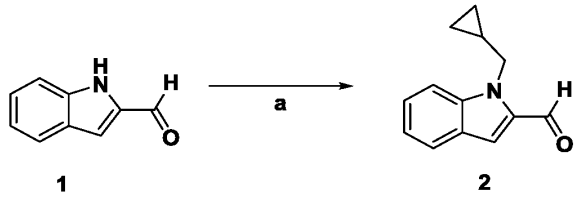
**Synthesis of 1-(4-chlorobenzyl)-1H-indole-2-carbaldehyde (Intermediate for Example-13)**



1 2

**[000304]** To a stirred solution 1H-indole-2-carbaldehyde (**1**, 0.5 g, 3.44 mmol) in DMF (10 mL), was added potassium carbonate (1.42 g, 10.3 mmol) followed by 1-(bromomethyl)-4-chlorobenzene (0.84 g, 4.13 mmol) and the reaction mixture was stirred at same temperature for 4 h. The reaction mixture was quenched with water, extracted with ethyl acetate (30 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate, filtered and evaporated to get crude product. Crude residue was purified by gradient column chromatography using 10-15% ethyl acetate in hexane to get the product as half white solid. (Yield: 93.4%, 0.86 g). $^1$HNMR (400 MHz, DMSO $d_6$) δ(ppm): 9.9 (s, 1H), 7.79 (d, *J* = 8 Hz, 1H), 7.60-7.56 (m, 2H), 7.39-7.36 (m, 1H), 7.31 (d, *J* = 8 Hz, 2H), 7.18-7.14 (m, 1H), 7.06 (d, *J* = 8 Hz, 2H), 5.8 (s, 2H). MS (ESI): mass calcd. for $C_{16}H_{12}ClNO$, 269.73; *m/z* found, 270.1 $(M+H)^+$.

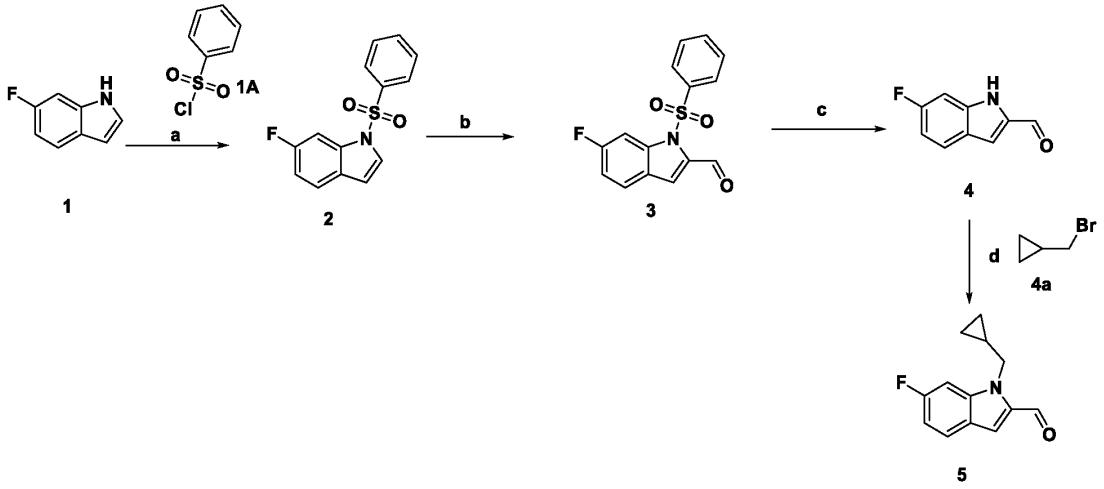
**Synthesis of 1-(cyclopropylmethyl)-1H-indole-2-carbaldehyde (Intermediate for Examples-1, 2, 4, 6, 7, 38, 62, 72, 76, 78, 79, 85 and 86)**




1 2

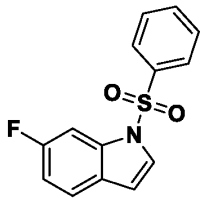
**[000305]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 1 g, 6.89 mmol) in DMF (20 mL), were added potassium carbonate (2.8 g, 20.67 mmol) and (bromomethyl)cyclopropane (0.68 mL, 7.58 mmol) at room temperature. The reaction mixture was stirred at room temperature for 12 h. The reaction mixture was diluted with water and extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using 3-7% ethyl acetate in hexane to afford the 1-(cyclopropylmethyl)-1H-indole-2-carbaldehyde as yellow solid (1 g, 76% Yield). $^1$HNMR (400 MHz, DMSO $d_6$) δ(ppm): 9.88 (s, 1H), 7.75 (d, $J$ = 8 Hz, 1H), 7.64 (d, $J$ = 8 Hz, 1H), 7.46 (s, 1H), 7.41-7.37 (m, 1H), 7.16-7.12 (m, 1H), 4.45 (d, $J$ = 8 Hz, 2H), 1.24-1.14 (m, 1H), 0.39-0.35 (m, 4H). MS (ESI): mass calcd. for $C_{13}H_{13}NO$, 199.1; *m/z* found, 200.1 $(M+H)^+$.

**Synthesisof1-(cyclopropylmethyl)-6-fluoro-1H-indole-2-carbaldehyde (Intermediate for Example-65)**




1 2 3

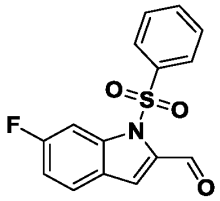
**Step 1: Preparation of 6-fluoro-1-(phenylsulfonyl)-1H-indole (2)**



2

**[000306]** To a solution of sodium hydride (0.88 g, 22.2 mmol) in DMF (50 mL) was added solution of 6-fluoro-1H-indole (**1**, 3.0 g, 22.2 mmol) in DMF at 0°C, dropwise over 15 min. Benzenesulfonyl chloride in DMF (2.86 mL, 22.2 mmol) was added at 0°C and stirred for 2 h at room temperature under $N_2$ atmosphere. To the reaction mixture was added ice cold water (50 mL), then filtered off the precipitate and washed with ice cold water to obtain white solid. (6.0 g, yield 98.19 %).

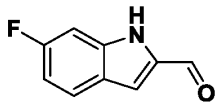
**Step 2: preparation 6-fluoro-1-(phenylsulfonyl)-1H-indole-2-carbaldehyde (3)**



3

**[000307]** To a solution of 6-fluoro-1-(phenylsulfonyl)-1H-indole (**2**, 6.0 g, 22.0 mmol) in dry THF (60 mL) was added lithium diisopropylamide 2M in THF (10.9 mL g, 22.0 mmol) at -78 °C and stirred for 5-8 min, followed by addition of dry DMF (2.5 mL, 33.0 mmol) at -78 °C and stirred for 10 min at -78 °C under $N_2$ atmosphere. To the reaction mixture was added aqueous ammonium chloride (20 mL), then extracted in to EtOAc. Organic layer was washed with saturated $NH_4Cl$ solution and brine, dried over sodium sulphate, filtered and concentrated under reduced pressure to obtain yellow solid (6.0 g, yield 90.90%). MS (ESI): *m/z* 304.2 $(M+H)^+$.

**Step 3: Preparation of 6-fluoro-1-(phenylsulfonyl)-1H-indole-2-carbaldehyde (4)**

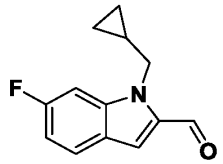


4

**[000308]** To the stirred solution of 6-Difluoro-1-(phenylsulfonyl)-1H-indole-2-carbaldehyde (**3**,1g, 3.3 mmol) in THF (50 mL), was added TBAF (1M in THF) (9.15 mL, 16.5mmol) at room temperature. The reaction mixture was stirred at room

temperature for 12 h. The reaction mixture was diluted with water and extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using 15-25% ethyl acetate in hexane to afford 6-fluoro-1-(phenylsulfonyl)-1H-indole-2-carbaldehyde as sticky solid (0.45 g, 90% Yield) MS (ESI): Mass calcd. for $C_9H_6FNO$, 163 m/z; found, 164 $(M+H)^+$.

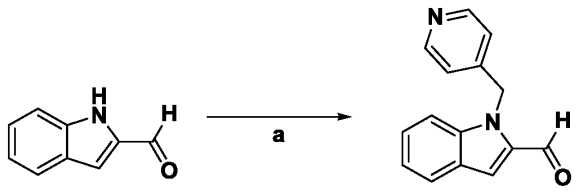
**Step 4: Preparation of1-(cyclopropylmethyl)-6-fluoro-1H-indole-2-carbaldehyde (5)**



**5**

**[000309]** To a stirred solution 6-fluoro-1H-indole-2-carbaldehyde (**4**, 0.5 g, 3.44 mmol) in DMF (10 mL), was added potassium carbonate (1.42 g, 10.3 mmol) followed by (bromomethyl)cyclopropane (0.84 g, 4.13 mmol) and the reaction mixture was stirred at same temperature for 4 h. The reaction mixture was quenched with water, extracted with ethyl acetate (30 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate, filtered and evaporated to get crude product. Crude residue was purified by gradient column chromatography using 10-15% ethyl acetate in hexane to get the product as half white solid. (Yield: 93.4%, 0.86 g). $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 9.81 (s, 1H), 7.69-7.66 (m, 1H), 7.25 (d, $J$ = 6.8 Hz, 1H), 7.07 (d, $J$ = 8 Hz, 1H), 6.97-6.91 (m, 1H), 4.43 (d, $J$ = 8 Hz, 2H), 1.32-1.25 (m, 1H), 0.5-0.45 (m, 2H), 0.42-0.38 (m, 2H). MS (ESI): mass calcd. for $C_{13}H_{12}FNO$, 217.09; *m/z* found, 218.0 $(M+H)^+$.

**Synthesis of 1-(pyridin-4-ylmethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-10)**

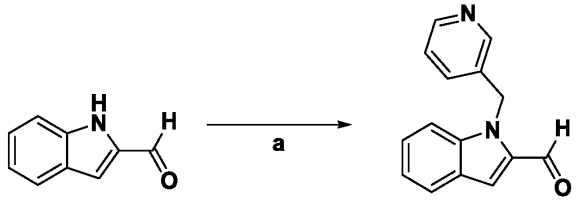



**1** **2**

**[000310]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 1 g, 6.89 mmol) in DMF (20 mL), were added cesium carbonate (6.7g, 20.68 mmol) and (4-(bromomethyl)pyridine (1.1 g, 6.89 mmol) at room temperature. The reaction mixture was refluxed at 80°C for 12 h. The reaction mixture was diluted with water and extracted

with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using 3-7% ethyl acetate in hexane to afford the 1-(pyridin-4-ylmethyl)-1H-indole-2-carbaldehyde as yellow solid (0.5 g, 31% Yield). $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): δ 9.92 (s, 1H), 8.54 (d, *J* = 8 Hz, 2H), 7.79 (d, *J* = 8 Hz, 1H), 7.67-7.64 (m, 1H), 7.56 (d, *J* =12 Hz, 2H), 7.37-7.33 (m, 1H), 7.22-7.19 (m, 1H), 6.88 (d, *J* = 8 Hz, 1H), 5.89 (s, 2H). MS (ESI): mass calcd. for $C_{15}H_{12}N_2O$, 236.09; *m/z* found, 237.0 $(M+H)^+$.

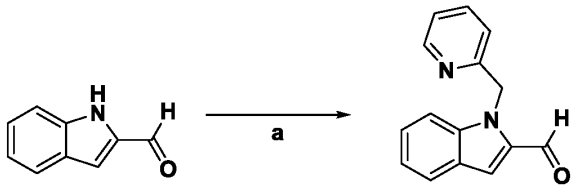
**Synthesis of 1-(pyridin-3-ylmethyl)-1H-indole-2-carbaldehyde (Intermediate for Examples-16, and 66)**




1 2

**[000311]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 1 g, 6.89 mmol) in DMF (20 mL), were added cesium carbonate (6.7g, 20.68 mmol) and 3-(chloromethyl)pyridine hydrochloride (1.1 g, 6.89 mmol) at room temperature. The reaction mixture was refluxed at 80°C for 12 h. The reaction mixture was diluted with water and extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using 3-7% ethyl acetate in hexane to afford the 1-(pyridin-3-ylmethyl)-1H-indole-2-carbaldehyde as yellow solid (0.4 g, 25% Yield). $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 9.92 (s, 1H), 8.41-8.38 (m, 2H), 7.80 (d, *J* = 8 Hz, 1H), 7.68 (d, *J* = 8.4 Hz, 1H ), 7.58 ( bs, 1H)), 7.42-7.38 (m, 2H), 7.28-7.25 (m, 1H), 7.18 (t, *J* = 16 Hz, 1H), 5.85 (s, 2H), MS (ESI): mass calcd. for $C_{15}H_{12}N_2O$, 236.27; *m/z* found, 237.1 $(M+H)^+$.

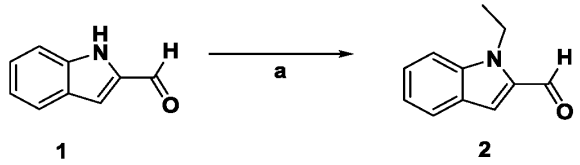
**Synthesis of 1-(pyridin-2-ylmethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-11 & 69)**




1 2

**[000312]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 1 g, 6.89 mmol) in DMF (20 mL), were added cesium carbonate (6.7g, 20.68 mmol) and 2-(bromomethyl)pyridine (1.1g, 6.89 mmol) at room temperature. The reaction mixture was refluxed at 80°C for 12 h. The reaction mixture was diluted with water and extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using 3-7% ethyl acetate in hexane to afford the 1-(pyridin-2-ylmethyl)-1H-indole-2-carbaldehyde as yellow solid (0.8 g, 50% Yield). $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 9.92 (s, 1H), 8.45 (d, $J$ = 4 Hz, 1H), 7.79 (d, $J$ = 8 Hz, 1H), 7.66 (m, 1H), 7.56 (d, $J$ = 12 Hz, 2H), 7.37-7.33 (m, 1H), 7.22-7.19 (m, 1H), 7.17-7.13 (m, 1H), 6.88 (d, $J$ = 8 Hz, 1H), 5.89 (s, 2H). MS (ESI): mass calcd. for $C_{16}H_{12}ClNO$, 269.73; *m/z* found, 270.1 $(M+H)^+$.

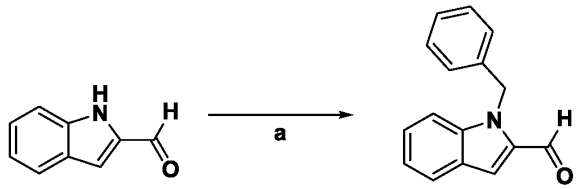
**Synthesis of 1-ethyl-1H-indole-2-carbaldehyde (Intermediate for Example-3)**




1 2

**[000313]** To a stirred solution 1H-indole-2-carbaldehyde (**1**, 1 g, 6.89 mmol) in DMF (15 mL), was added potassium carbonate (2.85 g, 20.6 mmol) followed by iodoethane (0.6 mL, 7.58 mmol) and the reaction mixture was stirred at same temperature for 4 h. Reaction mixture was poured into crushed ice, diluted with water and extracted with ethyl acetate. Organic layer was dried over anhydrous sodium sulfate evaporated under vacuum to give the crude. Crude was purified by flash column chromatography using ethyl acetate and hexane to obtain 1-ethyl-1H-indole-2-carbaldehyde as the viscous liquid. (Yield: 1g, 90%). $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 9.88 (s, 1H), 7.75 (d, $J$ = 8Hz, 1H), 7.61 (d, 1H, $J$ = 8 Hz, 1H), 7.44 (s, 1H), 7.41-7.37 (m, 1H), 7.16-7.12 (m, 1H), 4.58-4.52 (m, 2H), 1.26-1.23 (m, 3H). MS (ESI): mass calcd. for $C_{11}H_{11}NO$, 173.08; *m/z* found, 174.0 $(M+H)^+$.

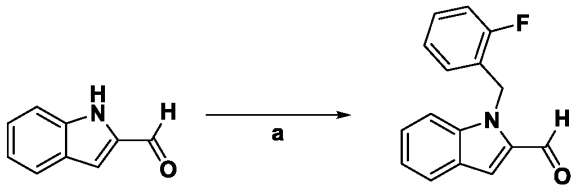
**Synthesis of 1-benzyl-1H-indole-2-carbaldehyde (Intermediate for Example-18)**




1 2

**[000314]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 1 g, 6.89 mmol) in DMF (20 mL), were added potassium carbonate (2.8 g, 20.68 mmol) and (bromomethyl)benzene (1.2 g, 7.58 mmol) at room temperature. The reaction mixture was stirred at room temperature for 12 h. The reaction mixture was diluted with water and extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to give the crude product. The crude residue was purified by gradient column chromatography using 3-7% ethyl acetate in hexane to afford the 1-benzyl-1H-indole-2-carbaldehyde as viscous liquid (0.5 g, 33% Yield). $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 9.92 (s, 1H), 7.78 (d, $J$ = 8 Hz, 1H), 7.58 (d, $J$ = 8 Hz, 1H), 7.54 (s, 1H), 7.38-7.35 (m, 1H), 7.26-7.20 (m, 2H), 7.18-7.13 (m, 2H), 7.05 (d, $J$ = 4 Hz, 2H), 5.82 (s, 2H). MS (ESI): mass calcd. for $C_{16}H_{13}NO$, 235.10; *m/z* found, 236.1 $(M+H)^+$.

**Synthesis of 1-(2-fluorobenzyl)-1H-indole-2-carbaldehyde (Intermediate for Example-14)**

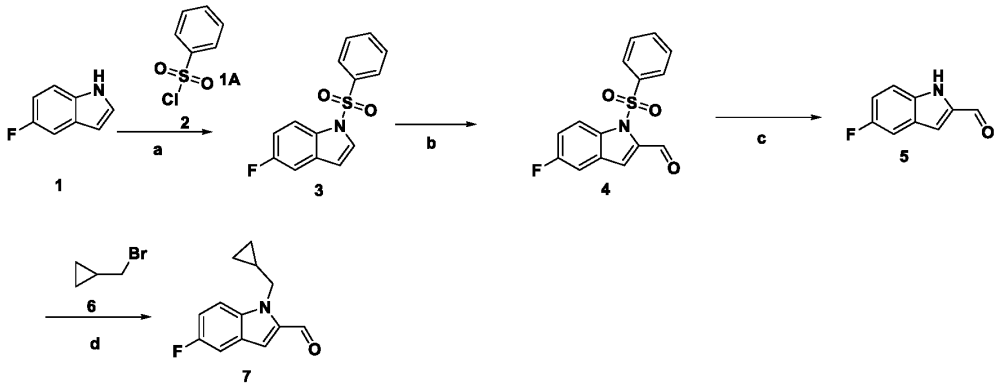



1 2

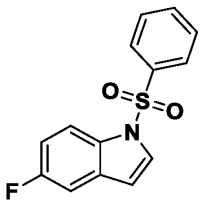
**[000315]** To a stirred solution 1H-indole-2-carbaldehyde (**1**, 1 g, 6.89 mmol) in DMF (15 mL), was added potassium carbonate (2.85 g, 20.6 mmol) followed by 1-(chloromethyl)-2-fluorobenzene (1.19 g, 8.26 mmol) and the reaction mixture was stirred at same temperature for 4 h. Reaction mixture was poured into crushed ice, diluted with water and extracted with ethyl acetate. Organic layer was dried over anhydrous sodium sulfate, evaporated under vacuum to give the crude. Crude was purified by flash column chromatography using ethyl acetate and hexane to afford the 1-(2-fluorobenzyl)-1H-indole-2-carbaldehyde as grey color solid (Yield:1.8g, 96.5%). $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 9.90 (s, 1H), 7.81 (d, $J$ = 8 Hz, 1H), 7.58-7.54 (m, 2H), 7.40-7.36 (m,

1H), 7.28-7.15 (m, 3H), 7.01-6.97 (m, 1H), 6.55-6.51 (m, 1H), 5.88 (s, 2H). MS (ESI): mass calcd. for $C_{16}H_{12}FNO$, 253.09; *m/z* found, 254.0 $(M+H)^+$.

**Synthesis of 1-(cyclopropylmethyl)-5-fluoro-1H-indole-2-carbaldehyde (Intermediate for Examples-9, 64 & 75)**



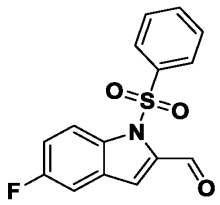

**Step 1: Preparation of 5-fluoro-1-(phenylsulfonyl)-1H-indole (3)**



**3**

**[000316]** To a solution of sodium hydride (0.06 g, 15 mmol) in DMF (10 mL) was added a solution of 5-fluoro-1H-indole (**1**, 0.2 g, 15 mmol) in DMF at 0 °C, drop wise over 15 min. followed by addition of a solution of benzenesulfonyl chloride (**2**, 0.26 g, 15 mmol) in DMF at 0 °C and the reaction mixture was stirred for 2 h at room temperature under $N_2$ atmosphere. To the reaction mixture was added ice cold water (50 mL), then the precipitate was filtered off and washed with ice cold water to obtain brown solid. (0.25 g, 62.50 % Yield). MS (ESI) *m/z* 275.0 $(M+H)^+$.

**Step 2: Preparation of 5-fluoro-1-(phenylsulfonyl)-1H-indole-2-carbaldehyde (4)**

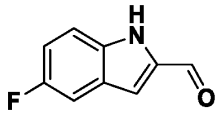


**4**

**[000317]** To a solution of 5-fluoro-1-(phenylsulfonyl)-1H-indole (**3**, 0.250 g, 1.0 mmol) in dry THF (50 mL) was added lithium diisopropylamide 1M in THF (0.5 mL g,

1.0 mmol) at -78 °C, followed by addition of dry DMF (0.11 mL, 1.5 mmol) at -78 °C and stirred for 10 min at -78 °C under $N_2$ atmosphere. To the reaction mixture was added aqueous ammonium chloride (20 mL) and extracted with EtOAc. Organic layer was washed with saturated $NH_4Cl$ solution and brine, dried over sodium sulphate, filtered and concentrated under reduced pressure to obtain brown solid. (0.150 g, 54.54 % Yield). MS (ESI) *m/z* 304.1 $(M+H)^+$.

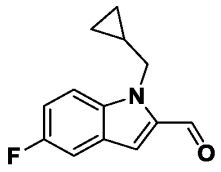
**Step 3: Preparation of 5-fluoro-1H-indole-2-carbaldehyde (5)**



**5**

**[000318]** To the stirred solution of 5-fluoro-1-(phenylsulfonyl)-1H-indole-2-carbaldehyde (**4**, 1.85 g, 6.105 mmol) in THF (50 mL), was added TBAF (1M in THF) (9.15 mL, 9.158 mmol) at room temperature. The reaction mixture was stirred at room temperature for 12 h. The reaction mixture was diluted with water and extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using 15-25% ethyl acetate in hexane to afford the 5-fluoro-1H-indole-2-carbaldehyde as sticky solid (0.65 g, 65% Yield) MS (ESI): Mass calcd. for $C_9H_6FNO$, 163.15; m/z found, 162.0 $[M-H]^-$.

**Step 4: Preparation of 1-(cyclopropylmethyl)-5-fluoro-1H-indole-2-carbaldehyde (7)**

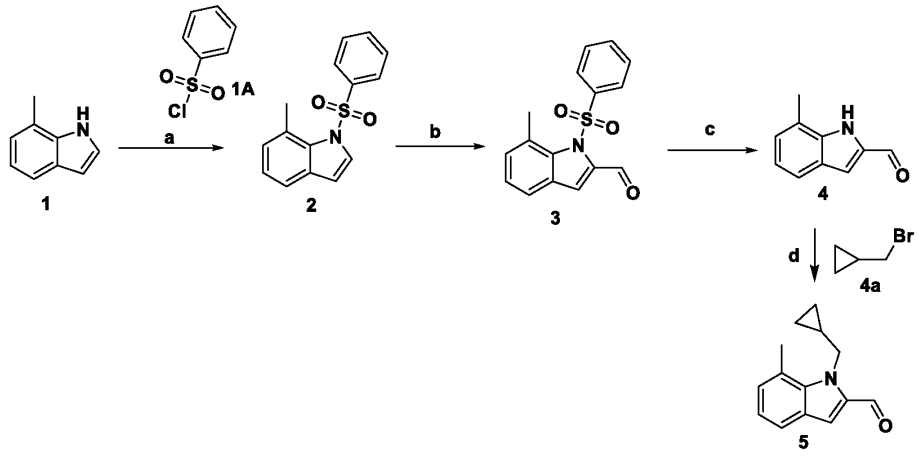


**7**

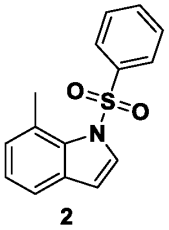
**[000319]** To the stirred solution of 5-fluoro-1H-indole-2-carbaldehyde (**5**, 0.65 g, 3.98 mmol) in DMF (50 mL), were added potassium carbonate (1.64 g, 11.94 mmol) and (bromomethyl)cyclopropane (**6**, 0.58 mL, 5.98 mmol) at room temperature. The reaction mixture was stirred at room temperature for 12 h. The reaction mixture was diluted with water and extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulphate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using 3-7% ethyl acetate

in hexane to afford the 1-(cyclopropylmethyl)-5-fluoro-1H-indole-2-carbaldehyde as sticky solid (0.76 g, 88% Yield). $^1$HNMR (400 MHz, DMSO-d6): δ 9.90 (s, 1H), 7.73-7.69 (m, 1H), 7.55-7.52 (m, 1H), 7.44 (s, 1H), 7.29-7.24 (m, 1H), 4.50 (d, *J* = 7.2 Hz, 2H), 1.23-1.16 (m, 1H), 0.41-0.32 (m, 4H). MS (ESI): Mass calcd. for $C_{13}H_{12}FNO$, 217.24: m/z found, 218.1 $[M+H]^+$.

**Synthesis of 1-(cyclopropylmethyl)-7-methyl-1H-indole-2-carbaldehyde (Intermediate for Example-8 & 84)**

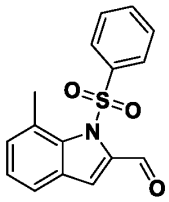



**Step 1: preparation of 7-methyl-1-(phenylsulfonyl)-1H-indole (2)**




**[000320]** To a solution of sodium hydride (0.92 g, 23 mmol) in DMF (10 mL) was added solution of 7-methyl-1H-indole (**1**, 3.0 g, 23 mmol) in DMF at 0 °C, dropwise over 15 min. Benzenesulfonyl chloride in DMF (2.96 mL, 23 mmol) was added at 0°C and stirred for 2 h at room temperature under $N_2$ atmosphere. To the reaction mixture was added ice cold water (50 mL), then filtered off the precipitate and washed with ice cold water to obtain brown solid (5.30 g, 85.50%). MS (ESI) *m/z* 272.1 $(M+H)^+$.

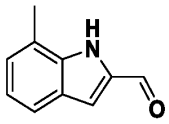
**Step 2: preparation 7-methyl-1-(phenylsulfonyl)-1H-indole-2-carbaldehyde (3)**



3

**[000321]** To a solution of 7-methyl-1-(phenylsulfonyl)-1H-indole (**2**, 5.3 g, 20.0 mmol) in dry THF (50 mL) was added lithium diisopropylamide 1.5M in THF (13.0 mL, 20.0 mmol) at -78 °C and stirred for 5-8 min, followed by addition of dry DMF (2.33 mL, 30.0 mmol) at -78 °C and stirred for 10 min at -78 °C under $N_2$ atmosphere. To the reaction mixture was added aqueous ammonium chloride (20 mL), then extracted in to EtOAc. Organic layer was washed with saturated $NH_4Cl$ solution and brine, dried over sodium sulphate, filtered and concentrated under reduced pressure to obtain red viscous liquid (5.0 g, 85.47 %). MS (ESI) *m/z* 300.2 $(M+H)^+$.

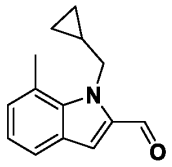
**Step 3: Preparation of 7-methyl-1H-indole-2-carbaldehyde (4)**



4

**[000322]** To the stirred solution of 7-methyl-1-(phenylsulfonyl)-1H-indole-2-carbaldehyde (**3**, 2 g, 6.68 mmol) in THF (20 mL), was added 1M solution of tetrabutyl ammonium fluoride in THF (10 mL, 10.2 mmol) and stirred at 80 °C for 1h. Reaction mixture was cooled to room temperature, added water (20 mL) and extracted with EtOAc (100 mL). Organic layer was dried over anhydrous $Na_2SO_4$ and evaporated under vacuum. Crude was purified by column chromatography using 15-20% EtOAc in Hexane to afford the product as brown solid. (0.8 g, 58% Yield). MS (ESI): Mass calcd. for $C_{10}H_9NO$, 159.07; *m/z* found 160.1 $(M+H)^+$.

**Step 4: 1-(cyclopropylmethyl)-7-methyl-1H-indole-2-carbaldehyde (5)**

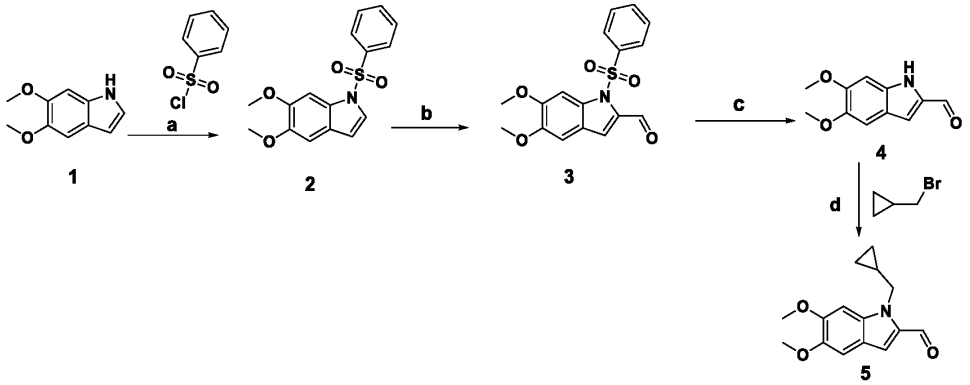


5

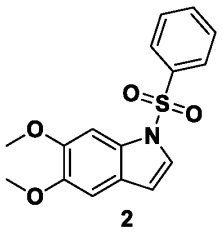
**[000323]** To the stirred solution of 7-methyl-1H-indole-2-carbaldehyde (**4**, 0.85 g, 5.345 mmol) in DMF (20 mL), were added potassium carbonate (2.21 g, 16.035 mmol)

and (bromomethyl)cyclopropane (4a, 0.78 mL, 8.018 mmol) at room temperature. The reaction mixture was stirred at room temperature for 12 h. The reaction mixture was diluted with water and extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using 3-7% ethyl acetate in hexane to afford the 1-(cyclopropylmethyl)-7-methyl-1H-indole-2-carbaldehyde as sticky solid (0.52 g, 45% Yield). $^1$HNMR (400 MHz, $CDCl_3$) δ(ppm): 9.82 (s, 1H), 7.58 (d, *J* = 8.0 Hz, 1H), 7.26 (s, 1H), 7.13 (d , *J* = 6.8 Hz, 1H), 6.26 (m, 1H), 4.83 (d , *J* = 6.8 Hz, 2H), 2.77 (s , 3H), 1.15-1.10 (m, 1H), 0.41-0.33 (m, 4H). MS (ESI): Mass calcd. for $C_{14}H_{15}NO$, 213.28; m/z found, 214.1 $[M+H]^+$.

**Synthesis of 1-(cyclopropylmethyl)-5,6-dimethoxy-1H-indole-2-carbaldehyde (Intermediate for Example-17)**

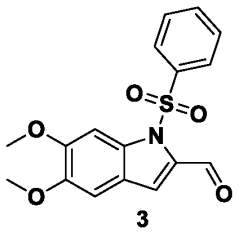



**Step 1: Preparation of 5,6-dimethoxy-1-(phenylsulfonyl)-1H-indole (2)**




**[000324]** To a solution of sodium hydride (0.56 g, 14 mmol) in DMF (50 mL) was added solution of 5,6-dimethoxy-1H-indole (**1**, 2.5 g, 14 mmol) in DMF at 0°C, dropwise over 15 min. Benzenesulfonyl chloride (1.8 mL, 14 mmol) in DMF was added at 0°C and stirred for 2 h at room temperature under $N_2$ atmosphere. To the reaction mixture was added ice cold water (50 mL), then filtered off the precipitate and washed with ice cold water to obtain white solid. (4.20 g, 93.95 % Yield). MS (ESI): mass calcd. for $C_{16}H_{15}NO_4S$, 317.07; m/z found, 318.1 $[M+H]^+$.

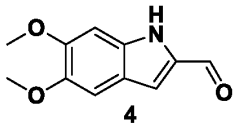
**Step 2: preparation 5,6-dimethoxy-1-(phenylsulfonyl)-1H-indole-2-carbaldehyde (3)**



3

**[000325]** To a solution of 5,6-dimethoxy-1-(phenylsulfonyl)-1H-indole (**2**, 4.2 g, 13.2 mmol) in dry THF (60 mL) was added lithium diisopropylamide 2M in THF (8.8 mL g, 13.2 mmol) at -78 °C and stirred for 5-8 min, followed by addition of dry DMF (1.54 mL, 20.0 mmol) at -78 °C and stirred for 10 min at -78 °C under $N_2$ atmosphere. To the reaction mixture was added aqueous ammonium chloride (20 mL), then extracted in to EtOAc. Organic layer was washed with saturated $NH_4Cl$ solution and brine, dried over sodium sulphate, filtered and concentrated under reduced pressure to obtain yellow solid (3.5 g, 78.26% Yield). MS (ESI): mass calcd. for $C_{17}H_{15}NO_5S$, 345.07; m/z found, 346.1 $[M+H]^+$.

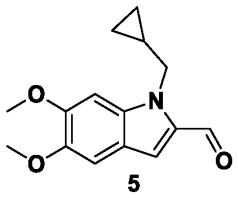
**Step 3: Preparation of 5,6-dimethoxy-1H-indole-2-carbaldehyde (4)**



4

**[000326]** To the stirred solution of 5,6-dimethoxy-1-(phenylsulfonyl)-1H-indole-2-carbaldehyde (**3**, 2 g, 5.5 mmol) in THF (50 mL), was added TBAF (1M in THF) (8.8 mL, 8.2 mmol) at room temperature. The reaction mixture was stirred at room temperature for 12 h. The reaction mixture was diluted with water and extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using 5-10% ethyl acetate in hexane to afford desired compound as gummy solid (1 g, 88.6% Yield). MS (ESI): mass calcd. for $C_{11}H_{11}NO3$, 205.07; m/z found, 206.1 $[M+H]^+$.

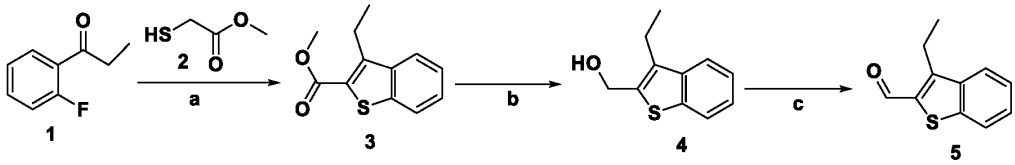
**Step 4: Preparation of 1-(cyclopropylmethyl)-5,6-dimethoxy-1H-indole-2-carbaldehyde (5)**



5

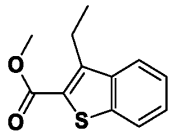
**[000327]** To the stirred solution of 5,6-dimethoxy-1H-indole-2-carbaldehyde (**4**, 1 g, 4.8 mmol) in DMF (20 mL), were added potassium carbonate (1.9 g, 14 mmol) and (bromomethyl)cyclopropane ( 0.7 g, 5.7 mmol) at room temperature. The reaction mixture was stirred at room temperature for 12 h. The reaction mixture was diluted with water and extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using 10% ethyl acetate in hexane to afford title compound as yellow solid (0.7 g, 56.3% Yield). $^1$HNMR (400 MHz, $CDCl_3$) δ(ppm): 9.71 (s, 1H), 7.12 (s, 1H), 7.06 (s, 1H), 6.78 (s, 1H), 4.47 (d, $J$ = 6.4 Hz, 2H), 3.99 (s, 3H), 3.93 (s, 3H), 1.30-1.25 (m, 1H), 0.49-0.41 (m, 4H). MS (ESI): Mass calcd. for $C_{15}H_{17}NO_3$, 259.31; m/z found, 260.2 $[M+H]^+$.

**Synthesis of Ethylbenzo[b]thiophene-2-carbaldehyde (Intermediate for Example-12)**



1 3 4 5

**Step 1: Methyl 3-ethylbenzo[b]thiophene-2-carboxylate (3)**

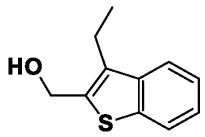


3

**[000328]** To a suspension of NaH (60% in oil, 0.17g, 4.27mmol) in THF (10 mL) was added methyl 2-mercaptoacetate (**2**, 0.41 g, 3.94 mmol) at room temperature and stirred at same temperature for 30 min. To the reaction was added solution of 1-(2-fluorophenyl)propan-1-one (**1**, 0.5 g, 3.28 mmol) in THF and allowed to reflux for 16 h (reaction condition **a**). Completion of the reaction was monitored by LCMS The reaction mixture was cooled to room temperature, diluted with EtOAc and washed with 1N NaOH and water. Organic layer was washed, dried over sodium sulphate, filtered and

concentrated under reduced pressure. The crude mixture was purified by column chromatography to obtain the product as brown oil (Yield: 0.4 g, 57.14 %). MS (ESI): mass calcd. for $C_{12}H_{12}O_2S$, 220.06; m/z found, 221.1 $(M+H)^+$.

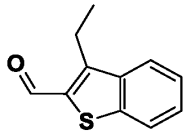
**Step 2: (3-Ethylbenzo[b]thiophen-2-yl) methanol (4)**



**4**

**[000329]** To a solution of methyl 3-ethylbenzo[b]thiophene-2-carboxylate (**3**, 0.5 g, 1.81 mmol) in THF (10 mL) was added 1M solution of LAH in THF (2.7 mL, 2.72 mmol) drop wise at 0°C. The reaction mixture was stirred for 2 h at $25^0$C (Reaction condition **b**). The reaction was monitored by TLC (1:1, EtOAc: hexane). The reaction mixture was quenched with saturated $NH_4Cl$ (10 mL), filtered through celite and extracted with EtOAc. Organic layer was washed with brine, dried over sodium sulphate, filtered and concentrated under reduced pressure. The crude mixture was purified by column chromatography to obtain the product as yellow oil (Yield: 0.24 g, 70.58 %). MS (ESI): mass calcd. for $C_{11}H_{12}OS$, 192.06; m/z found, 192.9 $(M+H)^+$.

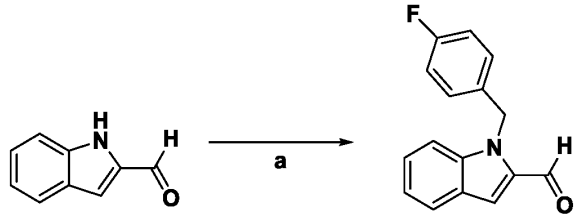
**Step 3: Ethylbenzo[b]thiophene-2-carbaldehyde (5)**



**5**

**[000330]** To a solution of (3-ethylbenzo[b]thiophen-2-yl) methanol (**4**, 0.24 g, 1.25 mmol) in DCM (10 mL) was added Dess martin periodinane (0.79 g, 1.87 mmol) at 0°C (Reaction condition **c**). The reaction mixture was stirred for 2 h at $25^0$C. The reaction was monitored by TLC (1:1, EtOAc: hexane). The reaction mixture was quenched with saturated $NaHCO_3$ (10 mL), filtered through celite and extracted with DCM. Organic layer was washed with brine, dried over sodium sulphate, filtered and concentrated under reduced pressure. The crude mixture was purified by column chromatography to obtain the product as yellow solid. (Yield: 0.18 g, 81.8 %).$^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 10.33 (s, 1H), 8.08-8.02 (m, 2H), 7.56 (t, $J$ = 6.8 Hz, 1H), 7.49 (t, $J$ = 7.6 Hz, 1H), 3.33-3.30 (m, 2H), 1.29 (t, $J$ = 7.2 Hz, 3H). MS (ESI): mass calcd. for $C_{11}H_{10}OS$, 190.05; m/z found, 191.0 $(M+H)^+$.

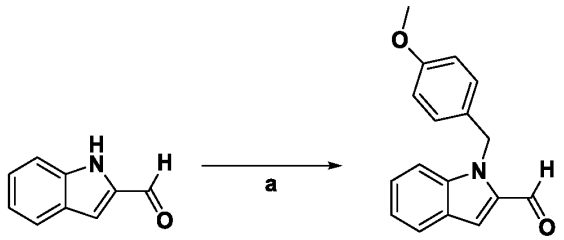
**Synthesis of 1-(4-fluorobenzyl)-1H-indole-2-carbaldehyde (Intermediate for Example-15)**




1 2

**[000331]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 0.5 g, 3.44 mmol) in DMF (20 mL), were added potassium carbonate (1.42 g, 10.34 mmol) and 1-(bromomethyl)-4-fluorobenzene (0.716 g, 3.79 mmol) at room temperature. The reaction mixture was stirred at room temperature for 12 h. The reaction mixture was diluted with water and extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to give the crude product. The crude residue was purified by gradient column chromatography using 3-7% ethyl acetate in hexane to afford the 1-(4-fluorobenzyl)-1H-indole-2-carbaldehyde as solid (0.8 g, 97% Yield). $^1$HNMR (400 MHz, $CDCl_3$) δ(ppm): 9.89 (s, 1H), 7.77 (d, $J$ = 8.4 Hz, 1H), 7.41 (m, 2H), 7.39 (s, 1H), 7.25-7.17 (m, 1H), 7.10-7.00 (m, 2H), 6.95 (t, $J$ = 8 Hz, 2H), 5.79 (s, 2H): MS (ESI): Mass calcd. for $C_{16}H_{12}FNO$, 253.28; m/z found, 254.0 $[M+H]^+$.

**Synthesis of 1-(4-methoxybenzyl)-1H-indole-2-carbaldehyde (Intermediate for Example-19)**

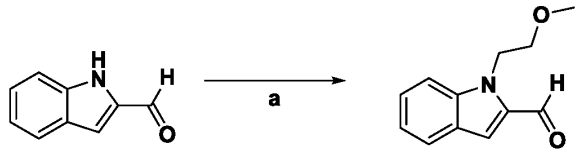



1 2

**[000332]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 0.5 g, 3.44 mmol) in DMF (20 mL), were added potassium carbonate (1.42 g, 10.34 mmol) and 1-(bromomethyl)-4-methoxybenzene (0.76 g, 3.79 mmol) at room temperature. The reaction mixture was stirred at room temperature for 12 h. The reaction mixture was diluted with water and extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude

product. The crude residue was purified by gradient column chromatography using 3-7% ethyl acetate in hexane to afford the 1-(4-methoxybenzyl)-1H-indole-2-carbaldehyde as solid (0.4 g, 43% Yield). $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 9.75 (s, 1H), 7.93 (d, *J* = 8.4 Hz, 1H), 7.82 (m, 2H), 7.36 (s, 1H), 7.25-7.17 (m, 1H), 7.12 (m, 2H), 6.83 (t, *J* = 8 Hz, 2H), 5.81 (s, 2H), 3.81 (s, 3H), MS (ESI): Mass calcd. for C17H15NO2, 265.31; m/z found, 266.1 $[M+H]^+$.

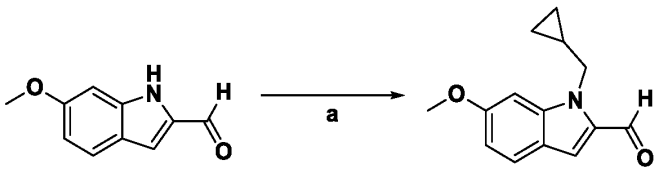
**Synthesis of 1-(2-methoxyethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-20)**




1 2

**[000333]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 0.80 g, 5.5 mmol) in *N, N*-dimethylformamide (20 mL), cesium carbonate (5.36 g, 90.5mmol) and 1-bromo-2-methoxyethane (0.62 mL, 6.7 mmol) were added at room temperature. The reaction mixture was stirred at 60 °C for 1 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (20 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 20% ethyl acetate in hexanes as eluent, to afford the 1-(2-methoxyethyl)-1H-indole-2-carbaldehyde as pale yellow oil. Yield: 3.0 g (42%). $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 9.89 (s, 1H), 7.75 (d, *J* = 7.9 Hz, 1H), 7.63 (d, *J* = 8.5 Hz, 1H), 7.47 (s, 1H), 7.39 (t, *J* = 7.2 Hz, 1H), 7.15 (t, *J* = 7.5 Hz, 1H), 4.70 (t, *J* = 5.44 Hz, 2H), 3.61 (t, *J* = 5.3 Hz, 2H), 3.15 (s, 3H).

**Synthesis of 1-(cyclopropylmethyl)-6-methoxy-1H-indole-2-carbaldehyde (Intermediate for Example-23)**

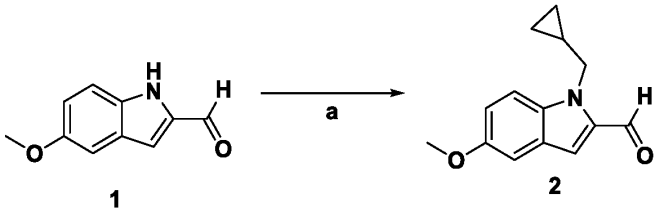



1 2

**[000334]** To the stirred solution of 6-methoxy-1H-indole-2-carbaldehyde (**1**, 2.0 g, 11.4 mmol) in *N, N*-dimethylformamide (20 mL), cesium carbonate (11.14 g, 34.3 mmol) and (bromomethyl)cyclopropane (1.41 mL, 13.7 mmol) were added at room temperature.

The reaction mixture was stirred at room temperature for 2 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (20 mL x 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 20% ethyl acetate in hexanes as eluent, to afford the 1-(cyclopropylmethyl)-6-methoxy-1H-indole-2-carbaldehyde as pale yellow oil. Yield: 0.80 g (31%), MS (ESI) 229.13; *m/z* found 230.1 $[M+H]^{+1}$.

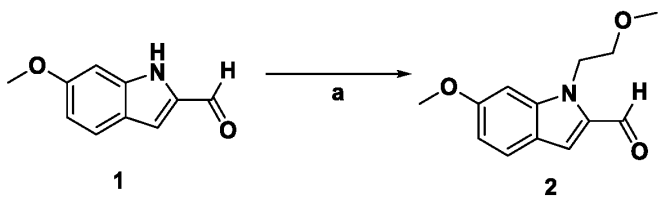
**Synthesis of 1-(cyclopropylmethyl)-5-methoxy-1H-indole-2-carbaldehyde (Intermediate for Example-60)**




1 2

**[000335]** To the stirred solution of 6-methoxy-1H-indole-2-carbaldehyde (**1**, 2.0 g, 11.4 mmol) in *N, N*-dimethylformamide (20 mL), cesium carbonate (11.14 g, 34.3 mmol) and (bromomethyl)cyclopropane (1.41 mL, 13.7 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 2 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (20 mL x 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 20% ethyl acetate in hexanes as eluent, to afford the 1-(cyclopropylmethyl)-5-methoxy-1H-indole-2-carbaldehyde as pale yellow oil. Yield: 0.79 g (30%), MS (ESI) 229.13; *m/z* found 230.1 $[M+H]^{+1}$.

**Synthesis of 6-methoxy-1-(2-methoxyethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-21)**

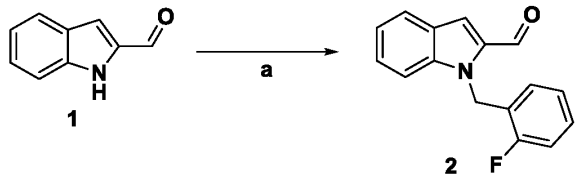



1 2

**[000336]** To the stirred solution of 6-methoxy-1H-indole-2-carbaldehyde (**1**, 0.80 g, 4.57 mmol) in *N, N*-dimethylformamide (3 mL), cesium carbonate (4.4 g, 13.7 mmol)

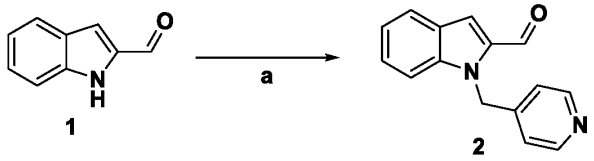
and 1-bromo-2-methoxyethane (0.51 mL, 5.48 mmol) were added at room temperature. The reaction mixture was stirred at 60 °C for 16 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (200 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by combiFlash using 12 g RediSep and 20% ethyl acetate in hexane as eluent to afford the 6-methoxy-1-(2-methoxyethyl)-1H-indole-2-carbaldehyde as off white semi solid. Yield: 0.60 g, 60%, MS (ESI): 235; *m/z* found 234.10 $[M-1]^{-1}$.

**Synthesis of 1-(2-fluorobenzyl)-1H-indole-2-carbaldehyde (Intermediate for Example-70)**




**[000337]** To a solution of 1H-indole-2-carbaldehyde (**1**, 2.0 g, 13.7 mmol) in *N, N*-dimethylformamide (15 mL), potassium carbonate (5.6 g, 41.1 mmol) and 1-(bromomethyl)-2-fluorobenzene (3.1 g, 16.5 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 4 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (20 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 20% ethyl acetate in hexane as eluent to afford 1-(2-fluorobenzyl)-1H-indole-2-carbaldehyde as yellow solid.

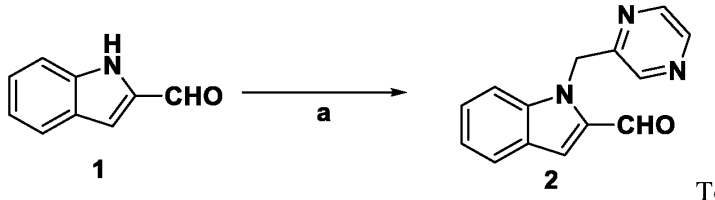
**Synthesis of 1-(pyridin-4-ylmethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-11 and 71)**




**[000338]** To a solution of 1H-indole-2-carbaldehyde (**1**, 1.50 g, 10.3 mmol) in *N, N*-dimethylformamide (40 mL), potassium carbonate (4.2 g, 31.0 mmol) and 4-(bromomethyl)pyridine hydrobromide (3.1 g, 12.4 mmol) were added at room temperature. The reaction mixture was stirred at 60 °C for 4 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (20 mL

× 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 10% ethyl acetate in hexane as eluent to afford 1-(pyridin-4-ylmethyl)-1H-indole-2-carbaldehyde as yellow oil. Yield: 1.0 g (40%). MS (ESI) 236.01; *m/z* found 2.37.12.1 $[M+H]^{+1}$.

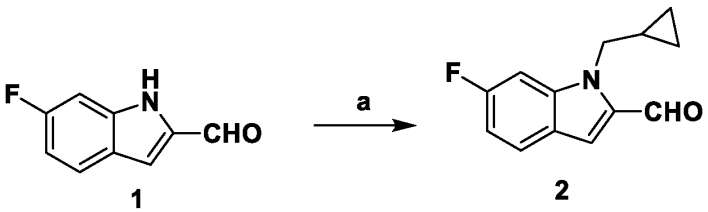
**Synthesis of 1-(pyrazin-2-ylmethyl)-1H-indole-2-carbaldehyde) (Intermediate for Example-25)**




1 2

**[000339]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 1.0 g, 6.81 mmol) in *N, N*-dimethylformamide (20.0 mL), cesium carbonate (11.2 g, 34.4 mmol) and 2-(chloromethyl)pyrazine (1.0 g, 8.27 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (30 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 10% ethyl acetate in hexane as eluent to afford 1-(pyrazin-2-ylmethyl)-1H-indole-2-carbaldehyde as yellow solid (**3a**). Yield: 0.80 g (48%). MS (ESI): 237.26, *m/z* found 238.12 $[M+H]^{+1}$.

**Synthesis of 1-(cyclopropylmethyl)-6-fluoro-1H-indole-2-carbaldehyde (Intermediate for Example-28)**

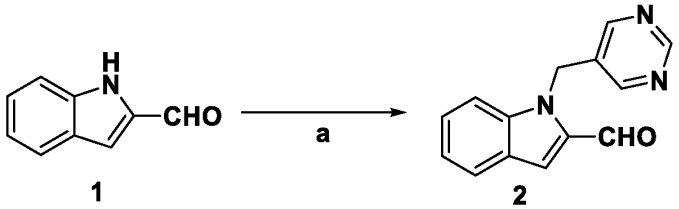



1 2

**[000340]** To the stirred solution of 6-fluoro-1H-indole-2-carbaldehyde (**1**, 1.5 g, 9.2 mmol) in *N, N*-dimethylformamide (30.0 mL), cesium carbonate (8.9 g, 27.6 mmol) and (bromomethyl)cyclopropane (1.47 g, 11.2 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction,

the reaction mixture was diluted with water and extracted with ethyl acetate (30 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 10% ethyl acetate in hexane as eluent to afford 1-(cyclopropylmethyl)-6-fluoro-1H-indole-2-carbaldehyde as yellow solid. Yield: 1.5 g (75%). MS (ESI): 217.24, *m/z* found 218.34 $[M+H]^{+1}$.

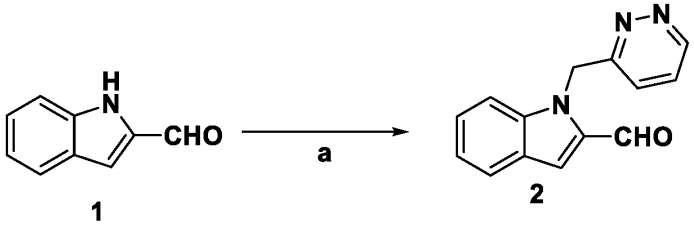
**Synthesis of 1-(pyrimidin-5-ylmethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-29)**




1 2

**[000341]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 1.20 g, 8.27 mmol) in *N, N*-dimethylformamide (20.0 mL), cesium carbonate (8.08 g, 24.01 mmol) and 5-(chloromethyl)pyrimidine (1.0 g, 8.27 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (30 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 10% ethyl acetate in hexane as eluent to afford 1-(pyrimidin-5-ylmethyl)-1H-indole-2-carbaldehyde as brown solid. Yield: 1.60 g (81%). MS (ESI): 237.26, *m/z* found 238.32 $[M+H]^{+1}$.

**Synthesis of 1-(pyridazin-3-ylmethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-30)**

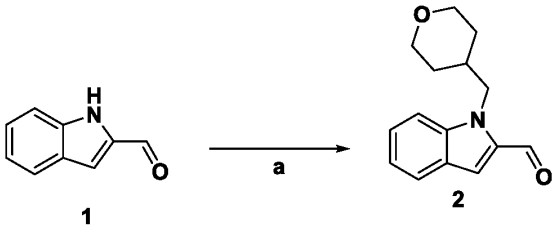



1 2

**[000342]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 1.0 g, 6.81 mmol) in *N, N*-dimethylformamide (10.0 mL), cesium carbonate (6.7 g, 20.01 mmol) and 3-(chloromethyl)pyridazine (1.0 g, 7.10 mmol) were added at room temperature. The

reaction mixture was stirred at room temperature for 3 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (30 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 10% ethyl acetate in hexane as eluent to afford 1-(pyridazin-3-ylmethyl)-1H-indole-2-carbaldehyde as brown solid (**3a**). Yield: 1.40 g (Crude). MS (ESI): 237.26, *m/z* found 238.42 $[M+H]^{+1}$.

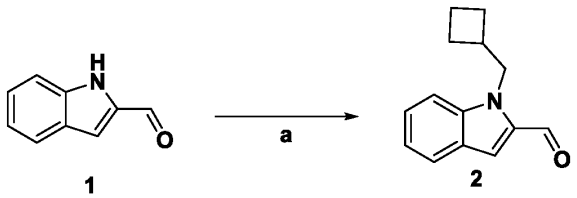
**Synthesis of 1-((tetrahydro-2H-pyran-4-yl)methyl)-1H-indole-2-carbaldehyde) (Intermediate for Example-40)**




1 2

**[000343]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 1.0 g, 6.89 mmol) in *N, N*-dimethylformamide (10 mL), cesium carbonate (6.70 g, 20.68 mmol) and 4-(bromomethyl)tetrahydro-2H-pyran (1.48 g, 8.27 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 1 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (200 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 5% ethyl acetate in hexane as eluent to afford 1-((tetrahydro-2H-pyran-4-yl)methyl)-1H-indole-2-carbaldehyde as white solid). Yield: 0.80 g (48%). MS (ESI);243.13 *m/z* found: 244.17$[M+H]^{+1}$.

**Synthesis of 1-(cyclobutylmethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-41)**



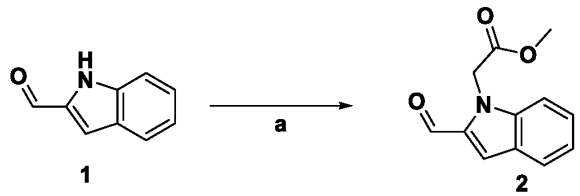

1 2

**[000344]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 0.50 g, 3.44 mmol) in *N, N*-dimethylformamide (10 mL), cesium carbonate (3.3 g, 10.34 mmol) and

cyclobutylmethyl methanesulfonate (**2b**, 0.84 g, 5.17 mmol) were added at room temperature. The reaction mixture was stirred at 100 °C for 1 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (200 mL x 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 5% ethyl acetate in hexane as eluent to afford 1-(cyclobutylmethyl)-1H-indole-2-carbaldehyde as oily liquid (**3a**). Yield: 0.650 g (88%). MS (ESI); 213.12 *m/z* found no ionization.

**[000345]** $^1$HNMR (400 MHz, DMSO-d6): δ 9.89 (s, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.46 (s, 1H), 7.40 (t, *J* = 7.2 Hz, 1H), 7.14 (t, *J* = 7.2 Hz, 1H), 4.60 (d, *J* = 6.8 Hz, 2H), 2.72 (t, *J* = 6.4 Hz, 1H), 1.87-1.71 (m, 6H).

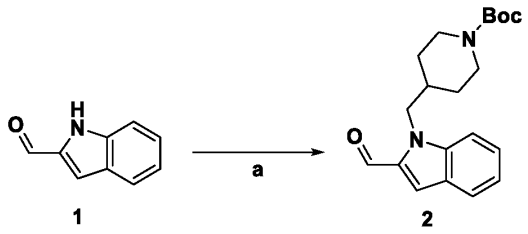
**Synthesis of methyl 2-(2-formyl-1H-indol-1-yl)acetate Intermediate for (Example-42)**




1 2

**[000346]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 1.5 g, 10.3 mmol) in *N, N*-dimethylformamide (40.0 mL), cesium carbonate (10.0 g, 30.9 mmol) and methyl 2-chloroacetate (**2a**, 1.35 g, 12.4 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 1 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (100 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 40 g RediSep and 5% ethyl acetate in hexane as eluent to afford methyl 2-(2-formyl-1H-indol-1-yl)acetate (**3a**) as yellow oil. Yield: 1.2 g (53%). MS (ESI): 217.04, *m/z* found 218.18 $[M+H]^{+1}$.

**Synthesis of tert-butyl 4-((2-formyl-1H-indol-1-yl)methyl)piperidine-1-carboxylate (Intermediate for Example-43)**

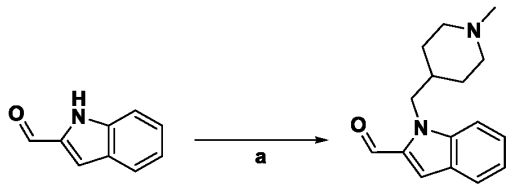



1 2

**[000347]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 1.0 g, 6.81 mmol) in *N, N*-dimethylformamide (10 mL), cesium carbonate (6.72 g, 20.0 mmol) and tert-butyl 4-(bromomethyl)piperidine-1-carboxylate (2.29 g, 8.11 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (50 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 20% ethyl acetate in hexane as eluent to afford the tert-butyl 4-((2-formyl-1H-indol-1-yl)methyl)piperidine-1-carboxylate as yellow solid.Yield: 2.0 g (86%). MS (ESI): found no ionization.

**[000348]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 9.89 (s, 1H), 7.77-7.76 (m, 1H), 7.70-7.68 (m, 1H), 7.49 (s, 1H), 7.40-7.38 (m, 1H), 7.17-7.14 (m, 1H), 4.44 (d, $J$ = 7.41 Hz, 2H), 3.89 (s, 2H), 1.99-1.89 (m, 1H), 1.37 (s, 13H) 1.18-1.13 (m, 2H).

**Synthesis of 1-((1-methylpiperidin-4-yl)methyl)-1H-indole-2-carbaldehyde (Intermediate for Example- 45)**

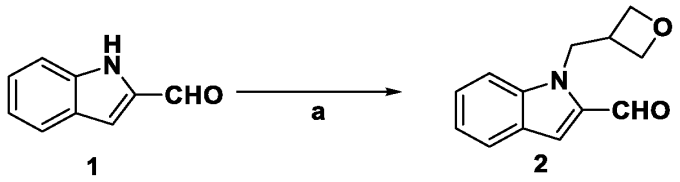



1 2

**[000349]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 1.0 g, 6.81 mmol) in *N, N*-dimethylformamide (10 mL), cesium carbonate (6.72 g, 20.0 mmol) and tert-butyl 4 4-(bromomethyl)-1-methylpiperidine (2.2 g, 8 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (50 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 20% ethyl acetate in hexane as

eluent to afford the 1-((1-methylpiperidin-4-yl)methyl)-1H-indole-2-carbaldehyde as solid. Yield: 2.2 g (85%).

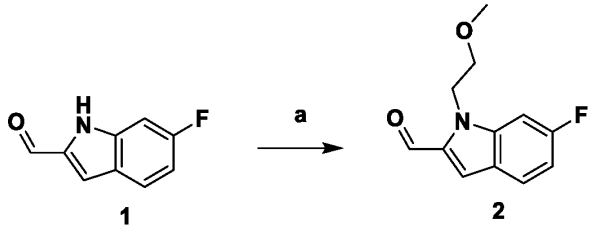
**Synthesis of 1-(oxetan-3-ylmethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-44)**




1 2

**[000350]** To the stirred solution of 1H-indole-2-carbaldehyde (1, 0.700 g, 4.82 mmol) in *N, N*-dimethylformamide (10.0 mL), cesium carbonate (4.7 g, 14.48 mmol) and (3-(chloromethyl)oxetane (0.562 g, 5.31 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 16 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (10 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 30% ethyl acetate in hexane as eluent to afford 1-(oxetan-3-ylmethyl)-1H-indole-2-carbaldehydeas yellow solid. Yield: 0.380 g (63%). MS (ESI): 215.09, *m/z* found 216.18 $[M+H]^{+1}$.

**Synthesis of 6-fluoro-1-(2-methoxyethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-52)**

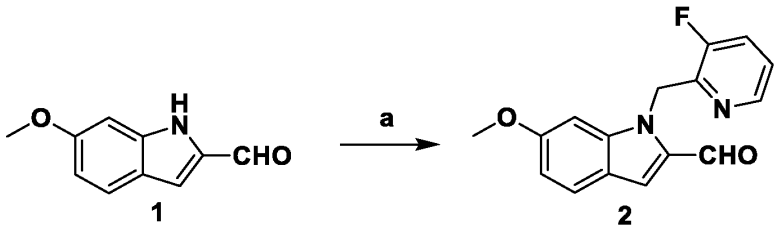



1 2

**[000351]** To the stirred solution of 6-fluoro-1H-indole-2-carbaldehyde (1, 0.90 g, 5.5 mmol) in *N, N*-dimethylformamide (20 mL), potassium carbonate (5.38 g, 16.5 mmol) and 1-bromo-2-methoxyethane (, 0.61 mL, 6.62 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (20 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 20% ethyl acetate in hexanes as eluent, to afford

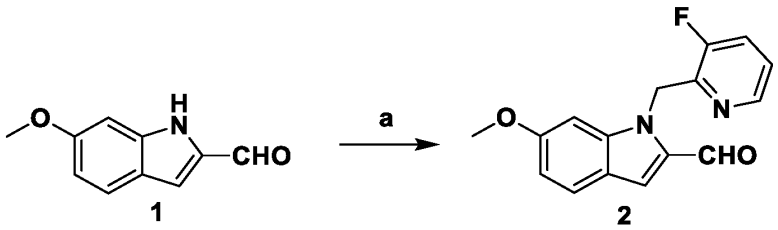
the 6-fluoro-1-(2-methoxyethyl)-1H-indole-2-carbaldehyde as sticky solid. Yield: 0.60 g (60%); MS (ESI) 221.09; *m/z* found 222.10 $[M+H]^{+1}$.

**Synthesis of 1-((3-fluoropyridin-2-yl)methyl)-6-methoxy-1H-indole-2-carbaldehyde (Intermediate for Example-26)**




**[000352]** To the stirred solution of 6-methoxy-1H-indole-2-carbaldehyde (**1**, 0.50 g, 2.85 mmol) in *N, N*-dimethylformamide (10.0 mL), cesium carbonate (2.7 g, 8.57 mmol) and 2-(chloromethyl)-3-fluoropyridine hydrochloride (0.452 g, 3.14 mmol) were added at room temperature. The reaction mixture was stirred at 60°C about 2 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (10 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 30% ethyl acetate in hexane as eluent to afford 1-((3-fluoropyridin-2-yl)methyl)-6-methoxy-1H-indole-2-carbaldehyde as solid Yield: 0.63 g (79%). MS (ESI): 284.10, *m/z* found 285.19 $[M+H]^{+1}$.

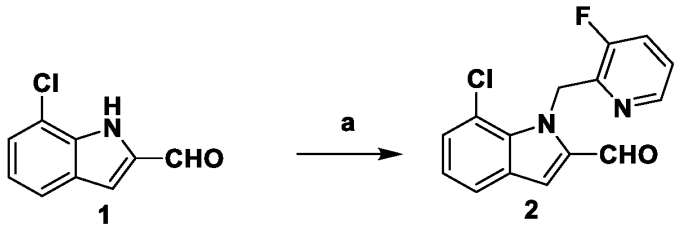
**Synthesis of 1-((3-fluoropyridin-2-yl)methyl)-6-methoxy-1H-indole-2-carbaldehyde (Intermediate for Example-33)**




**[000353]** To the stirred solution of 6-methoxy-1H-indole-2-carbaldehyde (**1**, 0.50 g, 2.85 mmol) in *N, N*-dimethylformamide (10.0 mL), cesium carbonate (2.7 g, 8.57 mmol) and 2-(chloromethyl)-3-fluoropyridine hydrochloride (0.45 g, 3.14 mmol) were added at room temperature. The reaction mixture was stirred at 60°C about 2 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (10 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 30% ethyl acetate in hexane as

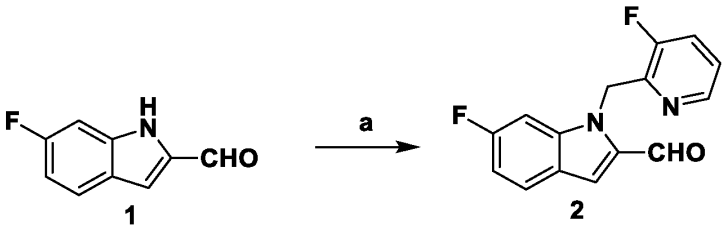
eluent to afford 1-((3-fluoropyridin-2-yl)methyl)-6-methoxy-1H-indole-2-carbaldehyde as yellow solid Yield: 0.66 g (81%). MS (ESI): 284.10, *m/z* found 285.19 $[M+H]^{+1}$.

**Synthesis of 7-chloro-1-((3-fluoropyridin-2-yl)methyl)-1H-indole-2carbaldehyde (Intermediate for Example-34)**




**[000354]** To the stirred solution of 7-chloro-1H-indole-2-carbaldehyde (**1**, 0.4 g, 2.23 mmol) in *N, N*-dimethylformamide (14.0 mL), cesium carbonate (2.1 g, 6.68 mmol) and 2-(chloromethyl)-3-fluoropyridine (0.39 g, 2.67 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (30 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 20% ethyl acetate in hexane as eluent to afford 7-chloro-1-((3-fluoropyridin-2-yl)methyl)-1H-indole-2-carbaldehyde as yellow oil. Yield: 0.30 g (46%). MS (ESI): 288.0, *m/z* found 289.01 $[M+H]^{+1}$.

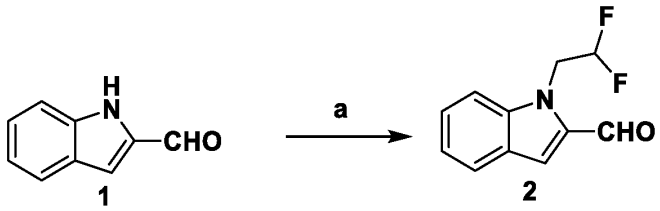
**Synthesis of 6-fluoro-1-((3-fluoropyridin-2-yl)methyl)-1H-indole-2-carbaldehyde (Intermediate for Example-35)**




**[000355]** To the stirred solution of 6-fluoro-1H-indole-2-carbaldehyde (**1**, 0.5 g, 3.06 mmol) in *N, N*-dimethylformamide (6.0 mL), cesium carbonate (2.99 g, 9.2 mmol) and 2-(chloromethyl)-3-fluoropyridine hydrochloride (0.53 g, 3.6 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (20 mL × 2). The combined organic extracts were washed with brine, dried

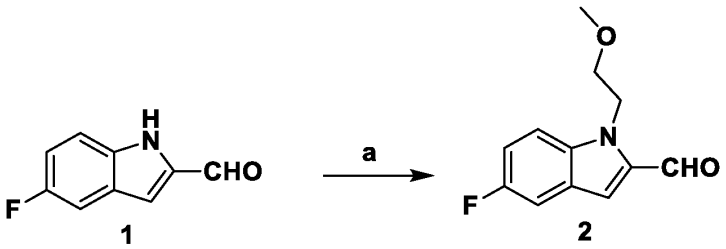
over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 5% ethyl acetate in hexane as eluent to afford 6-fluoro-1-((3-fluoropyridin-2-yl)methyl)-1H-indole-2-carbaldehyde as yellow solid. Yield: 0.72 g (86%). MS (ESI): 272.12, *m/z* found no ionization. $^1$HNMR (400 MHz, DMSO-d6): δ 9.80 (s, 1H), 8.15 (d, *J* = 4.5 Hz, 1H), 7.85-7.82 (m, 1H), 7.73 (t, *J* = 9.1 Hz, 1H), 7.54 (s, 1H), 7.50 (d, *J* = 10.6 Hz, 1H), 7.35-7.28 (m, 1H), 7.05-7.02 (m, 1H), 5.97 (s, 2H).

**Synthesis of 1-(2,2-difluoroethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-47)**



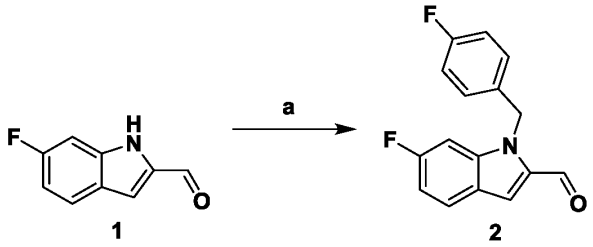

**[000356]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 1.0 g, 6.81 mmol) in *N, N*-dimethylformamide (10.0 mL), cesium carbonate (6.7 g, 20.01 mmol) and 2-bromo-1,1-difluoroethane (1.78 mL, 20.6 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (30 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 10% ethyl acetate in hexane as eluent to afford 1-(2,2-difluoroethyl)-1H-indole-2-carbaldehyde as brown solid. Yield: 0.91 g (63%). MS (ESI): 209.26, *m/z* found no ionization. $^1$HNMR (400 MHz, DMSO-d6): δ 9.98 (s, 1H), 7.82 (d, *J* = 8.1 Hz, 1H), 7.79 (d, *J* = 7.9 Hz, 1H), 7.57 (s, 1H), 7.45 (t, *J* = 8.0 Hz, 1H), 7.20 (t, *J* = 7.6 Hz, 1H), 6.33 (t, *J* = 54.3 Hz, 1H), 5.09-5.01 (m, 2H).

**Synthesis of 5-fluoro-1-(2-methoxyethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-48)**



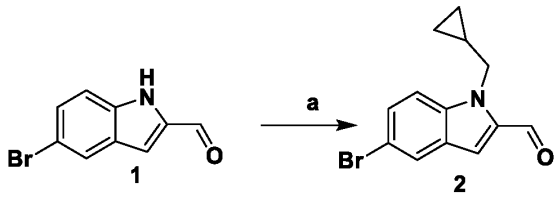
**[000357]** To the stirred solution of 5-fluoro-1H-indole-2-carbaldehyde (**1**, 0.5 g, 3.06 mmol) in *N, N*-dimethylformamide (20.0 mL), cesium carbonate (3.0 g, 9.18 mmol) and 1-bromo-2-methoxyethane (**2a**, 0.34 mL, 3.68 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 2 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (20 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 20% ethyl acetate in hexane as eluent to afford 5-fluoro-1-(2-methoxyethyl)-1H-indole-2-carbaldehyde as brown oil. Yield: 0.58 g (85%), MS (ESI) 221.0; *m/z* found 221.95 $[M+H]^{+1}$.

**Synthesis of 6-fluoro-1-(4-fluorobenzyl)-1H-indole-2-carbaldehyde (Intermediate for Example-49)**



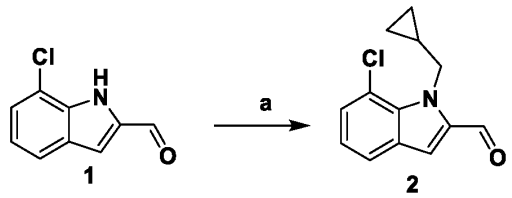

**[000358]** To the stirred solution of 6-fluoro-1H-indole-2-carbaldehyde (1, 1.00 g, 6.13 mmol) in *N, N*-dimethylformamide (10 mL), cesium carbonate (5.98 g, 18.4 mmol) and 1-(bromomethyl)-4-fluorobenzene (1.38 g, 7.36 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 1 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (200 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 5% ethyl acetate in hexane as eluent to afford 6-fluoro-1-(4-fluorobenzyl)-1H-indole-2-carbaldehyde as off white solid. Yield: 1.20 g (75%). MS (ESI); 271.08 *m/z* found: 272.19.

**Synthesis of 5-bromo-1-(cyclopropylmethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-67)**



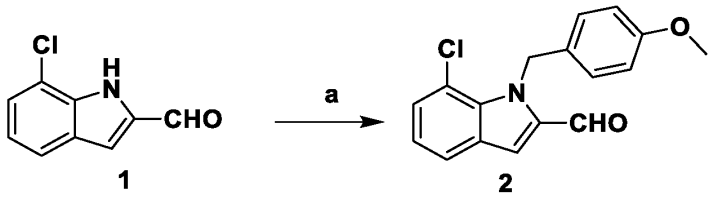

**[000359]** To the stirred solution of 5-bromo-1H-indole-2-carbaldehyde (1, 5 g, 32.9 mmol) in *N, N*-dimethylformamide (60 mL), cesium carbonate (29.5g, 90.5mmol) and (bromomethyl)cyclopropane (4.8 mL, 36.2 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (200 mL x 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by combi flash using 12 g Redisep and 20% ethyl acetate in hexane to afford the 5-bromo-1-(cyclopropylmethyl)-1H-indole-2-carbaldehyde as solid. Yield: 3.5 g (55%). MS (ESI): 278.06; *m/z* found 279.19.

**Synthesis of 1-(cyclopropylmethyl)-7-chloro-1H-indole-2-carbaldehyde (Intermediate for Example-57)**




**[000360]** To the stirred solution of 7-chloro-1H-indole-2-carbaldehyde (1, 5.4 g, 30.9 mmol) in *N, N*-dimethylformamide (60 mL), cesium carbonate (29.5g, 90.5mmol) and (bromomethyl)cyclopropane (4.8 mL, 36.2 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (200 mL x 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by combi flash using 12 g Redisep and 20% ethyl acetate in hexane to afford the 1-(cyclopropylmethyl)-7-chloro-1H-indole-2- carbaldehyde as sticky solid. Yield: 3.0 g (42%). $^1$HNMR (400 MHz, DMSO-d6): δ(ppm): 9.92 (s, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.62 (s, 1H) 7.47 (d, *J* = 8.0 Hz, 1H), 7.16 (t, *J* = 7.6 Hz, 1H), 4.80 (d, *J* = 6.92 Hz, 2H), 1.26 (m, 1H), 0.42-0.34 (m, 4H). MS (ESI): 233.06; *m/z* found 234.19.

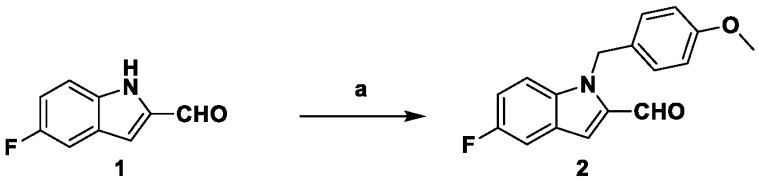
**Synthesis of 7-chloro-1-(4-methoxybenzyl)-1H-indole-2-carbaldehyde (Intermediate for Example-39)**




1 2

**[000361]** To the stirred solution of 7-chloro-1H-indole-2-carbaldehyde, 0.5 g, 2.78 mmol) in *N, N*-dimethylformamide (10.0 mL), cesium carbonate (2.7 g, 8.35 mmol) and 1-(chloromethyl)-4-methoxybenzene (0.52 g, 3.34 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (30 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 10% ethyl acetate in hexane as eluent to afford 7-chloro-1-(4-methoxybenzyl)-1H-indole-2-carbaldehyde as yellow oil. Yield: 0.40 g (47%). MS (ESI): 299.0, *m/z* found 300.19 $[M+H]^{+1}$.

**Synthesis of 5-fluoro-1-(4-methoxybenzyl)-1H-indole-2-carbaldehyde (Intermediate for Example-46)**

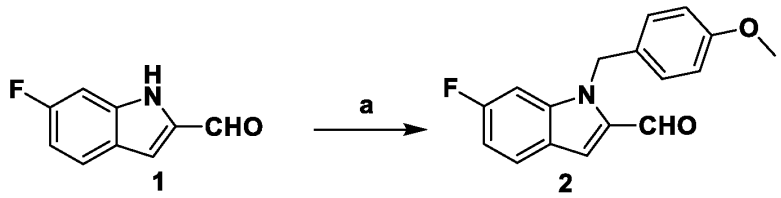



1 2

**[000362]** To the stirred solution of 5-fluoro-1H-indole-2-carbaldehyde (1, 0.5 g, 3.06 mmol) in *N, N*-dimethylformamide (20.0 mL), cesium carbonate (3.0 g, 9.18 mmol) and 1-(chloromethyl)-4-(methoxymethyl)benzene (0.72 mL, 3.68 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 2 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (25 mL x 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 20% ethyl acetate in hexane as eluent to afford 5-fluoro-1-(4-methoxybenzyl)-1H-indole-2-carbaldehyde as yellow oil. Yield: 0.52 g (60%). MS (ESI): 283.06; *m/z* found no ionization. $^1$HNMR (400 MHz,

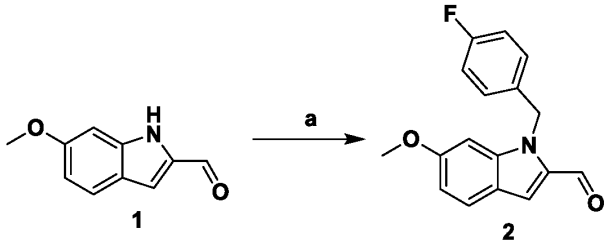
DMSO-d6): δ 9.95 (s, 1H), 7.74 (d, *J* = 6.28 Hz, 1H), 7.70 (d, *J* = 4.28 Hz, 1H), 7.52 (s, 1H), 7.30-7.27 (m, 1H), 7.08 (d, *J* = 13.5 Hz, 2H), 6.82 (d, *J* = 8.7 Hz, 2H), 5.76 (s, 2H), 3.67 (s, 3H).

**Synthesis of 6-fluoro-1-(4-methoxybenzyl)-1H-indole-2-carbaldehyde (Intermediate for Example-50)**




**[000363]** To the stirred solution of 6-fluoro-1H-indole-2-carbaldehyde ( 0.5 g, 3.06 mmol) in *N, N*-dimethylformamide (20.0 mL), cesium carbonate (3.0 g, 9.18 mmol) and 1-bromo-2-methoxyethane ( 0.34 mL, 3.68 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 2 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (20 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 20% ethyl acetate in hexane as eluent to afford 6-fluoro-1-(4-methoxybenzyl)-1H-indole-2-carbaldehyde as brown oil. Yield: 0.51 g (58%), MS (ESI) 283.1; *m/z* found 284.22 $[M+H]^{+1}$.

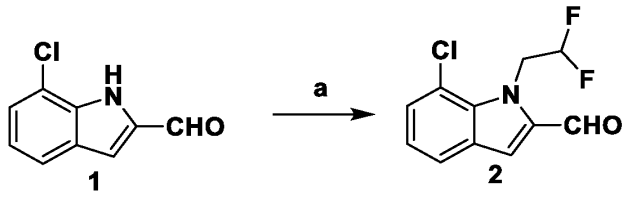
**Synthesis of 1-(4-fluorobenzyl)-6-methoxy-1H-indole-2-carbaldehyde (Intermediate for Example-51)**




**[000364]** To the stirred solution of 6-methoxy-1H-indole-2-carbaldehyde (, 0.70 g, 5.5 mmol) in *N, N*-dimethylformamide (10 mL), cesium carbonate (5.31 g, 16.3 mmol) and 1-(bromomethyl)-4-fluorobenzene (1.22 g, 5.6 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 1 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (200 mL × 2). The combined organic extracts were washed with brine, dried over

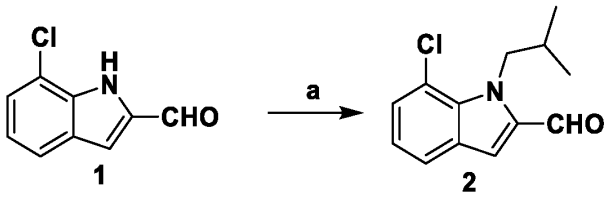
anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 5% ethyl acetate in hexane as eluent to afford 1-(4-fluorobenzyl)-6-methoxy-1H-indole-2-carbaldehyde as yellow solid. Yield: 1.0 g (90%). MS (ESI);283.1 *m/z* found: 284.18.

**Synthesis of 7-chloro-1-(2,2-difluoroethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-56)**




**[000365]** To the stirred solution of 7-chloro-1H-indole-2-carbaldehyde (0.9 g, 5.0 mmol) in *N, N*-dimethylformamide (20.0 mL), cesium carbonate (4.9 g, 15 mmol) and 2-bromo-1,1-difluoroethane (0.868 g, 6.0 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (30 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated to afford **7**-chloro-1-(2,2-difluoroethyl)-1H-indole-2-carbaldehyde. Yield: 1.46 g (Crude). MS (ESI): 243.03, *m/z* found 244.00$[M+H]^{+1}$.

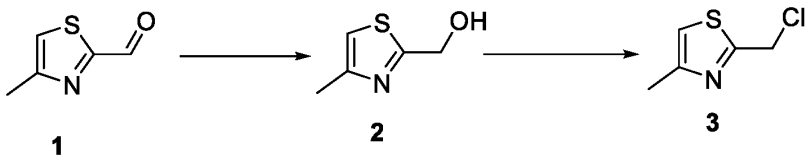
**Synthesis of 7-chloro-1-isobutyl-1H-indole-2-carbaldehyde (Intermediate for Example-55)**



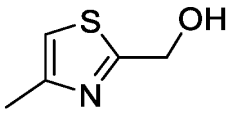

**[000366]** To the stirred solution of 7-chloro-1H-indole-2-carbaldehyde (0.7 g, 3.90 mmol) in *N, N*-dimethylformamide (20.0 mL), cesium carbonate (3.8 g, 11.69 mmol) and 1-bromo-2-methylpropane (0.53 g, 3.90 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (30 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 5% ethyl acetate in hexane as eluent to afford 7-

chloro-1-isobutyl-1H-indole-2-carbaldehyde as yellow oil. Yield: 0.50 g (54%). MS (ESI): 235.71, *m/z* found 236.62 $[M+H]^{+1}$.

**Synthesis of2-(chloromethyl)-4-methylthiazole (Intermediate for Example -59)**

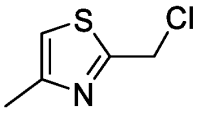



**Step A: (4-methylthiazol-2-yl)methanol**



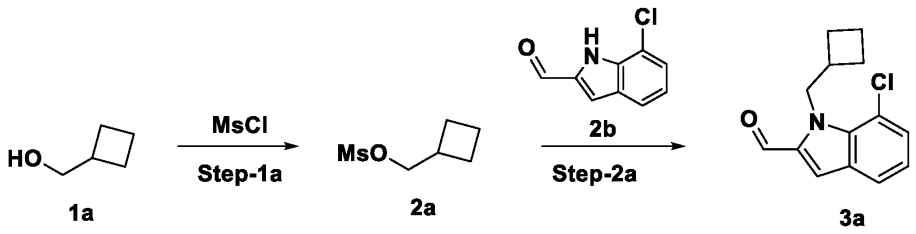

**[000367]** To the stirred solution of 4-methylthiazole-2-carbaldehyde (**1**, 1.0 g, 7 mmol) in MeOH (30 mL) at 0 °C, was added sodium borohydrate (0.52 g, 14 mmol) lot wise. The reaction mixture was stirred at room temperature for 2h. The reaction mixture was diluted with water (15 mL) and extracted with EtOAc (2 X 25 mL). Organic layer was washed with brine (15mL) solution, dried over anhydrous $Na_2SO_4$ and evaporated. The crude residue was purified by gradient column chromatography using 40-60% EtOAc in Hexane to afford the product as pale yellow gummy. (0.9g, 90%, Yield). MS (ESI): mass calcd.for $C_5H_7NOS$, 129.02; *m/z* found 130.1 $(M+H)^+$.

**Step B: 2-(chloromethyl)-4-methylthiazole**



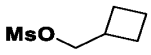

**[000368]** To a stirred solution of (4-methylthiazol-2-yl)methanol (**2**, 0.9 g, 6.97 mmol) in DCM (5 mL), was added $SOCl_2$ (0.83 mL, 11 mmol) drop wise at 0 °C and the reaction mixture was stirred at room temperature for 1 h. The reaction mixture was neutralized using cold $NaHCO_3$ (5 mL) solution and extracted with DCM (2 X 25 mL). Organic layer was washed with brine (5mL) solution, dried over anhydrous $Na_2SO_4$ and evaporated to afford the product as yellow oil. (1 g). MS (ESI): mass calcd.for $C_5H_6ClNS$ , 146.99; *m/z* found 148.1 $(M+H)^+$.

**Synthesis of 7-chloro-1-(cyclobutylmethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-53)**



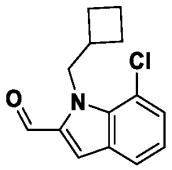

1a 2a 3a

**Step -1a: preparation of cyclobutylmethyl methanesulfonate (2a)**



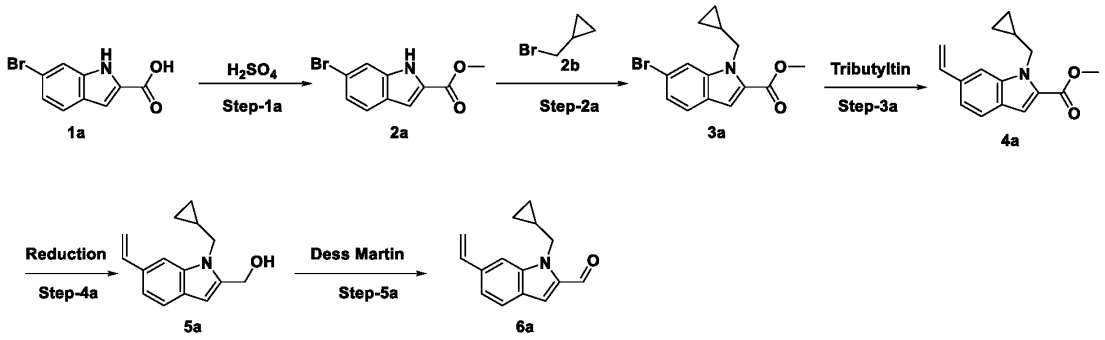

**[000369]** To the stirred solution of cyclobutylmethanol (**1a**, 2.00 g, 23.2 mmol) in dichloromethane (20 mL), triethylamine (6.50 mL, 46.5 mmol) and *N,N*-dimethylaminopyridine (0.28 g, 2.3 mmol) were added at room temperature, mesyl chloride (2.27 mL, 27.9 mmol) was added at 0 °C. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, reaction mixture was diluted with water and extracted with dichloromethane (20 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g Redisep and 10% ethyl acetate in hexanes as eluent, to afford the cyclobutylmethyl methanesulfonate as colorless oil (**2a**). Yield: 2.50 g (66%); MS (ESI) 164.05; *m/z* found no ionization. $^1$HNMR (400 MHz, DMSO-d6): δ(ppm): 4.16 (d, *J* = 6.76 Hz, 2H), 3.16 (s, 3H), 2.67-2.60 (m, 1H), 2.05-1.98 (m, 2H), 1.94-1.76 (m, 4H).

**Step-2a: Synthesis of 7-chloro-1-(cyclobutylmethyl)-1H-indole-2-carbaldehyde (3a)**

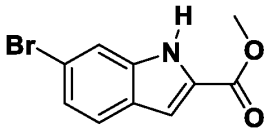



**[000370]** To the stirred solution of 7-chloro-1H-indole-2-carbaldehyde (**2b**, 0.90 g, 5.0 mmol) in *N, N*-dimethylformamide (10 mL), cesium carbonate (4.90 g, 15.1 mmol) and cyclobutylmethyl methanesulfonate (**2a**, 0.98 g, 6.0 mmol) were added at room temperature. The reaction mixture was stirred at 60 °C for 3 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (20 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g Redisep and 20% ethyl acetate in hexanes as eluent, to afford the 7-chloro-1-(cyclobutylmethyl)-1H-indole-2-carbaldehyde as pale yellow sticky solid (**3a**). Yield: 0.32 g (26%); MS (ESI) 247.08; *m/z* found 248.10 $[M+H]^{+1}$.

**Synthesis of 1-(cyclopropylmethyl)-6-vinyl-1H-indole-2-carbaldehyde (Intermediate for Example-61)**

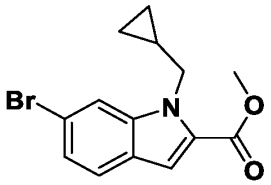



**Step-1a preparation of methyl-6-bromo-1H-indole-2-carboxylate (2a)**




**[000371]** To the stirred solution of 6-bromo-1H-indole-2-carboxylic acid (**1a**, 5.0 g, 20.83 mmol) in methanol (50.0 mL), sulphuric acid (9 mL, 1.8 vol) was added at 0 °C. The reaction mixture was stirred at 80 °C for 12 h. After completion of reaction, the reaction mixture was quenched with ice and precipitated solid was filtered and washed with water (100 mL × 2). The compound obtained was dried under vacuum. The crude was purified by CombiFlash using 40 g RediSep and 10% ethyl acetate in hexane as eluent to afford methyl-6-bromo-1H-indole-2-carboxylate as white solid (**2a**). Yield: 4.5 g (86%). MS (ESI): 252.99 *m/z* found 253.99 $[M+H]^{+1}$.

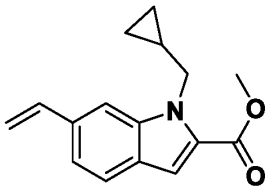
**Step-2a:preparation of methyl 6-bromo-1-(cyclopropylmethyl)-1H-indole-2-carboxylate (3a)**




**[000372]** To the stirred solution of 1H-indole-2-carbaldehyde (**2a**, 4.5 g, 17.85 mmol) in *N, N*-dimethylformamide (40 mL), cesium carbonate (17.4 g, 53.27 mmol) and (bromomethyl)cyclopropane (**2b**, 2.8 g, 21.42 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 2 h. After completion of

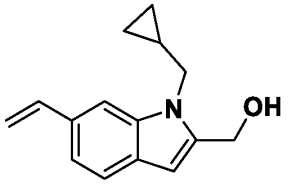
reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (30 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 10% ethyl acetate in hexane as eluent to afford methyl-6-bromo-1-(cyclopropylmethyl)-1H-indole-2-carboxylate as white solid (**3a**). Yield: 4.0 g (74%). MS (ESI): 307.18, *m/z* found 308.04 $[M+H]^{+1}$.

**Step-3a: preparation of methyl-1-(cyclopropylmethyl)-6-vinyl-1H-indole-2-carboxylate (4a)**



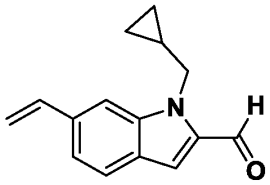

**[000373]** To the stirred solution of methyl-6-bromo-1-(cyclopropylmethyl)-1H-indole-2-carboxylate (**3a**, 4.0 g, 13.02 mmol) in *N, N*-dimethylformamide (40.0 mL), lithium chloride (0.656 g, 15.63 mmol) and tributyl vinyl tin (4.9 g, 15.63 mmol) were added at room temperature. Argon was purged for15 min, tetrakis(triphenylphosphine) palladium (0) (0.75 g, 0.65 mmol) was added at room temperature. The reaction mixture was stirred at 90 °C for 4 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (40 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 40 g RediSep and 5%-10% ethyl acetate in hexane as eluent to afford methyl 1-(cyclopropylmethyl)-6-vinyl-1H-indole-2-carboxylate as brown solid (**4a**). Yield: 3.1 g (92%). MS (ESI): 255.13, *m/z* found 256.11 $[M+H]^{+1}$.

**Step-4a: preparation of (1-(cyclopropylmethyl)-6-vinyl-1H-indol-2-yl) methanol (5a)**



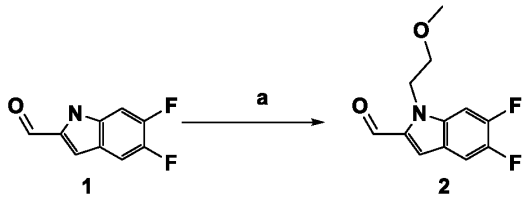
**[000374]** To the stirred solution of methyl-1-(cyclopropylmethyl)-6-vinyl-1H-indole-2-carboxylate (**4a**, 2.7 g, 10.5 mmol) in tetrahydrofuran (30.0 mL), 1.0 M lithium aluminum hydrate in tetrahydrofuran (20 mL, 21.0 mmol) were added at 0 °C . The reaction mixture was stirred at room temperature for 2 h. After completion of reaction, the reaction mixture was diluted with ammonium chloride and extracted with ethyl acetate (30 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12.0 g Redisep and 20% ethyl acetate in hexane as eluent to afford (1-(cyclopropylmethyl)-6-vinyl-1H-indol-2-yl)methanol as white solid (**5a**).Yield: 2.0 g (83%). MS (ESI): 227.13, *m/z* found 228.13 $[M+H]^{+1}$.

**Step-5a: preparation of 1-(cyclopropylmethyl)-6-vinyl-1H-indole-2-carbaldehyde**



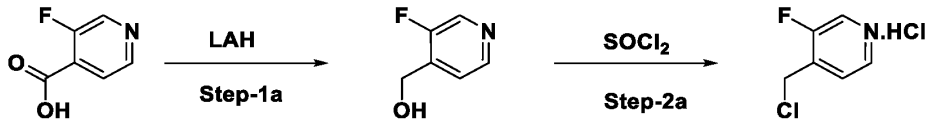

**[000375]** To the stirred solution of (1-(cyclopropylmethyl)-6-vinyl-1H-indol-2-yl)methanol ( 2.0 g, 8.73 mmol) in dichloromethane (20.0 mL), Dess Martin periodinane (4.4g, 10.48 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 4 h. After completion of reaction, the reaction mixture was diluted with water and extracted with dichloromethane (20 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 30% ethyl acetate in hexane as eluent to afford 1-(cyclopropylmethyl)-6-vinyl-1H-indole-2-carbaldehyde as white solid (**6a**). Yield: 1.1 g (55%). MS (ESI): 225.12, *m/z* found 226.12 $[M+H]^{+1}$.

**Synthesis of 5,6-difluoro-1-(2-methoxyethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-54)**



**[000376]** To the stirred solution of 5,6-difluoro-1H-indole-2-carbaldehyde (1, 0.50 g, 2.76 mmol) in *N, N*-dimethylformamide (10 mL), cesium carbonate (2.69 g, 8.28 mmol) and 1-bromo-2-methoxyethane (0.32 mL, 3.31 mmol) were added at room temperature. The reaction mixture was stirred at 60 °C for 3 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (200 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 10% ethyl acetate in hexane as eluent to afford 5,6-difluoro-1-(2-methoxyethyl)-1H-indole-2-carbaldehyde as yellow solid. Yield: 0.66 g (45%). MS (ESI); 239.08 *m/z* found 240.04 $[M+H]^{+1}$.

**Synthesis of 4-(chloromethyl)-3-fluoropyridine hydrochloride (Intermediate for Example-24)**




1a 2a 3a

**Step-1a: preparation of (3-fluoropyridin-4-yl)methanol (2a)**



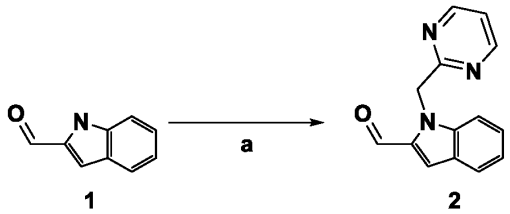

**[000377]** To a solution of 3-fluoroisonicotinic acid (**1a**, 2.0 g, 14.2 mmol) in tetrahydrofuran (20 mL), Lithium aluminium hydride (1M in tetrahydrofuran), (12.0 mL, 21.3 mmol) was added drop wise over 10 min at 0 °C and reaction mixture was stirred for 2 h at 0 °C. After completion of reaction, 40% potassium hydroxide solution was (60 mL) was added to reaction mixture. The solid precipitated was filtered off and washed with diethyl ether. The crude was purified by CombiFlash using 12 g RediSep and 20% ethyl acetate in hexane as eluent to afford (3-fluoropyridin-4-yl) methanol (**2a**) as off white solid. Yield: 0.50 g (28%). MS (ESI): 127.04; *m/z* found, 128.01 $[M+H]^{+1}$.

**Step 2a: *preparation* of 4-(chloromethyl)-3-fluoropyridine hydrochloride (3a)**



**[000378]** To a stirred solution of (3-fluoropyridin-4-yl)methanol (**2a**, 0.70 g, 5.51 mmol) in N,N-dichloromethane (5.0 mL), at 0 °C, was added thionyl chloride (1.00 g, 13.78 mmol), the reaction mixture was then stirred at room temperature for 1 h. After completion of reaction dichloromethane was removed under reduced pressure and crude obtained was washed with diethyl ether and dried to afford 4-(chloromethyl)-3-fluoropyridine hydrochloride **3a** as light brown solid. Yield: 1.0 g (90%). MS (ESI): 180.99; m/z found, 182.02$[M+H]^+$.

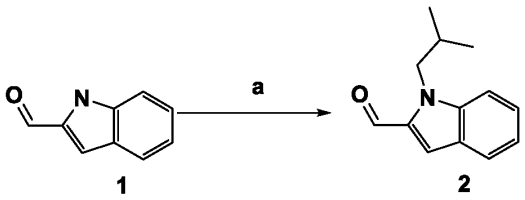
**Synthesis of 1-(pyrimidin-2-ylmethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-27)**




**[000379]** To the stirred solution of 1H-indole-2-carbaldehyde (1, 0.70 g, 4.82 mmol) in *N, N*-dimethylformamide (10 mL), cesium carbonate (7.8 g, 24.1mmol) and 2-(chloromethyl)pyrimidine (0.98 g, 7.24 mmol) were added at room temperature. The reaction mixture was stirred at 60 °C for 3 h. After completion of reaction, reaction mixture was cooled to room temperature, diluted with water and extracted with ethyl acetate (200 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 10% ethyl acetate in hexane as eluent to afford 1-(pyrimidin-2-ylmethyl)-1H-indole-2-carbaldehyde as brown crystalline solid. Yield: 1.30 g (81%). MS (ESI): 237.09; *m/z* found 238.14 $[M+H]^{+1}$.

**[000380]** $^1$HNMR (400 MHz, DMSO-d6): δ 9.87 (s, 1H), 8.68 (d, *J* = 4.8 Hz, 2H), 7.80 (d, *J* = 8.0 Hz, 1H) 7.55 (d, *J* = 5.84 Hz, 2H), 7.36 (d, *J* = 4.72 Hz, 2H), 7.16(t, *J* = 7.36 Hz, 1H), 6.0 (s, 2H).

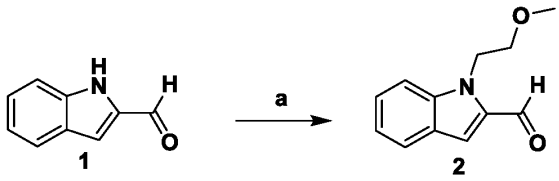
**Synthesis of 1-isobutyl-1H-indole-2-carbaldehyde (Intermediate for Example-31)**



**[000381]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 0.70 g, 4.82 mmol) in *N, N*-dimethylformamide (10 mL), cesium carbonate (7.8 g, 24.1mmol) and (1-bromo-2-methylpropane (0.98 g, 7.24 mmol) were added at room temperature. The reaction mixture was stirred at 60 °C for 3 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (200 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 10% ethyl acetate in hexane as eluent to afford 1-isobutyl-1H-indole-2-carbaldehyde as oily liquid. Yield: 0.80 g (82%). MS (ESI); 201.12 *m/z* found 202.30 $(M+H)^+$.

**[000382]** $^1$HNMR (400 MHz, DMSO-d6): δ 9.89 (s, 1H), 7.77 (d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 8.44 Hz, 1H), 7.48 (s, 1H), 7.39 (t, *J* = 7.5 Hz, 1H), 7.15 (t, *J* = 7.4 Hz, 1H), 4.37 (d, *J* = 7.4 Hz, 2H), 2.11-2.04 (m, 1H), 0.81 ((d, *J* = 6.64 Hz, 6H).

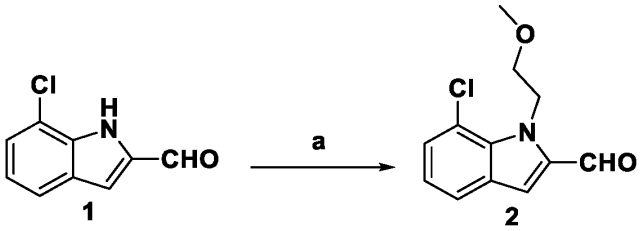
**Synthesis of 1-(2-methoxyethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-22)**




**[000383]** To the stirred solution of 1H-indole-2-carbaldehyde (1, 1.0 g, 6.0 mmol) in *N, N*-dimethylformamide (6.0 mL), cesium carbonate (6.6 g, 20.6 mmol) and 1-bromo-2-methoxyethane (0.76 mL, 8.0 mmol) were added at room temperature. The reaction mixture was stirred at 60 °C for 1.5 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (200 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 20% ethyl acetate in hexane as eluent to afford the 1-(2-methoxyethyl)-1H-indole-2-carbaldehyde as light yellow solid. Yield: 0.9 g (64%). MS (ESI): 203; *m/z* found no ionization.

**[000384]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 9.89 (s, 1H), 7.75 (d, *J* = 8.4 Hz, 1H), 7.63 (d, *J* = 8.8 Hz, 1H) 7.47 (s, 1H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.15 (t, *J* = 7.6 Hz, 1H), 4.70 (t, *J* = 5.6 Hz, 2H), 3.61 (t, *J* = 5.2 Hz, 2H), 3.17 (s, 3H).

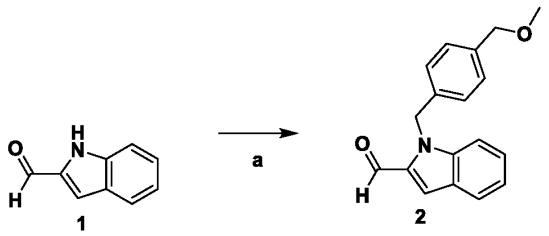
**Synthesis of 7-chloro-1-(2-methoxyethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-36)**




**[000385]** To the stirred solution of 7-chloro-1H-indole-2-carbaldehyde (**1**, 0.5 g, 2.79 mmol) in *N, N*-dimethylformamide (15 mL), cesium carbonate (2.7 g, 8.37 mmol) and 1-bromo-2-methoxyethane (0.31 mL, 3.35 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (50 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 20% ethyl acetate in hexane as eluent to afford 7-chloro-1-(2-methoxyethyl)-1H-indole-2-carbaldehyde as yellow oil. Yield: 0.34 g (52%). MS (ESI): 237.06; *m/z* found no ionization.

**[000386]** $^1$HNMR (400 MHz, DMSO-d6): δ(ppm): 9.93 (s, 1H), 7.77 (d, *J* = 8.0 Hz, 1H), 7.56 (s, 1H) 7.45 (d, *J* = 7.5 Hz, 1H), 7.15 (t, *J* = 7.8 Hz, 1H), 5.13 (t, *J* = 5.9 Hz, 2H), 3.62 (t, *J* = 5.9 Hz, 2H), 3.16 (s, 3H).

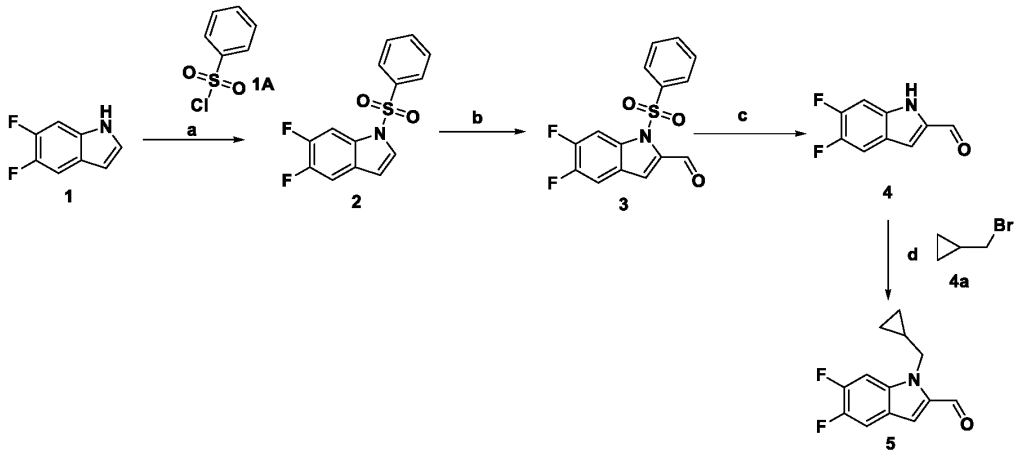
**Synthesis of 1-(4-(methoxymethyl)benzyl)-1H-indole-2-carbaldehyde (Intermediate for Example-37)**



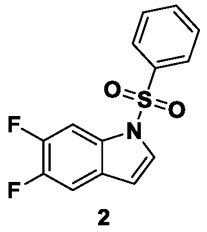

**[000387]** To the stirred solution of 1H-indole-2-carbaldehyde (1, 1.0 g, 6.0 mmol) in *N, N*-dimethylformamide (5.0 mL), cesium carbonate (0.58 g, 1.79 mmol) and (41-(bromomethyl)-4-(methoxymethyl)benzene (0.14 g, 0.72 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (20 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude

was purified by CombiFlash using 12 g RediSep and 5% methanol in dichloromethane as eluent to afford the 1-(4-(methoxymethyl)benzyl)-1H-indole-2-carbaldehyde.

**Synthesis of 1-(cyclopropylmethyl)-5,6-difluoro-1H-indole-2-carbaldehyde (Intermediate for Example-32 & 77)**

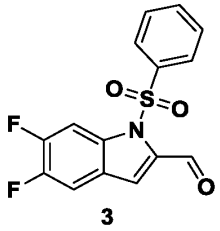



**Step 1a: Preparation of 5,6-Difluoro-1-(phenylsulfonyl)-1H-indole (2)**



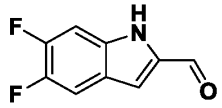

**[000388]** To a solution of sodium hydride (0.26 g, 13 mmol) in DMF (10 mL) was added solution of 5,6-difluoro-1H-indole (**1**, 0.52 g, 13 mmol) in DMF at 0 °C, drop wise over 15 min. Followed by addition of solution of benzenesulfonyl chloride in DMF (1.4 g, 13 mmol) at 0 °C and stirred for 2 h at room temperature under $N_2$ atmosphere. To the reaction mixture was added ice cold water (50 mL), then filtered off the precipitate and washed with ice cold water to obtain brown solid. (1 g, 26 % Yield). MS (ESI) *m/z* 293.0 $(M+H)^+$.

**Step 2b: Preparation of 5,6-Difluoro-1-(phenylsulfonyl)-1H-indole-2-carbaldehyde (3)**



**[000389]** To a solution of 5,6-difluoro-1-(phenylsulfonyl)-1H-indole (**2**, 1 g, 3.42 mmol) in dry THF (50 mL) was added lithium diisopropylamide 1M in THF (3.4 mL g, 6.84mmol) at -78 °C and stirred for 5-8 min, followed by addition of dry DMF (0.5mL, at -78°C and stirred for 10 min at -78°C under $N_2$ atmosphere. To the reaction mixture was added aqueous ammonium chloride (20 mL), then extracted in to EtOAc. Organic layer was washed with saturated $NH_4Cl$ solution and brine, dried over sodium sulphate, filtered and concentrated under reduced pressure to obtain brown solid (0.7 g, 70 %). MS (ESI) *m/z* 322.0 $(M+H)^+$.

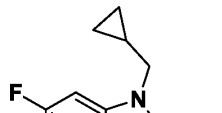
**Step 3c: Preparation of 5,6-Difluoro-1H-indole-2-carbaldehyde (4)**



**4**

**[000390]** To the stirred solution of 5,6-Difluoro-1-(phenylsulfonyl)-1H-indole-2-carbaldehyde (**3**, 0.8 g, 2.49 mmol) in THF (50 mL), was added TBAF (1M in THF) (9.15 mL, 12.45 mmol) at room temperature. The reaction mixture was stirred at room temperature for 12 h. The reaction mixture was diluted with water and extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using 15-25% ethyl acetate in hexane to afford the 5-fluoro-1H-indole-2-carbaldehyde as sticky solid (0.4 g, 88% Yield) MS (ESI): Mass calcd. for $C_9H_5F_2NO$, 181.145; m/z found, 182 $(M+H)^+$.

**Step 4d: Preparation of 1-(cyclopropylmethyl)-5,6-difluoro-1H-indole-2-carbaldehyde (5)**

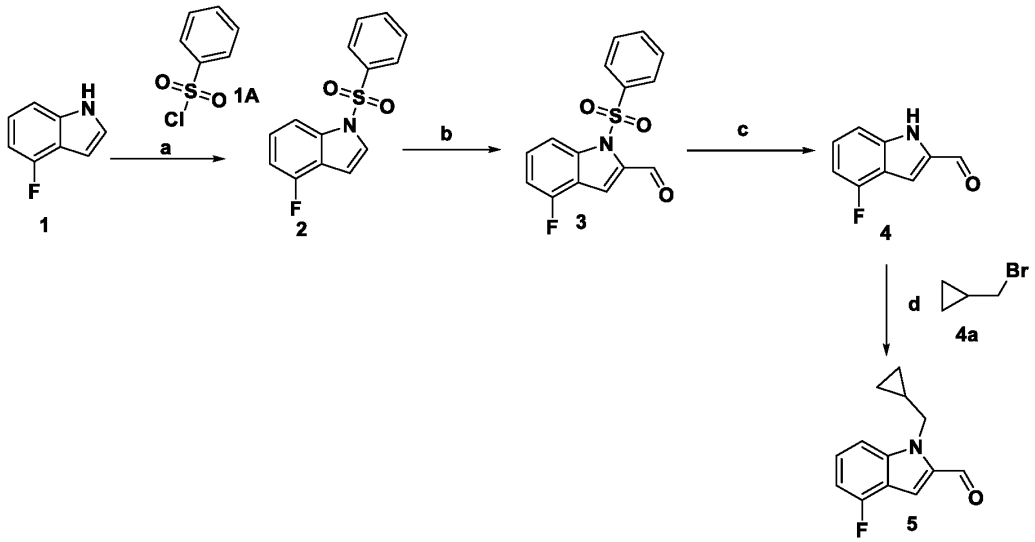


**5**

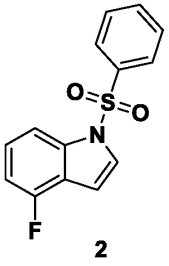
**[000391]** To the stirred solution of 5,6-difluoro-1H-indole-2-carbaldehyde (**4**, 0.3 g, 1.65 mmol) in DMF (20 mL), were added potassium carbonate (0.68g, 4.97 mmol) and (bromomethyl)cyclopropane (4a, 0.16 mL, 1.82 mmol) at room temperature. The reaction mixture was stirred at room temperature for 12 h. The reaction mixture was diluted with water and extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude product. The

crude residue was purified by gradient column chromatography using 3-7% ethyl acetate in hexane to afford the 1-(cyclopropylmethyl)-5,6-difluoro-1H-indole-2-carbaldehyde as off white solid (0.2 g, 48% Yield). $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 9.86 (s, 1H), 7.90-7.78 (m, 2H), 7.48 (s, 1H), 4.42 (d, $J$ = 6.8 Hz, 2H), 1.20 ( bs, 1H), 0.39-0.35 (m, 4H), MS (ESI): Mass calcd. for $C_{13}H_{11}F_2NO$, 235.23; m/z found, 236.1 $[M+H]^+$.

**Synthesis of 1-(cyclopropylmethyl)-4-fluoro-1H-indole-2-carbaldehyde (Intermediate for Example-80)**

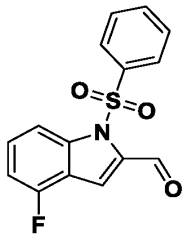



**Step 1: Preparation of 4-fluoro-1-(phenylsulfonyl)-1H-indole (2)**




**[000392]** To a solution of sodium hydride (0.88 g, 22.2 mmol) in DMF (50 mL) was added solution of 4-fluoro-1H-indole (**1**, 3.0 g, 22.2 mmol) in DMF at 0 °C, dropwise over 15 min. Benzenesulfonyl chloride in DMF (2.86 mL, 22.2 mmol) was added at 0$^0$C and stirred for 2 h at room temperature under $N_2$ atmosphere. To the reaction mixture was added ice cold water (50 mL), then filtered off the precipitate and washed with ice cold water to obtain white solid. (7.0 g - crude).

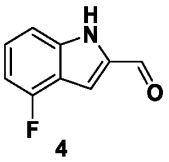
**Step 2: Preparation of 4-fluoro-1-(phenylsulfonyl)-1H-indole-2-carbaldehyde (3)**



3

**[000393]** To a solution of 4-fluoro-1-(phenylsulfonyl)-1H-indole (**2**, 7.0 g, 22.0 mmol) in dry THF (60 mL) was added lithium diisopropylamide 2M in THF (10.9 mL, 22.0 mmol) at -78 °C and stirred for 5-8 min, followed by addition of dry DMF (2.5 mL, 33.0 mmol) at -78 °C and stirred for 10 min at -78 °C under $N_2$ atmosphere. To the reaction mixture was added aqueous ammonium chloride (20 mL), then extracted in to EtOAc. Organic layer was washed with saturated $NH_4Cl$ solution and brine, dried over sodium sulphate, filtered and concentrated under reduced pressure to obtain red liquid (6.80 g, 88.31 %).

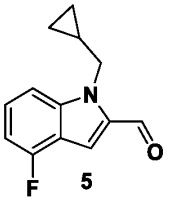
**Step 3: Preparation of 4-fluoro-1H-indole-2-carbaldehyde (4)**



4

**[000394]** To a solution of 4-fluoro-1-(phenylsulfonyl)-1H-indole-2-carbaldehyde (**4,** 3.0 g, 9.9 mmol) in dry THF (20 mL) was added tetrabutyl ammonium fluoride 1M in THF (14.8 mL) and the reaction mixture was stirred for about 12 h under room temperature. The reaction mixture was quenched with water and, then extracted with ethyl acetate (50 mL x 3). Combined organic extracts were washed with brine, dried over sodium sulfate, filtered and evaporated to get crude product. Crude residue was purified by gradient column chromatography using 5-10% ethyl acetate in hexane to get the product as yellow solid. (Yield: 99%, 1.6 g). MS (ESI): Mass calcd. for $C_9H_6FNO$, 163.04; *m/z* found 164 $(M+H)^+$.

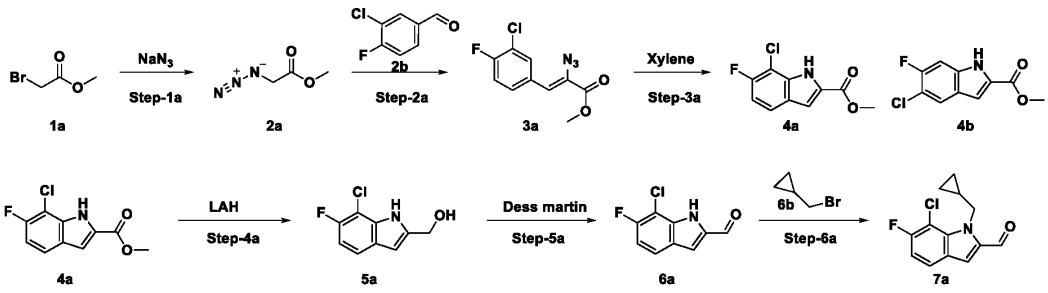
**Step- 4: Preparation of 1-(cyclopropylmethyl)-4-fluoro-1H-indole-2-carbaldehyde (5)**



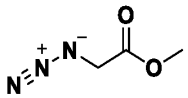
5

**[000395]** To a stirred solution of 4-fluoro-1H-indole-2-carbaldehyde (**4**, 1.6 g, 9.877 mmol) in DMF (10 mL), was added potassium carbonate (6.8g, 49.38mmol) followed by (bromomethyl)cyclopropane (6, 1.4 mL, 10.65 mmol) and the reaction mixture was stirred at room temperature for 12h. The reaction mixture was quenched with water, extracted with ethyl acetate (30 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate, filtered and evaporated to get crude product. Crude residue was purified by gradient column chromatography using 5-10% ethyl acetate in hexane to get the product as brown liquid. (Yield: 47.6%, 1 g). $^1$HNMR (400 MHz, DMSO-$d_6$): δ 9.90 (s, 1H), 7.55-7.50 (m, 2H), 7.40-7.35 (m, 1H), 6.95-6.90 (m, 1H), 4.46 (d, *J* = 8 Hz, 2H), 1.22-1.21 (m, 1H), 0.42-0.36 (m, 4H). MS (ESI): Mass calcd. for $C_{13}H_{12}FNO$, 217.24; m/z found, 218 $[M+H]^+$.

**Synthesis of 7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indole-2-carbaldehyde (Intermediate for Example-87)**

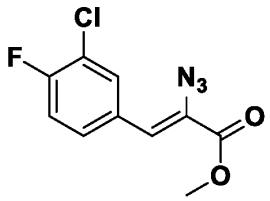



**Step-1a: Synthesis of methyl-2-azidoacetate (2a)**



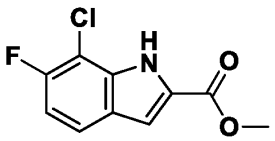
**[000396]** To a stirred solution of methyl-2-bromoacetate (**1a**, 20.0 g, 131.5 mmol) in *N, N*-dimethylformamide (40.0 mL), sodium azide (10.2 g, 157.8 mmol) was added at 0 °C. The reaction mixture was stirred at room temperature for 16 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (100 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure to afford methyl 2-azidoacetate as oily liquid (**2a**). Yield: 11.2 g (74%). ELSD MS (ESI): 115.04, *m/z* found 116.10 $[M+H]^{+1}$.

**Step-2a: Synthesis of methyl (Z)-2-azido-3-(3-chloro-4-fluorophenyl)acrylate (3a)**

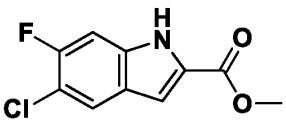



**[000397]** To a stirred solution of methanol (25 mL), sodium metal (1.09 g, 47.46 mmol) was added at room temperature and allowed to stir at room temperature for 10 min. Methyl-2-azidoacetate (**2a**, 2.50 g, 15.80 mmol) and 3-chloro-4-fluorobenzaldehyde (**2b**, 6.10 g, 53.70 mmol) solution in methanol (5.0 mL) were added at -15 °C. The reaction mixture was stirred at -15 °C for 4 h. After completion of reaction, the reaction mixture was neutralized with 1 N Hydrogen chloride at 0 °C up to pH ~7. The precipitated solid was filtered, washed with water (10 mL × 2). The compound obtained was dried under vacuum to afford methyl (Z)-2-azido-3-(3-chloro-4-fluorophenyl)acrylate (**3a**) as light yellow solid. Yield: 1.8 g (45%). MS (ESI): 255.02, *m/z* found 256.25 $[M+H]^{+1}$.

**Step-3a: Synthesis of methyl-7-chloro-6-fluoro-1H-indole-2-carboxylate (4a)**



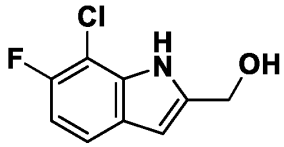

**4a**




**4b**

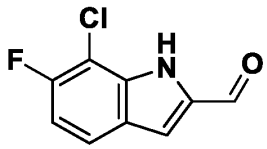
**[000398]** The stirred solution of methyl (Z)-2-azido-3-(3-chloro-4-fluorophenyl)acrylate (**3a**, 1.80 g, 7.05 mmol) in *p*-xylene (80.0 mL) was refluxed at 140 °C for 2 h. After completion of reaction, the reaction mixture was concentrated under reduced pressure. The resulting crude was purified by CombiFlash using 40.0 g RediSep column. Desired methyl-7-chloro-6-fluoro-1H-indole-2-carboxylate (**4a**) was obtained at 2% ethyl acetate in hexanes and methyl 5-chloro-6-fluoro-1H-indole-2-carboxylate (**4b**) was obtained at 5% ethyl acetate in hexanes. Desired fraction was concentrated to afford methyl-7-chloro-6-fluoro-1H-indole-2-carboxylate (**4a**) as light brown solid. Yield: 1.1 g (Crude). MS (ESI): 227.01, *m/z* found 228.01 $[M+H]^{+1}$.

**Step-4a: Synthesis of (7-chloro-6-fluoro-1H-indol-2-yl)methanol (5a)**



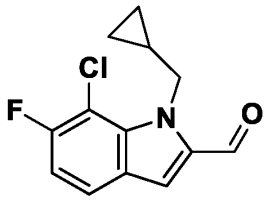

**[000399]** To a stirred solution of methyl-7-chloro-6-fluoro-1H-indole-2-carboxylate (**4a**, 1.0 g, 4.4 mmol) in tetrahydrofuran (20.0 mL), 1.0 M lithium aluminum hydrate in tetrahydrofuran (8.8 ml, 8.80 mmol) was added at 0 °C . The reaction mixture was stirred at room temperature for 2 h. After completion of reaction, the reaction mixture was diluted with ammonium chloride and extracted with ethyl acetate (30 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 40 g RediSep column and 20% ethyl acetate in hexane as eluent to afford (7-chloro-6-fluoro-1H-indol-2-yl)methanol as sticky solid (**5a**). Yield: 8.24 g (91%). MS (ESI): 199.02, *m/z* found 200.05 $[M+H]^{+1}$.

**Step-5a: Synthesis of 7-chloro-6-fluoro-1H-indole-2-carbaldehyde (6a)**



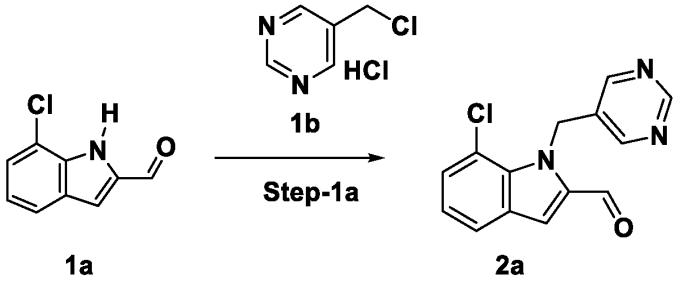

**[000400]** To a stirred solution of (7-chloro-6-fluoro-1H-indol-2-yl)methanol (**5a**, 0.80 g, 4.00 mmol) in dichloromethane (30.0 mL), Dess Martin periodinane (3.4 g, 8.00 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 4 h. After completion of reaction, the reaction mixture was diluted with water and extracted with dichloromethane (20 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12.0 g RediSep column and 2-5% ethyl acetate in hexane as eluent to afford 7-chloro-6-fluoro-1H-indole-2-carbaldehyde as white solid (**6a**). Yield: 0.63 g (75%). MS (ESI): 197.0, *m/z* found 198.12 $[M+H]^{+1}$.

**Step-6a: Synthesis of 7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indole-2-carbaldehyde (7a)**




**[000401]** To a stirred solution of 7-chloro-6-fluoro-1H-indole-2-carbaldehyde (**6a**, 0.30 g, 1.52 mmol) in *N, N*-dimethylformamide (15.0 mL), cesium carbonate (1.40 g, 4.56 mmol) and (bromomethyl)cyclopropane (**6b**, 0.29 mL, 3.04 mmol) were added at room temperature. The reaction mixture was stirred at 60 °C for 30 min. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (30 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12.0 g RediSep column and 10% ethyl acetate in hexane as eluent to afford 7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indole-2-carbaldehyde as sticky solid (**7a**). Yield: 0.33 g (88%). MS (ESI): 251.05, *m/z* found 252.25 $[M+H]^{+1}$.

**Synthesis of 7-chloro-1-(pyrimidin-5-ylmethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-88)**




**[000402]** To a stirred solution of 7-chloro-1H-indole-2-carbaldehyde (**1a**, 0.500 g, 2.79 mmol) in *N, N*-dimethylformamide (10.0 mL), cesium carbonate (2.7 g, 8.37 mmol) and 5-(chloromethyl) pyrimidine hydrochloride (**1b**, 0.429 g, 3.34 mmol) were added at room temperature. The reaction mixture was stirred at room temperature about 16 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (10 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12.0 g RediSep and 30% ethyl acetate in hexane as eluent to afford 7-chloro-1-(pyrimidin-5-ylmethyl)-1H-indole-2-carbaldehyde as yellow solid (**2a**). Yield: 0.260 g (34%). MS (ESI): 271.10, *m/z* found 272.19 $[M+H]^{+1}$.

## BIOLOGICAL ASSAYS:

### FP Binding assay

**[000403]** Binding of compounds with PAD4 enzyme was detected by FP assay. PAD4 enzyme was diluted to 1 uM in assay buffer (100 mM HEPES, 50 mM NaCl, 1 mM DTT, 5% Glycerol and 1 mM CHAPS) and added to wells containing various concentration of compounds or DMSO vehicle (1%) in a 384 well black plate. 10 nM of fluorescein labelled probe (JPAD -00085) was added to the plate. Assay plate was incubated for 60 minutes at room temperature before measuring FP reading at FP module (λex 485/λem 535 nm) on Pherastar. $IC_{50}$ was calculated using XL-fit software model 205. (Ref: Nat Chem Biol. 2015 Mar;11(3):189-91).

### Ammonia Release Biochemical assay

Citrullination assay was detected via ammonia release. PAD4 enzyme was diluted to 120 nM in assay buffer (100 mM HEPES, 50 mM NaCl, 2 mM DDT, 0.6 mg/mL BSA, pH 7.4) added to wells containing various concentration of compound or DMSO vehicle (1 % final) in black 384 well plate. Following a 60-min preincubation at room temperature, the reaction was initiated by the addition of substrate (1.5 mM BAEE in 200 mM HEPES, 50 mM NaCl, 350 uM CaCl2, 2 mM, pH 7.4). The reaction was stopped after 60 min by addition of stop/detection buffer containing 50 mM EDTA, 2.6 mM of o-phthaladehyde and 2.6 mM DTT. Assay was incubated at room temperature for 90 min before measuring fluorescence's (λex 405/λem 460 nm) on Tecan reader. $IC_{50}$ was calculated using XL-fit software model 205. (Ref: Nat Chem Biol. 2015 Mar;11(3):189-91).

### Anti-PAD4 activity:

**[000404]** **Table 1**, below, shows the activity of selected compounds of this disclosure in the PAD4 assays described above. Compounds having an activity designated as "**A**" provided $IC_{50} \leq$ 1uM; compounds having an activity designated as "**B**" provided $IC_{50}$ 1 – 10 uM; and compounds having an activity designated as "C" provided $IC_{50} \geq$10 uM.

**Table 1:** PAD4 enzymatic activity

| Example No. | NH3 release; PAD4 $IC_{50}$ (uM) | FP PAD4 $IC_{50}$ (uM) |
|---|---|---|
| 1 | A | B |

| | | |
|---|---|---|
| 2 | B | nd |
| 3 | B | nd |
| 4 | C | C |
| 5 | B | B |
| 6 | B | nd |
| 7 | B | nd |
| 8 | A | A |
| 9 | A | A |
| 10 | A | A |
| 11 | A | A |
| 12 | A | A |
| 13 | A | B |
| 14 | B | A |
| 15 | A | B |
| 16 | A | B |
| 17 | A | B |
| 18 | A | B |
| 19 | A | A |
| 20 | A | nd |
| 21 | A | nd |
| 22 | A | nd |
| 23 | A | nd |
| 24 | A | nd |
| 25 | A | nd |
| 26 | A | nd |
| 27 | A | nd |
| 28 | A | nd |
| 29 | B | nd |

| | | |
|---|---|---|
| 30 | B | nd |
| 31 | A | nd |
| 32 | A | nd |
| 33 | A | nd |
| 34 | A | nd |
| 35 | A | nd |
| 36 | A | nd |
| 37 | A | nd |
| 38 | C | nd |
| 39 | A | nd |
| 40 | B | nd |
| 41 | A | nd |
| 42 | C | nd |
| 43 | C | nd |
| 44 | B | nd |
| 45 | C | nd |
| 46 | A | nd |
| 47 | A | nd |
| 48 | A | nd |
| 49 | A | nd |
| 50 | A | nd |
| 51 | A | nd |
| 52 | B | nd |
| 53 | A | nd |
| 54 | B | nd |
| 55 | A | nd |
| 56 | A | nd |
| 57 | A | nd |
| 58 | B | nd |

| | | |
|---|---|---|
| **59** | **A** | **nd** |
| **60** | **A** | **nd** |
| **61** | **A** | **nd** |
| **62** | **C** | **nd** |
| **63** | **A** | **A** |
| **64** | **A** | **A** |
| **65** | **A** | **A** |
| **66** | **A** | **B** |
| **67** | **A** | **nd** |
| **68** | **B** | **nd** |
| **69** | **A** | **nd** |
| **70** | **A** | **nd** |
| **71** | **A** | **nd** |
| **72** | **A** | **A** |
| **73** | **A** | **A** |
| **74** | **A** | **nd** |
| **75** | **A** | **nd** |
| **76** | **A** | **B** |
| **77** | **A** | **A** |
| **78** | **A** | **nd** |
| **79** | **B** | **nd** |
| **80** | **B** | **nd** |
| **81** | **C** | **nd** |
| **82** | **B** | **nd** |
| **83** | **B** | **nd** |
| **84** | **A** | **nd** |
| **85** | **A** | **nd** |
| **86** | **A** | **nd** |
| **87** | **A** | **nd** |

| | | |
|---|---|---|
| **88** | **B** | **nd** |

nd= not determined

**[000405]** Table 1 illustrates that most of the compounds (from Examples 1-88) were found to be active against the PAD4 enzyme when evaluated through both Ammonia Release Biochemical and FP Binding assays. The $IC_{50}$ values display the efficacy of the compounds in inhibiting the PAD4 enzyme activity. $IC_{50}$ value indicates how much of a particular drug or a compound is needed to inhibit a given biological process or component of a process such as an enzyme. A low value of $IC_{50}$ denotes high inhibition efficacy of the test compound (Examples 1-88 as described herein). However, in the above Table 1, high efficacy is denoted by "A" , "B", and "C", wherein "A" having least value of $IC_{50}$ and thus most effective.

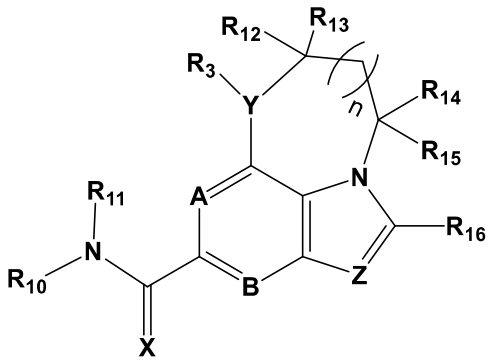
**[000406]** The Ammonia Release Biochemical assay showed that 62 out of 88 compounds showed an $IC_{50}$ value of $\leq$ 1µM denoted by "A". These 62 compounds were Examples- 1, 8-13, 15-28, 31-37, 39, 41, 46-51, 53, 55-57, 59-61, 63-67, 69-78, and 84-88.

**[000407]** On the other hand, the FP Binding assay showed 13 out of 23 tested compounds to be actively inhibiting PAD4 enzyme activity. The individual examples being Examples- 8-12, 14, 19, 63-65, 72, 73, and 77 respectively.

**[000408]** Therefore, it may be inferred that Examples- 1, 8-13, 15-28, 31-37, 39, 41, 46-51, 53, 55-57, 59-61, 63-67, 69-78, and 84-87 are identified, and could be developed, as potential drugs for alleviating PAD4 enzyme activity and thus treating PAD4 mediated disorders.

**I/We claim**:

**1.** A compound of Formula (I)




Formula (I)

their stereoisomers and pharmaceutically acceptable salts thereof, wherein

X is O or S;

Y is O or N;

Z is N;

A is $CR_1$;

B is $CR_2$;

n is 0-1;

$R_1$ and $R_2$ are independently selected from hydrogen;

$R_3$ is absent or is selected from hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2C_6$ aryl, and $SO_2C_{1-6}$ alkyl, wherein $SO_2C_{1-6}$ alkyl, and $SO_2C_6$ aryl is optionally substituted with $C_{1-6}$ alkoxy, halogen, and $C_6$ aryl;

$R_{10}$ and $R_{11}$ are taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein,

the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from amino, $-NHC(O)CH=CHCH_2N(CH_3)_2$, or $C_{1-6}$ alkylamino;

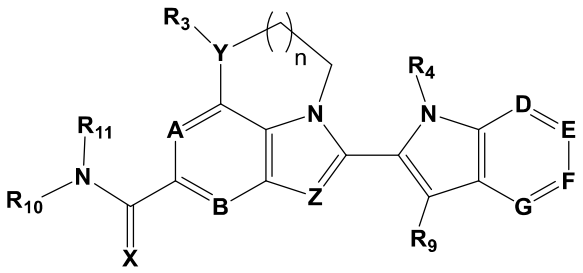
$R_{12}$, $R_{13}$, $R_{14}$ and $R_{15}$ are independently selected from hydrogen or $C_{1-6}$ alkyl; and

$R_{16}$ is 5-10 membered bicyclic heteroaryl with 1-2 heteroatoms selected from N or S, wherein,

5-10 membered bicyclic heteroaryl is optionally substituted with 1-3 substituents selected from the group consisting of halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl- $C_6$ aryl, $C_{2-6}$ alkenyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-}$

$_6$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and -COOH.

**2.** A compound of Formula (II)




Formula (II)

their stereoisomers and pharmaceutically acceptable salts thereof,

wherein,

X is O or S;

Y is O or N;

Z is N;

A is $CR_1$;

B is $CR_2$;

D is selected from N or $CR_5$;

E is $CR_6$;

F is $CR_7$;

G is $CR_8$;

n is 1-2;

$R_1$, $R_2$ and $R_9$ are independently selected from hydrogen;

$R_5$, $R_6$, $R_7$ and $R_8$ are independently selected from the group consisting of hydrogen, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{2-6}$ alkenyl- $C_6$ aryl, and $C_{1-6}$ heteroaryl;

$R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $SO_2C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, and $SO_2C_6$ aryl, wherein, $SO_2C_6$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, and $C_6$ aryl;

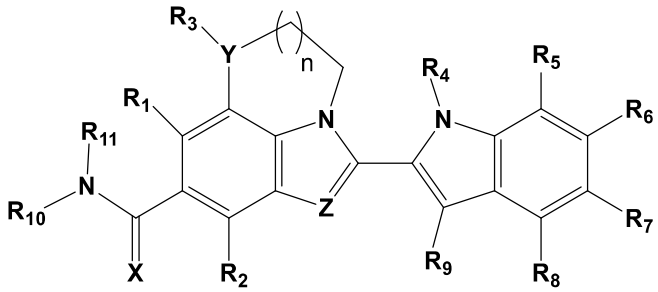
$R_4$ is selected from the group consisting of $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, is

optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and -COOH; and

$R_{10}$ and $R_{11}$ are taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein,

the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, and -$NHC(O)CH=CHCH_2N(CH_3)_2$.

**3.** A compound of Formula (III)




Formula (III)

their stereoisomers and pharmaceutically acceptable salts thereof,

wherein,

X is O or S;

Y is O or N;

Z is N;

n is 1-2;

$R_1$, $R_2$ and $R_9$ are independently selected from hydrogen;

$R_5$, $R_6$, $R_7$ and $R_8$ are independently selected from the group consisting of hydrogen, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{2-6}$ alkenyl- $C_6$ aryl, and $C_{1-6}$ heteroaryl;

$R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $SO_2C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, and $SO_2C_6$ aryl, wherein, $SO_2C_6$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, and $C_6$ aryl;

$R_4$ is selected from the group consisting of $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and -COOH; and

$R_{10}$ and $R_{11}$ are taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein,

the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, and -$NHC(O)CH=CHCH_2N(CH_3)_2$.

**4.** The compound of Formula (I) as claimed in claim 1 or its stereoisomers and pharmaceutically acceptable salts thereof, which is selected from a group consisting of:

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(1)**,

(R)-(3-aminopyrrolidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(2)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-ethyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(3)**,

(2-(aminomethyl)piperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(4)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-ethyl-1H-pyrrolo[2,3-b]pyridin-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(5)**,

(R)-(3-aminopiperidin-1-yl)(1-(1-(cyclopropylmethyl)-1H-indol-2-yl)-8,9-dihydro-7H-6-oxa-2,9a-diazabenzo[cd]azulen-4-yl)methanone **(6)**,

(R)-(3-aminopyrrolidin-1-yl)(1-(1-(cyclopropylmethyl)-1H-indol-2-yl)-8,9-dihydro-7H-6-oxa-2,9a-diazabenzo[cd]azulen-4-yl)methanone **(7)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-methyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(8)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(9)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-4-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(10)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-2-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(11)**,

(R)-(3-aminopiperidin-1-yl)(2-(3-ethylbenzo[b]thiophen-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(12)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(4-chlorobenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(13)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(2-fluorobenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(14)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(4-fluorobenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(15)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-3-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(16)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5,6-dimethoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(17)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-benzyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(18)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(4-methoxybenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(19)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(20)**,
(R)-(3-aminopiperidin-1-yl)(2-(6-methoxy-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(21)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(2-hydroxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(22)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-methoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(23)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-((3-fluoropyridin-4-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(24)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(pyrazin-2-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(25)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-((3-fluoropyridin-2-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(26)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(pyrimidin-2-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(27)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(28)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(pyrimidin-5-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(29)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridazin-3-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(30)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-isobutyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(31)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5,6-difluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(32)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-((3-fluoropyridin-2-yl)methyl)-6-methoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(33)**,
(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-((3-fluoropyridin-2-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(34)**,
(R)-(3-aminopiperidin-1-yl)(2-(6-fluoro-1-((3-fluoropyridin-2-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(35)**,
(*R*)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(36)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(4-(hydroxymethyl)benzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone trifluoroacetic acid salt **(37)**,
(R,E)-N-(1-(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)-4-(dimethylamino)but-2-enamide trifluoroacetic acid salt **(38)**,
(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(4-methoxybenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(39)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-((tetrahydro-2H-pyran-4-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(40)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclobutylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(41)**,
(R)-2-(2-(7-(3-aminopiperidine-1-carbonyl)-3,4-dihydro-5-ox1,2adiazaacenaphthylen-2-yl)-1H-indol-1-yl)acetic acid **(42)**,
(R)- (3-aminopiperidin-1-yl)(2-(1-(piperidin-4-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(43)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(oxetan-3-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(44)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-((1-methylpiperidin-4-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(45)**,
(*R*)-(3-aminopiperidin-1-yl)(2-(5-fluoro-1-(4-methoxybenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(46)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(2,2-difluoroethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(47)**,
(*R*)-(3-aminopiperidin-1-yl)(2-(5-fluoro-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(48)**,
(R)-(3-aminopiperidin-1-yl)(2-(6-fluoro-1-(4-fluorobenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(49)**,
(*R*)-(3-aminopiperidin-1-yl)(2-(6-fluoro-1-(4-methoxybenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(50)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(4-fluorobenzyl)-6-methoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(51)**,
3-aminopiperidin-1-yl)(2-(6-fluoro-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(52)**,
(*R*)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(cyclobutylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(53)**,
(R)-(3-aminopiperidin-1-yl)(2-(5,6-difluoro-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(54)**,
(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-isobutyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(55)**,
(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(2,2-difluoroethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(56)**,
(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(57)**,
(R,E)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-styryl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(58)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-((4-methylthiazol-2-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(59)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-methoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(60)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-(hydroxymethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl) methanone **(61)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,3-dimethyl-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(62)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(63)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(64)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(65)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-3-ylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(66)**,
(R)-(3-aminopiperidin-1-yl)(2-(5-bromo-1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(67)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-(pyridin-3-yl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(68)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-2-ylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(69)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(2-fluorobenzyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(70)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-4-ylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(71)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-methyl-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(72)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-methoxy-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(73)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-methoxy-1H-indol-2-yl)-6-methyl-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(74)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-6-methyl-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(75)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(methylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(76)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5,6-difluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(77)**,
(R)-(3-aminopiperidin-1-yl)(6-cyclopropyl-2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(78)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(phenethylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(79)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-4-fluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(80)**,

(R)-(3-aminopiperidin-1-yl)(6-((4-chlorophenyl)sulfonyl)-2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(81)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(cyclopropylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(82)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-((2-ethoxyethyl)sulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(83)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-methyl-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(84)**,

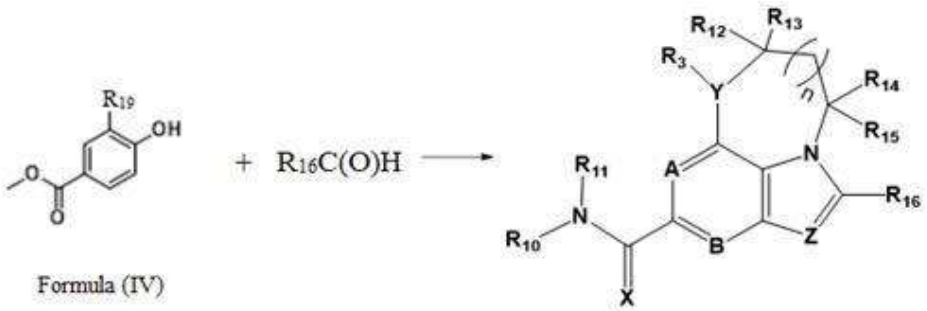
(R)-1-(8-(3-aminopiperidine-1-carbonyl)-2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-4,5-dihydro-6H-imidazo[1,5,4-de]quinoxalin-6-yl)ethan-1-one **(85)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanethione **(86)**,

(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(87)**, and

(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(pyrimidin-5-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(88)**.

**5.** A process of preparation of compounds of Formula (I) as claimed in any of claims 1 and 4 or its stereoisomers and pharmaceutically acceptable salts thereof, the process comprising reacting Formula (IV) and $R_{16}C(O)H$



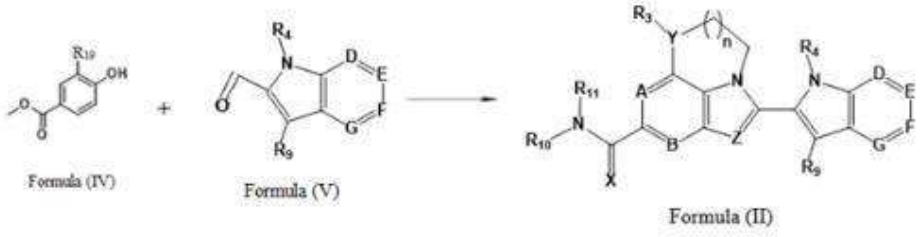

Formula (IV)

Formula (I)

wherein $R_{19}$ of Formula (IV) is selected from nitro and $C_{1-6}$ alkoxy; $R_{16}$ of $R_{16}C(O)H$ is 5-10 membered bicyclic heteroaryl with 1-2 heteroatoms selected from N or S, wherein, 5-10 membered bicyclic heteroaryl is optionally substituted with 1-3 substituents selected from the group consisting of halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{2-6}$ alkenyl- $C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$

heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and -COOH; X of Formula (I) is selected from O or S; Y is selected from O or N; Z is N; A is $CR_1$; B is $CR_2$; n is 0-1; $R_1$ and $R_2$ are independently selected from hydrogen; $R_3$ is absent or is selected from hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $SO_2C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, and $SO_2C_6$ aryl, wherein, $SO_2C_6$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, and $C_6$ aryl; $R_{10}$ and $R_{11}$ are taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein, the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from amino, $C_{1-6}$ alkylamino, and -$NHC(O)CH=CHCH_2N(CH_3)_2$; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from hydrogen and $C_{1-6}$ alkyl; $R_{16}$ is 5-10 membered bicyclic heteroaryl with 1-2 heteroatoms selected from N or S, wherein, 5-10 membered bicyclic heteroaryl is optionally substituted with 1-3 substituents selected from the group consisting of halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{2-6}$ alkenyl- $C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and -COOH.

**6.** A process of preparation of compounds of Formula (II) as claimed in any of claims 2 and 4 or its stereoisomers and pharmaceutically acceptable salts thereof, the process comprising reacting Formula (IV) and Formula (V)

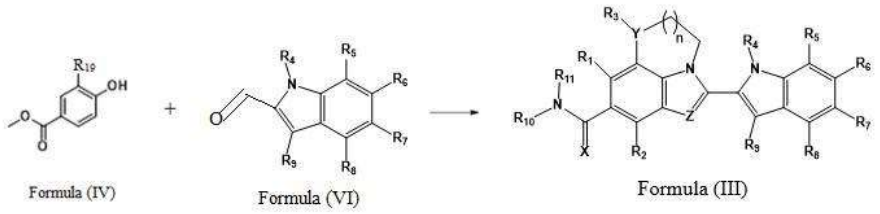



Formula (IV) Formula (V) Formula (II)

wherein $R_{19}$ of Formula (IV) is selected from nitro and $C_{1-6}$ alkoxy; X of Formula (II) is selected from O or S; Y is selected from O or N; Z is N; A is $CR_1$; B is $CR_2$; D is selected from N or $CR_5$; E is $CR_6$; F is $CR_7$; G is $CR_8$; n is 1-2; $R_1$, $R_2$ and $R_9$ are independently selected from hydrogen; $R_5$, $R_6$, $R_7$ and $R_8$ are independently selected

from the group consisting of hydrogen, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{2-6}$ alkenyl- $C_6$ aryl, and $C_{1-6}$ heteroaryl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $SO_2C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, and $SO_2C_6$ aryl, wherein, $SO_2C_6$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, and $C_6$ aryl; $R_4$ is selected from the group consisting of $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, $-CH_2OH$, and -COOH; $R_{10}$ and $R_{11}$ are taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, and $-NHC(O)CH=CHCH_2N(CH_3)_2$; D of Formula (V) is selected from N or $CR_5$; E is $CR_6$; F is $CR_7$; G is $CR_8$, $R_9$ is H; and $R_4$ is selected from the group consisting of $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, $-CH_2OH$, and -COOH.

**7.** A process of preparation of compounds of Formula (III) as claimed in any of claims 3-4 or its stereoisomers and pharmaceutically acceptable salts thereof, the process comprising reacting Formula (IV) and Formula (VI)




wherein $R_{19}$ of Formula (IV) is selected from nitro and $C_{1-6}$ alkoxy; X of Formula (III) is selected from O or S; Y is O or N; Z is N; n is 1-2; $R_1$, $R_2$ and $R_9$ are independently selected from hydrogen; $R_5$, $R_6$, $R_7$ and $R_8$ are independently selected from the group consisting of hydrogen, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{2-6}$ alkenyl- $C_6$ aryl, and $C_{1-6}$ heteroaryl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $SO_2C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, and $SO_2C_6$ aryl, wherein, $SO_2C_6$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy,

halogen, and $C_6$ aryl; $R_4$ is selected from the group consisting of $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and COOH; $R_{10}$ and $R_{11}$ are taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein, the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, and -$NHC(O)CH=CHCH_2N(CH_3)_2$; and $R_9$ of formula (VI) is hydrogen; $R_5$, $R_6$, $R_7$ and $R_8$ are independently selected from the group consisting of hydrogen, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{2-6}$ alkenyl- $C_6$ aryl, and $C_{1-6}$ heteroaryl; $R_4$ is selected from the group consisting of $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and COOH.

**8.** A pharmaceutical composition comprising a compound of Formula (I), Formula (II), and Formula (III) or a pharmaceutically acceptable salt thereof as claimed in any of claims 1-4 together with a pharmaceutically acceptable carrier, optionally in combination with one or more other pharmaceutical compositions.

**9.** The pharmaceutical composition as claimed in claim 8, wherein the composition is in the form selected from the group consisting of a tablet, capsule, powder, syrup, solution, aerosol, and suspension.

**10.** Compounds as claimed in any of the claims 1-4 or a pharmaceutically acceptable salt thereof for use as a medicament.

**11.** An *in vitro* method for inhibiting one or more PAD family in a cell with an effective amount of the compound as claimed in any of the claims 1-4.

**12.** Use of a pharmaceutical composition as claimed in any one of the claim 8 or 9 in the manufacture of a medicament for treating a condition selected from vasculitis, systemic lupus erythematosus, cancer, asthma, rheumatoid arthritis, ulcerative colitis, psoriasis, cystic fibrosis and cutaneous lupus erythematosus.

**13.** Use of the compound of Formula (I), Formula (II), and Formula (III) as claimed in any one of claims 1-4 in the manufacture of a medicament for the treatment of

rheumatoid arthritis, vasculitis, systemic lupus erythematosus, ulcerative colitis, cancer, cystic fibrosis, asthma, cutaneous lupus erythematosus and psoriasis.

**14.** Use of the compound as claimed in any one of claims 1-4 or the pharmaceutical composition as claimed in claim 8, or 9 together with other clinically relevant agents or biological agents in the manufacture of a medicament for the treatment and/or prevention of treatment of rheumatoid arthritis, vasculitis, systemic lupus erythematosus, ulcerative colitis, cancer, cystic fibrosis, asthma, cutaneous lupus erythematosus and psoriasis.

**15.** Use of the compound as claimed in any one of claims 1-4 or the pharmaceutical composition as claimed in claim 8, or 9 together with other clinically relevant agents or biological agents in the manufacture of a medicament for the treatment and/or prevention of acid-induced lung injury, respiratory distress syndrome, allergen induced asthma, allergic bronchopulmonary, chronic lung disease of prematurity, chronic obstructive pulmonary disease, colitis, cystic fibrosis, gouty arthritis, inflammatory bowel disease, inflammatory lung disease, inflammatory pain, juvenile rheumatoid arthritis, kidney disease, kidney injury caused by parasitic infections, kidney transplant rejection prophylaxis, lung injury, lupus, lupus nephritis, multiple sclerosis, muscular dystrophy, non-allergen induced asthma, osteoarthritis, periodontitis, peritoneal endometriosis, psoriasis, pulmonary disease, pulmonary fibrosis, pyogenic sterile arthritis, renal disease, rheumatic disease, rheumatoid arthritis, sepsis, severe pain and ulcerative colitis.

**16.** Use of a therapeutically effective amount of the compound as claimed in any one of the claims 1-4, or the pharmaceutical composition as claimed in claim 8 or 9 in the manufacture of a medicament for the treatment and/or prevention of a condition selected from acid-induced lung injury, respiratory distress syndrome, allergen induced asthma, allergic bronchopulmonary, chronic lung disease of prematurity, chronic obstructive pulmonary disease, colitis, cystic fibrosis, gouty arthritis, inflammatory bowel disease, inflammatory lung disease, inflammatory pain, juvenile rheumatoid arthritis, kidney disease, kidney injury caused by parasitic infections, kidney transplant rejection prophylaxis, lung injury, lupus, lupus nephritis, multiple sclerosis, muscular dystrophy, non-allergen induced asthma, osteoarthritis, periodontitis, peritoneal endometriosis, psoriasis, pulmonary disease, pulmonary fibrosis, pyogenic sterile arthritis, renal disease, rheumatic disease, rheumatoid arthritis, sepsis, severe pain and ulcerative colitis.

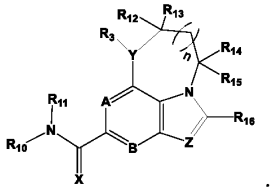
**17.** Use of a combination of the compounds as claimed in any of claims 1-4 or the pharmaceutical composition as claimed in claim 8 or 9, with other clinically relevant agents or biological agents in the manufacture of a medicament for the treatment of rheumatoid arthritis.

**18.** Use of a combination of the compounds as claimed in any of claims 1-4 or the pharmaceutical composition as claimed in claim 8 or 9, with other clinically relevant immune modulators agents in the manufacture of a medicament for the treatment of cancer.

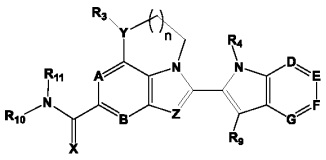
# HETEROCYCLIC COMPOUNDS AS PAD INHIBITORS

## TECHNICAL FIELD OF THE INVENTION

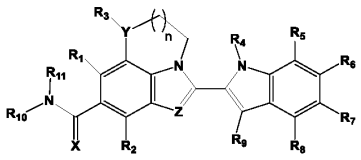
**[0001]** The present disclosure is directed to novel heterocyclic compounds of Formula (I), (II), and (III) along with their polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof which act as PAD4 inhibitors.



**Formula (I)**



**Formula (II)**



**Formula (III)**

The process for the preparation of the above heterocyclic compounds of the Formula (I), (II), and (III), their polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, pharmaceutical compositions, and metabolites, are also described herein which are useful in the preparation of such compounds.

**[0002]** The compounds described herein are PAD4 inhibitors and may be useful in the treatment of various disorders, for example rheumatoid arthritis, vasculitis, systemic lupus erythematosis, cutaneous lupus erythematosis, ulcerative colitis, cancer, cystic fibrosis, asthma, multiple sclerosis, and psoriasis.

## BACKGROUND OF THE INVENTION

**[0003]** The PAD (protein arginine de-iminase) consists of a family of enzymes that convert peptidyl-arginine to peptidyl citrulline. The process for this conversion is known as citrullination (J. E. Jones, et al. Curr. Opin. Drug Discov. Devel., 2009, 12, 616-627). There are five isozymes of the PAD family found in mammals, *viz*. PAD1, PAD2, PAD3, PAD4, and PAD6. The amino acid sequence of these isozymes share a sequence similarity of 70 – 95 % with mammals. Citrullination which is a post-translational modification of arginine to citrulline by the closely related enzymes of PAD family affect numerous physiological and pathological processes.

**[0004]** Citrullination has been implicated in various ailments, for example, cell differentiation (K. Nakashima et al., J. Biol. Chem., 1999, 274, 27786-27792), stem cell pluripotency (M. A. Christophorou et al., Nature, 2014, 507, 104-108), apoptosis (G. Y.

Liu, Apoptosis, 2006, 11, 183-196), neutrophil extracellular trap (NET) formation (Y. Wang et al., J. Cell Biol., 2009, 184, 205-213), transcriptional regulation (P. Li et al., Mol. Cell Biol., 2008, 28, 4745-4758), antigen processing in autophagy (J. M. Ireland et al., J. Exp. Med., 2011, 208, 2625-2632), inflammation (D. Makrygiannakis et al., Ann. Rheum. Dis., 2006, 65, 1219-1222), the cornification of skin (E. Candi et al., Nat. Rev. Mol. Cell Biol., 2005, 6, 328-340), demyelination in multiple sclerosis (F. G. Mastronardi et al., J. Neurosci., 2006, 26, 11387-11396), chemokine regulation (T. Loos et al., Blood, 2008, 112, 2648-2656), spinal cord injury repair (S. Lange et al., Dev. Biol., 2011, 355, 205-214), and various normal cellular processes.

**[0005]** The role of PAD in pathogenesis of many diseases has become increasingly evident as the enzymes that catalyze citrullination, also produce autoantibodies that recognize the citrullinated proteins. The introduction of citrulline, resultant of PAD activity, changes both the structure and function of proteins. At physiological activity levels, PADs regulate many cell-signaling pathways like cell differentiation, apoptosis, and gene transcription (György et al. Int. J. Biochem. Cell Biol., 2006, 38, 1662-1677). Over the past decade, it is becoming increasingly apparent that aberrant PAD activity is involved in many human inflammatory diseases such as, rheumatoid arthritis (RA), Alzheimer's disease, and multiple sclerosis (N. K. Acharya, J. Autoimmun., 2012, 38, 369-380).

**[0006]** PAD4 have also been known for the deamination or citrullination of a variety of proteins both *in vitro* and *in vivo*, with consequences of diverse functional response in a variety of diseases, such as, rheumatoid arthritis (RA), diseases with neutrophilic contributions to pathogenesis (for example, vasculitis, systemic lupus erythematosus, ulcerative colitis), along with oncology indications (J. E. Jones, et al. Curr. Opin. Drug Discov. Devel., 2009, 12, 616-627). PAD4 has been found to be involved in the formation of neutrophil extracellular traps (NETs) and more specifically in the histone citrullination that occurs during NETosis (J. Cedervall, A. -K. Olsson, Oncoscience, 2015, 2(11), 900-901). Thus, PAD4 enzyme is linked to diseases characterized by abnormal levels of neutrophil extracellular traps (NETs). The proposed role of PAD4 in NETosis is pertinent for rheumatoid arthritis (RA) as NETs are deficient in the absence of PAD4 and PAD4 is released extracellulary in RA joints, probably due to the pathological status of RA neutrophils.

**[0007]** Considering the fact that NETs are implicated in many diseases, the therapeutic potential of PAD inhibitor drugs would be significant. PAD4 inhibitors may also have

wider applicability as tools and therapeutics for human disease through epigenetic mechanisms.

**[0008]** In literature, a number of PAD inhibitors that are selective for PAD4 are known (H. D. Lewis *et al.*, Nature Chemical Biology, 2015, 11, 189-191). Some of these compounds are chloro-amidine, fluoro-chloridine and their related analogs act as mechanism-based inhibitors that irreversibly inactivate PAD4 and other PAD isozymes. The PAD4 inhibitor compounds have utility against rheumatoid arthritis (RA). PAD4, detected in synovial tissue, has been found to be responsible for citrullination of a variety of joint proteins. These citrullinated protein substrates produce anti-citrullinated antibodies which are responsible for disease pathogenesis (Y. Kochi et al., Ann. Rheum. Dis., 2011, 70, 512-515).

**[0009]** PAD4 inhibitors have also been known for alleviating pathological activity in a variety of diseases. Some specific studies show that the defence mechanism of neutrophils to eliminate pathogens, also known as NET formation is associated with histone citrullination (I. Neeli et al., J. Immunol., 2008, 180, 1895-1902). Therefore, PAD4 inhibitor compounds can be utilized in injuries and disease pathologies where NET formation in tissues occurs. In addition, PAD4 inhibitors have wider applicability to neutrophilic diseases.

**[00010]** US20170105971 discloses the alleviation, treatment and/ or prevention of auto immune diseases like, rheumatoid arthritis, osteoarthritis and arthralgia by using amidines as PAD inhibitor compounds. Another application US20050159334 also discusses the treatment of rheumatoid arthritis (RA) with the administration of suitable PAD inhibitor.

**[00011]** The PAD inhibitor compound chloro-amidine, has been widely studied to demonstrate their efficacy in several animal disease models like, collagen-induced arthritis (V. C. Willis et al., J. Immunol., 2011, 186(7), 4396-4404), dextran sulfate sodium (DSS)-induced experimental colitis (A. A. Chumanevich et al., Am. J. Physiol. Gastrointest. Liver Physiol., 2011, 300(6), G929-G938), lupus-prone MRL/lpr mice atherosclerosis and arterial thrombosis (J. S. Knight et al., Circ. Res., 2014, 114(6), 947-956), spinal cord injury repair (S. Lange et al., Dev. Biol., 2011, 355(2), 205-214), and experimental autoimmune encephalomyelitis (EAE). The study on DSS colitis demonstrated that chloro-amidine drives *in vitro* and *in vivo* apoptosis of inflammatory cells, indicating the efficacy of PAD4 inhibitors in treating inflammatory diseases.

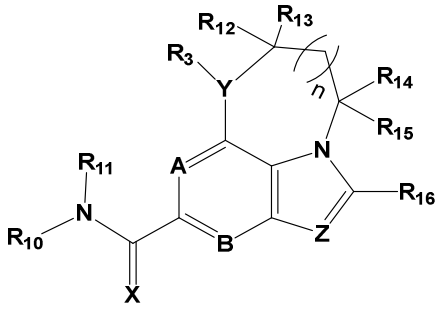
**[00012]** PAD4 is predominantly expressed in granulocytes and is strongly linked to diverse diseases. In multiple tumors, PAD4 is found to be overexpressed affecting the p53 function and downstream pathways. Calcium binding to PAD promotes the bioactive conformation, increasing PAD4 activity by ten thousand times.

**[00013]** Slack *et al.* demonstrated the use of PAD4 inhibitors in the treatment of cancers (J. L. Slack et al., Cellular and Molecular Life Sciences, 2011, 68(4), 709-720). Overexpression of PAD4 had already been demonstrated in numerous cancers (X. Chang et al., BMC Cancer, 2009, 9, 40). It is suggested that PAD4 inhibitors have an anti-proliferative role as well. PAD4 deiminases arginine residues in histones at the promoters of p53- target genes such as p21, which are involved in cell cycle arrest and induction of apoptosis (P. Li et al., Molecular & Cell Biology, 2008, 28(15), 4745-4758).

**[00014]** PAD inhibition is a viable strategy for the treatment of numerous diseases mentioned above. The use of PAD inhibitors in various other diseases where dysregulated PAD activity is implicated needs to be explored. Although a definitive role for dysregulated PAD activity in these diseases has not been established, a direct link is plausible. However, there remains an unmet need to identify and develop PAD4 inhibitors which may treat PAD4 mediated disorders with efficacy.

**SUMMARY**

**[00015]** The present invention refers to subject matter as defined in the attached set of claims. In one example, present disclosure discloses a compound of Formula (I)




**Formula (I)**

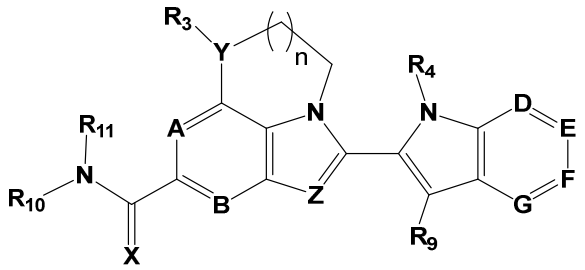
their polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof,

wherein X is selected from O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy,

$C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10

membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00016]** In another example, present disclosure also discloses compound of Formula (II)




**Formula (II)**

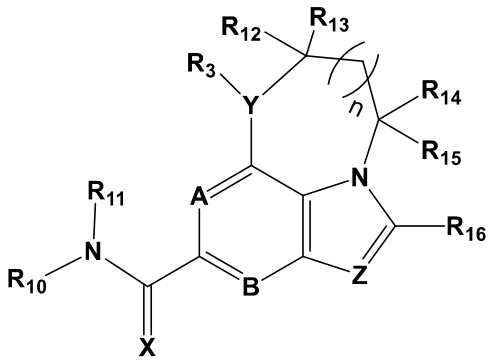
their polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof,

wherein

X is selected from O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; D is selected from N or $CR_5$; E is selected from N or $CR_6$; F is selected from N or $CR_7$; G is selected from N or $CR_8$; n is 0-2; $R_1$, $R_2$, $R_5$, $R_6$, $R_7$, $R_8$, and $R_9$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl,

wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_4$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, -COOH, and cyano; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of $C_{1-6}$ alkylamino, and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00016a]** In another aspect, there is provided a compound of Formula (I)




Formula (I)

their stereoisomers and pharmaceutically acceptable salts thereof, wherein

X is O or S;

Y is O or N;

Z is N;

A is $CR_1$;

B is $CR_2$;

n is 0-1;

$R_1$ and $R_2$ are independently selected from hydrogen;

$R_3$ is absent or is selected from hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2C_6$ aryl, and $SO_2C_{1-6}$ alkyl, wherein $SO_2C_{1-6}$ alkyl, and $SO_2C_6$ aryl is optionally substituted with $C_{1-6}$ alkoxy, halogen, and $C_6$ aryl;

$R_{10}$ and $R_{11}$ are taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein,

the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from amino, $-NHC(O)CH=CHCH_2N(CH_3)_2$, or $C_{1-6}$ alkylamino;

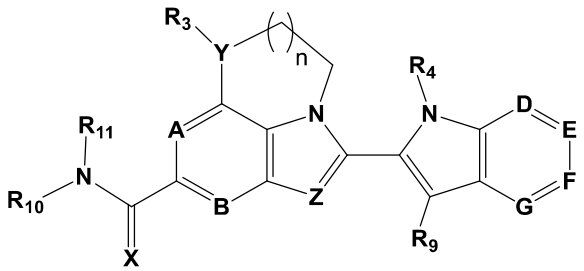
$R_{12}$, $R_{13}$, $R_{14}$ and $R_{15}$ are independently selected from hydrogen or $C_{1-6}$ alkyl; and

$R_{16}$ is 5-10 membered bicyclic heteroaryl with 1-2 heteroatoms selected from N or S, wherein,

5-10 membered bicyclic heteroaryl is optionally substituted with 1-3 substituents selected from the group consisting of halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl- $C_6$ aryl, $C_{2-6}$ alkenyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one

or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and -COOH.

**[00016b]** In another aspect, there is provided a compound of Formula (II)




Formula (II)

their stereoisomers and pharmaceutically acceptable salts thereof,

wherein,

X is O or S;

Y is O or N;

Z is N;

A is $CR_1$;

B is $CR_2$;

D is selected from N or $CR_5$;

E is $CR_6$;

F is $CR_7$;

G is $CR_8$;

n is 1-2;

$R_1$, $R_2$ and $R_9$ are independently selected from hydrogen;

$R_5$, $R_6$, $R_7$ and $R_8$ are independently selected from the group consisting of hydrogen, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{2-6}$ alkenyl- $C_6$ aryl, and $C_{1-6}$ heteroaryl;

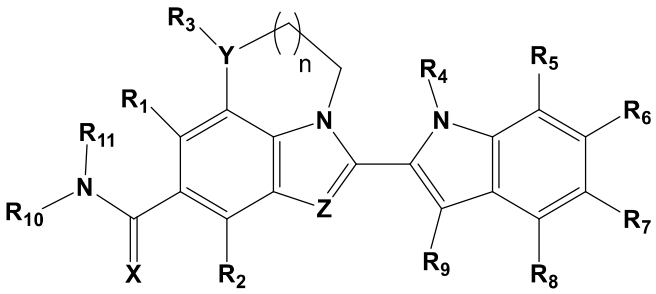
$R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $SO_2C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, and $SO_2C_6$ aryl, wherein, $SO_2C_6$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, and $C_6$ aryl;

$R_4$ is selected from the group consisting of $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and -COOH; and

$R_{10}$ and $R_{11}$ are taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein,

the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, and -$NHC(O)CH=CHCH_2N(CH_3)_2$.

**[00016c]** In another aspect, there is provided a compound of Formula (III)




Formula (III)

their stereoisomers and pharmaceutically acceptable salts thereof,

wherein,

X is O or S;

Y is O or N;

Z is N;

n is 1-2;

$R_1$, $R_2$ and $R_9$ are independently selected from hydrogen;

$R_5$, $R_6$, $R_7$ and $R_8$ are independently selected from the group consisting of hydrogen, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{2-6}$ alkenyl- $C_6$ aryl, and $C_{1-6}$ heteroaryl;

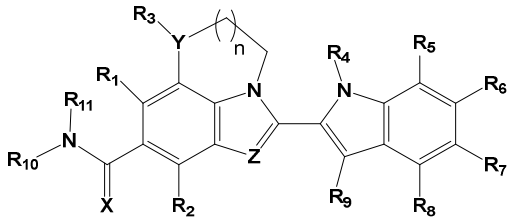
$R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $SO_2C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, and $SO_2C_6$ aryl, wherein, $SO_2C_6$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, and $C_6$ aryl;

$R_4$ is selected from the group consisting of $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and -COOH; and

$R_{10}$ and $R_{11}$ are taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein,

the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, and -$NHC(O)CH=CHCH_2N(CH_3)_2$.

**[0017]** In yet another example, present disclosure further dislcoses compound of Formula (III)



**Formula (III)**

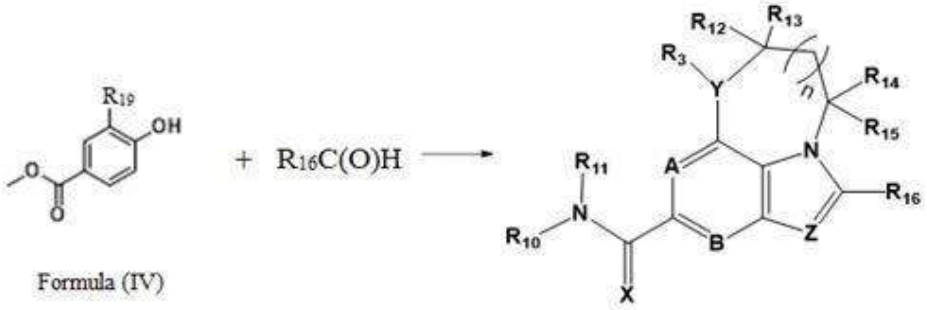
their polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof, wherein X is selected from O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; n is 0-2; $R_1$, $R_2$, $R_5$, $R_6$, $R_7$, $R_8$, and $R_9$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_4$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $CH_2OH$, COOH, and cyano; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$

alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $-NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00018]** The present disclosure further describes the process of preparation of compounds of Formula (I), Formula (II), and Formula (III) or its polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof.

**[00019]** The present disclosure further discloses a pharmaceutical composition comprising a compound of Formula (I), Formula (II), and Formula (III) or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier, optionally in combination with one or more other pharmaceutical compositions.

**[00019a]** In an aspect, there is provided a process of preparation of compounds of Formula (I) as defined above or its stereoisomers and pharmaceutically acceptable salts thereof, the process comprising reacting Formula (IV) and $R_{16}C(O)H$



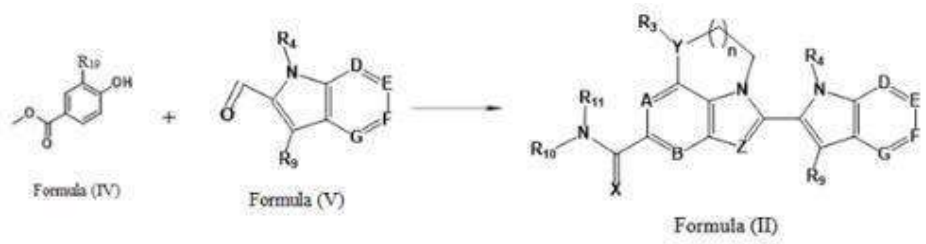

Formula (IV)

Formula (I)

wherein $R_{19}$ of Formula (IV) is selected from nitro and $C_{1-6}$ alkoxy; $R_{16}$ of $R_{16}C(O)H$ is 5-10 membered bicyclic heteroaryl with 1-2 heteroatoms selected from N or S, wherein, 5-10 membered bicyclic heteroaryl is optionally substituted with 1-3 substituents selected from the group consisting of halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{2-6}$ alkenyl- $C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and -COOH; X of Formula (I) is selected from O or S; Y is selected from O or N; Z is N; A is $CR_1$; B is $CR_2$; n is 0-1; $R_1$ and $R_2$ are independently selected from hydrogen; $R_3$ is absent or is selected from hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $SO_2C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, and $SO_2C_6$ aryl, wherein, $SO_2C_6$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, and $C_6$ aryl; $R_{10}$ and $R_{11}$ are taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein, the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from amino, $C_{1-6}$ alkylamino, and -$NHC(O)CH=CHCH_2N(CH_3)_2$; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from hydrogen and $C_{1-6}$ alkyl; $R_{16}$ is 5-10 membered bicyclic heteroaryl with 1-2 heteroatoms selected from N or S, wherein, 5-10 membered bicyclic heteroaryl is optionally substituted with 1-3 substituents selected from the group consisting of halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{2-6}$ alkenyl- $C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and

$C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and -COOH.

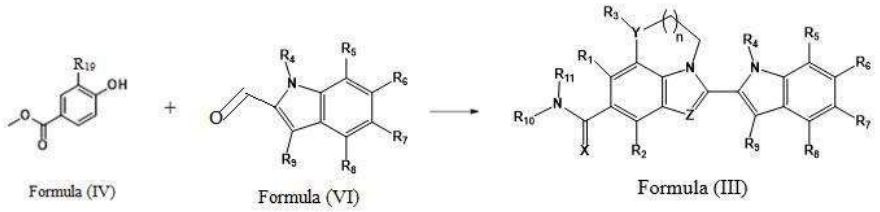
**[00019b]** In another aspect, there is provided a process of preparation of compounds of Formula (II) as defined above or its stereoisomers and pharmaceutically acceptable salts thereof, the process comprising reacting Formula (IV) and Formula (V)




wherein $R_{19}$ of Formula (IV) is selected from nitro and $C_{1-6}$ alkoxy; X of Formula (II) is selected from O or S; Y is selected from O or N; Z is N; A is $CR_1$; B is $CR_2$; D is selected from N or $CR_5$; E is $CR_6$; F is $CR_7$; G is $CR_8$; n is 1-2; $R_1$, $R_2$ and $R_9$ are independently selected from hydrogen; $R_5$, $R_6$, $R_7$ and $R_8$ are independently selected from the group consisting of hydrogen, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{2-6}$ alkenyl- $C_6$ aryl, and $C_{1-6}$ heteroaryl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $SO_2C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, and $SO_2C_6$ aryl, wherein, $SO_2C_6$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, and $C_6$ aryl; $R_4$ is selected from the group consisting of $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and -COOH; $R_{10}$ and $R_{11}$ are taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, and -$NHC(O)CH=CHCH_2N(CH_3)_2$; D of Formula (V) is selected from N or $CR_5$; E is $CR_6$; F is $CR_7$; G is $CR_8$, $R_9$ is H; and $R_4$ is selected from the group consisting of $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, is

optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and -COOH.

**[00019c]** In another aspect, there is provided a process of preparation of compounds of Formula (III) as defined above or its stereoisomers and pharmaceutically acceptable salts thereof, the process comprising reacting Formula (IV) and Formula (VI)




wherein $R_{19}$ of Formula (IV) is selected from nitro and $C_{1-6}$ alkoxy; X of Formula (III) is selected from O or S; Y is O or N; Z is N; n is 1-2; $R_1$, $R_2$ and $R_9$ are independently selected from hydrogen; $R_5$, $R_6$, $R_7$ and $R_8$ are independently selected from the group consisting of hydrogen, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{2-6}$ alkenyl- $C_6$ aryl, and $C_{1-6}$ heteroaryl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $SO_2C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, and $SO_2C_6$ aryl, wherein, $SO_2C_6$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, and $C_6$ aryl; $R_4$ is selected from the group consisting of $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and COOH; $R_{10}$ and $R_{11}$ are taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein, the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, and -$NHC(O)CH=CHCH_2N(CH_3)_2$; and $R_9$ of formula (VI) is hydrogen; $R_5$, $R_6$, $R_7$ and $R_8$ are independently selected from the group consisting of hydrogen, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{2-6}$ alkenyl- $C_6$ aryl, and $C_{1-6}$ heteroaryl; $R_4$ is selected from the group consisting of $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and COOH.

**[00019d]** In yet another aspect, the present disclosure provides a pharmaceutical composition comprising a compound of Formula (I), Formula (II), and Formula (III) or a pharmaceutically acceptable salt thereof as provided herein with a pharmaceutically acceptable carrier, optionally in combination with one or more other pharmaceutical compositions.

**[0019e]** In yet another aspect, the present disclosure provides compounds as claimed herein or a pharmaceutically acceptable salt thereof for use as a medicament

**[00020]** In yet another example, the present disclosure further discloses a method for inhibiting one or more PAD family in a cell with an effective amount of the compound of the present disclosure.

**[0020a]** In yet another aspect, there is provided an *in vitro* method for inhibiting one or more PAD family in a cell with an effective amount of the compound as defined herein.

**[00021]** The present disclosure further discloses a method of treating a condition mediated by one or more PAD's, the method comprising administering to a subject suffering from a condition mediated by one or more PAD family, a therapeutically effective amount of the compound of Formula (I), Formula (II), and Formula (III) or the pharmaceutical composition of the present disclosure with other clinically relevant agents or biological agents to a subject in need thereof.

**[00021a]** In yet another aspect, the present disclosure provides use of a pharmaceutical composition provided herein in the manufacture of a medicament for treating a condition selected from vasculitis, systemic lupus erythematosus, cancer, asthma, rheumatoid arthritis, ulcerative colitis, psoriasis, cystic fibrosis and cutaneous lupus erythematosus.

**[00021b]** In yet another aspect, the present disclosure provides use of the compound of Formula (I), Formula (II), and Formula (III) as provided herein in the manufacture of a medicament for the treatment of rheumatoid arthritis, vasculitis, systemic lupus erythematosus, ulcerative colitis, cancer, cystic fibrosis, asthma, cutaneous lupus erythematosis, and psoriasis.

**[00022]** In yet another aspect, the present disclosure further discloses use of the compound of Formula (I), Formula (II) and Formula (III) as defined above in the manufacture of a medicament for the treatment of rheumatoid arthritis, vasculitis, systemic lupus erythematosus, ulcerative colitis, cancer, cystic fibrosis, asthma, cutaneous lupus erythematosus, and psoriasis.

**[00022a]** In yet another aspect, the present disclosure provides use of the compound provided herein or the pharmaceutical composition provided herein together with other clinically relevant agents or biological agents in the manufacture of a medicament for the treatment and/or prevention of treatment of rheumatoid arthritis, vasculitis, systemic lupus erythematosus, ulcerative colitis, cancer, cystic fibrosis, asthma, cutaneous lupus erythematosus and psoriasis.

**[00022b]** In yet another aspect, the present disclosure provides use of the compound provided herein or the pharmaceutical composition provided herein together with other clinically relevant agents or biological agents in the manufacture of a medicament for the treatment and/or prevention of acid-induced lung injury, respiratory distress syndrome, allergen induced asthma, allergic bronchopulmonary, chronic lung disease of prematurity, chronic obstructive pulmonary disease, colitis, cystic fibrosis, gouty arthritis, inflammatory bowel disease, inflammatory lung disease, inflammatory pain, juvenile rheumatoid arthritis, kidney disease, kidney injury caused by parasitic infections, kidney transplant rejection prophylaxis, lung injury, lupus, lupus nephritis, multiple sclerosis, muscular dystrophy, non-allergen induced asthma, osteoarthritis, periodontitis, peritoneal endometriosis, psoriasis,pulmonary disease, pulmonary fibrosis, pyogenic sterile arthritis, renal disease, rheumatic disease, rheumatoid arthritis, sepsis, severe pain and ulcerative colitis.

**[00022c]** In yet another aspect, the present disclosure provides use of a therapeutically effective amount of the compound provided herein or the pharmaceutical composition provided herein in the manufacture of a medicament for the treatment and/or prevention of a condition selected from acid-induced lung injury, respiratory distress syndrome, allergen induced asthma, allergic bronchopulmonary, chronic lung disease of prematurity, chronic obstructive pulmonary disease, colitis, cystic fibrosis, gouty arthritis, inflammatory bowel disease, inflammatory lung disease, inflammatory pain, juvenile rheumatoid arthritis, kidney disease, kidney injury caused by parasitic

infections, kidney transplant rejection prophylaxis, lung injury, lupus, lupus nephritis, multiple sclerosis, muscular dystrophy, non-allergen induced asthma, osteoarthritis, periodontitis, peritoneal endometriosis, psoriasis, pulmonary disease, pulmonary fibrosis, pyogenic sterile arthritis, renal disease, rheumatic disease, rheumatoid arthritis, sepsis, severe pain and ulcerative colitis.

**[00022d]** In yet another aspect, the present disclosure provides use of a combination of the compounds provided herein or the pharmaceutical composition provided herein with other clinically relevant agents or biological agents in the manufacture of a medicament for the treatment of rheumatoid arthritis.

**[00022e]** In yet another aspect, the present disclosure provides use of a combination of the compounds provided herein or the pharmaceutical composition provided herein with other clinically relevant immune modulators agents in the manufacture of a medicament for the treatment of cancer.

**[00023]** These and other features, aspects, and advantages of the present subject matter will become better understood with reference to the following description. This summary is provided to introduce a selection of concepts in a simplified form. This summary is not intended to identify key features or essential features of the disclosure, nor is it intended to be used to limit the scope of the subject matter.

## DETAILED DESCRIPTION

**[00024]** Those skilled in the art will be aware that the present disclosure is subject to variations and modifications other than those specifically described. It is to be understood that the present disclosure includes all such variations and modifications. The disclosure also includes all such steps, features, compositions and compounds referred to or indicated in this specification, individually or collectively, and any and all combinations of any or more of such steps or features.

*Definitions*

**[00025]** For convenience, before further description of the present disclosure, certain terms employed in the specification, and examples are collected here. These definitions should be read in the light of the remainder of the disclosure and understood as by a person of skill in the art. The terms used herein have the meanings recognized and known to those of skill in the art, however, for convenience and completeness, particular terms and their meanings are set forth below.

**[00026]** The articles “a”, “an” and “the” are used to refer to one or to more than one (i.e., to at least one) of the grammatical object of the article.

**[00027]** Throughout the description and the claims which follow, unless the context requires otherwise, the word “comprise”, and variations such as “comprises” and “comprising”, will be understood to imply the inclusion of a stated integer or step or group of integers but not to the exclusion of any other integer or step or group of integers or steps.

**[00028]** The term “including” is used to mean “including but not limited to”. “Including” and “including but not limited to” are used interchangeably.

**[00029]** In the structural formulae given herein and throughout the present disclosure, the following terms have been indicated meaning, unless specifically stated otherwise.

**[00030]** Furthermore, the compound of Formula (I), Formula (II), and Formula (III) can be its derivatives, analogs, stereoisomer's, diastereomers, geometrical isomers, polymorphs, solvates, co-crystals, intermediates, metabolites, prodrugs or pharmaceutically acceptable salts and compositions.

**[00031]** The compounds according to Formula (I), Formula (II), and Formula (III) contain one or more asymmetric centres (also referred to as a chiral centres) and may, therefore, exist as individual enantiomers, diastereoisomers, or other stereoisomeric forms, or as mixtures thereof. Chiral centres, such as chiral carbon atoms, may also be present in a substituent such as an alkyl group. Where the stereochemistry of a chiral centre present in Formula (I), Formula (II), and Formula (III), or in any chemical structure illustrated herein, is not specified, the structure is intended to encompass any stereoisomer and all mixtures thereof. Thus, compounds according to Formula (I), Formula (II), and Formula (III) containing one or more chiral centres may be used as racemic modifications including racemic mixtures and racemates, enantiomerically-enriched mixtures, or as enantiomerically-pure individual stereoisomers.

**[00032]** Individual stereoisomers of a compound according to Formula (I), Formula (II), and Formula (III) which contain one or more asymmetric centres may be resolved by methods known to those skilled in the art. For example, such resolution may be carried out (1) by formation of diastereoisomeric salts, complexes or other derivatives; (2) by selective reaction with a stereoisomer-specific reagent, for example by enzymatic oxidation or reduction; or (3) by gas-liquid or liquid chromatography in a chiral environment, for example, on a chiral support such as silica with a bound chiral ligand or in the presence of a chiral solvent. It will be appreciated that where the desired stereoisomer is converted into another chemical entity by one of the separation procedures described above, a further step is required to liberate the desired form.

**[00033]** Alternatively, specific stereoisomers may be synthesised by asymmetric synthesis using optically active reagents, substrates, catalysts or solvents, or by converting one enantiomer to the other by asymmetric transformation.

**[00034]** It is to be understood that the references herein to compounds of Formula (I), Formula (II), and Formula (III) and salts thereof covers the compounds of Formula (I), Formula (II), and Formula (III) as free bases, or as salts thereof, for example as pharmaceutically acceptable salts thereof. Thus, in one embodiment, the disclosure is

directed to compounds of Formula (I), Formula (II), and Formula (III) as the free base. In another embodiment, the disclosure is directed to compounds of Formula (I), Formula (II), and Formula (III) and salts thereof. In a further embodiment, the disclosure is directed to compounds of Formula (I), Formula (II), and Formula (III) and pharmaceutically acceptable salts thereof.

**[00035]** It will be appreciated that pharmaceutically acceptable salts of the compounds according to Formula (I, II and III) may be prepared. Indeed, in certain embodiments of the disclosure, pharmaceutically acceptable salts of the compounds according to Formula (I), Formula (II), and Formula (III) may be preferred over the respective free base because such salts impart greater stability or solubility to the molecule thereby facilitating formulation into a dosage form. Accordingly, the disclosure is further directed to compounds of Formula (I), Formula (II), and Formula (III) and pharmaceutically acceptable salts thereof.

**[00036]** "Enantiomeric excess" (ee) is the excess of one enantiomer over the other expressed as a percentage. In a racemic modification, since both enantiomers are present in equal amounts, the enantiomeric excess is zero (0% ee). However, if one enantiomer were enriched such that it constitutes 95% of the product, then the enantiomeric excess would be 90% ee (the amount of the enriched enantiomer, 95%, minus the amount of the other enantiomer, 5%).

**[00037]** "Enantiomerically enriched" refers to products whose enantiomeric excess (ee) is greater than zero. For example, 'enantiomerically enriched' refers to products whose enantiomeric excess is greater than 50% ee, greater than 75% ee, and greater than 90% ee. 'Enantiomerically pure' refers to products whose enantiomeric excess is 99% or greater.

**[00038]** Included within the scope of the 'compounds of the disclosure' are all solvates (including hydrates), complexes, polymorphs, prodrugs, radiolabelled derivatives, and stereoisomers of the compounds of Formula (I), Formula (II), and Formula (III) and salts thereof.

**[00039]** The compounds of the disclosure may exist in solid or liquid form. In the solid state, the compounds of the disclosure may exist in crystalline or non-crystalline form, or as a mixture thereof. For compounds of the disclosure that are in crystalline form, the skilled artisan will appreciate that pharmaceutically acceptable solvates may be formed wherein solvent molecules are incorporated into the crystalline lattice during crystallization. Solvates may involve non-aqueous solvents such as ethanol, iso-propyl

alcohol, N,N- dimethylsulfoxide (DMSO), acetic acid, ethanolamine, and ethyl acetate, or they may involve water as the solvent that is incorporated into the crystalline lattice. Solvates wherein water is the solvent that is incorporated into the crystalline lattice are typically referred to as 'hydrates'. Hydrates include stoichiometric hydrates as well as compositions containing variable amounts of water. The disclosure includes all such solvates.

**[00040]** It will be further appreciated that certain compounds of the disclosure that exist in crystalline form, including the various solvates thereof, may exhibit polymorphism (i.e. the capacity to occur in different crystalline structures). These different crystalline forms are typically known as 'polymorphs'. The disclosure includes such polymorphs. Polymorphs have the same chemical composition but differ in packing, geometrical arrangement, and other descriptive properties of the crystalline solid state. Polymorphs, therefore, may have different physical properties such as shape, density, hardness, deformability, stability, and dissolution properties. Polymorphs typically exhibit different melting points, IR spectra, and X-ray powder diffraction patterns, which may be used for identification. It will be appreciated that different polymorphs may be produced, for example, by changing or adjusting the reaction conditions or reagents, used in making the compound. For example, changes in temperature, pressure, or solvent may result in polymorphs. In addition, one polymorph may spontaneously convert to another polymorph under certain conditions.

**[00041]** The disclosure also includes isotopically-labelled compounds, which are identical to the compounds of Formula (I, II and III) and salts thereof, but for the fact that one or more atoms are replaced by an atom having an atomic mass or mass number different from the atomic mass or mass number most commonly found in nature. Examples of isotopes that can be incorporated into the compounds of the disclosure include isotopes of hydrogen, carbon, nitrogen, oxygen and fluorine, such as $^{3}H$, $^{11}C$, $^{14}C$ and $^{18}F$.

**[00042]** The term "co-crystals" refers to solids that are crystalline single-phase materials composed of two or more different molecular and/or ionic compounds generally in a stoichiometric ratio which are neither solvates nor simple salts.

**[00043]** The term "substituted" in reference to a group indicates that a hydrogen atom attached to a member atom within a group is replaced. It should be understood that the term 'substituted' includes the implicit provision that such substitution be in accordance with the permitted valence of the substituted atom and the substituent and that the

substitution results in a stable compound (i.e. one that does not spontaneously undergo transformation such as rearrangement, cyclisation, or elimination). In certain embodiments, a single atom may be substituted with more than one substituent as long as such substitution is in accordance with the permitted valence of the atom. Suitable substituents are defined herein for each substituted or optionally substituted group.

**[00044]** The term "polymorphs" refers to crystal forms of the same molecule, and different polymorphs may have different physical properties such as, for example, melting temperatures, heats of fusion, solubilities, dissolution rates and/or vibrational spectra as a result of the arrangement or conformation of the molecules in the crystal lattice.

**[00045]** The term "prodrugs" refers to the precursor of the compound of Formula (I, II, and III) which on administration undergoes chemical conversion by metabolic processes before becoming active pharmacological substances. In general, such prodrugs will be functional derivatives of a compound of the disclosure, which are readily convertible *in vivo* into a compound of the disclosure.

**[00046]** The term "alkyl" refers to a saturated hydrocarbon chain having the specified number of carbon atoms. For example, which are not limited, $C_{1\text{-}6}$ alkyl refers to an alkyl group having from 1 – 6 carbon atoms, or 1 – 3 carbon atoms. Alkyl groups may be straight or branched chained groups. Representative branched alkyl groups have one, two, or three branches. Preferred alkyl groups include, without limitation, methyl, ethyl, n-propyl, isopropyl, butyl, and isobutyl.

**[00047]** The term "C(O) alkyl" refers to an alkyl group as defined above attached via carbonyl linkage to the rest of the molecule. For example, $C(O)C_{1\text{-}6}$ alkyl refers to an alkyl group having from 1 – 6 carbon atoms, or 1 – 3 carbon atoms attached via carbonyl linkage to the rest of the molecule. Preferred C(O) alkyl groups include, without limitation, $-C(O)CH_3$, $-C(O)CH_2CH_3$, and the like.

**[00048]** The term "$SO_2$ alkyl" refers to an alkyl group as defined above attached via sulfonyl linkage to the rest of the molecule. For example, $SO_2C_{1\text{-}6}$ alkyl refers to an alkyl group having from 1 – 6 carbon atoms, or 1 – 3 carbon atoms attached via sulfonyl linkage to the rest of the molecule. Preferred $SO_2$ alkyl groups include, without limitation, $-SO_2CH_3$, $-SO_2CH_2CH_3$, and the like.

**[00049]** The term "alkoxy" refers to an alkyl group attached via an oxygen linkage to the rest of the molecule. For example, $C_{1\text{-}6}$ alkoxy refers to an alkyl group having from 1 – 6 carbon atoms, or 1 – 3 carbon atoms attached via an oxygen linkage to the rest of the

molecule. Preferred alkoxy groups include, without limitation, –$OCH_3$ (methoxy), –$OC_2H_5$ (ethoxy) and the like.

**[00050]** The term "alkylamino" refers to an alkyl group as defined above attached via amino linkage to the rest of the molecule. For example, $C_{1-6}$ alkylamino refers to an alkyl group having from 1 – 6 carbon atoms, or 1 – 3 carbon atoms attached via amino linkage to the rest of the molecule. Preferred alkylamino groups include, without limitation, -$NHCH_3$, -$N(CH_3)_2$, and the like.

**[00051]** The term "C(O)NR" refers to an alkylamino group as defined above attached via a carbonyl linkage to the rest of the molecule. Preferred C(O)NR groups include, $C(O)NCH_3$, $C(O)NCH_2CH_3$, and the like.

**[00052]** The term "$SO_2NR$" refers to an alkylamino group as defined above attached via a sulfonyl linkage to the rest of the molecule. Preferred $SO_2NR$ groups include, $SO_2NCH_3$, $SO_2NCH_2CH_3$, and the like.

**[00053]** The term "C(O) alkylamino" refers to an alkylamino group as defined above attached via carbonyl linkage to the rest of the molecule. For example, $C(O)C_{1-6}$ alkylamino refers to an alkylamino group having from 1 – 6 carbon atoms, or 1 – 3 carbon atoms attached via carbonyl linkage to the rest of the molecule. Preferred C(O) alkylamino groups include, without limitation, -$C(O)NHCH_3$, -$C(O)N(CH_3)_2$, and the like.

**[00054]** The term "$SO_2$ alkylamino" refers to an alkylamino group as defined above attached via sulfonyl linkage to the rest of the molecule. For example, $SO_2C_{1-6}$ alkylamino refers to an alkylamino group having from 1 – 6 carbon atoms, or 1 – 3 carbon atoms attached via sulfonyl linkage to the rest of the molecule. Preferred $SO_2$ alkylamino groups include, without limitation, -$SO_2NHCH_3$, -$SO_2N(CH_3)_2$, and the like.

**[00055]** The term "acylamino" refers to an acyl group attached via amino linkage to the rest of the molecule. For example, $C_{1-6}$ acylamino refers to an acyl group having from 1 – 6 carbon atoms, or 1 – 3 carbon atoms attached via amino linkage to the rest of the molecule. Preferred acylamino groups include, without limitation, -$(CO)NHCH_3$, -$(CO)N(CH_3)_2$, and the like.

**[00056]** The term "haloalkyl" refers to an alkyl group as defined above attached via halo linkage to the rest of the molecule. For example, $C_{1-6}$ haloalkyl refers to an alkyl group having from 1 – 6 carbon atoms, or 1 – 3 carbon atoms attached via halo linkage to the rest of the molecule. Preferred haloalkyl groups include, without limitation, -$CH_2Cl$, -$CHCl_2$, and the like.

**[00057]** The term "C(O) haloalkyl" refers to an haloalkyl group as defined above attached via carbonyl linkage to the rest of the molecule. For example, $C(O)C_{1-6}$ haloalkyl refers to an haloalkyl group having from 1 – 6 carbon atoms, or 1 – 3 carbon atoms attached via carbonyl linkage to the rest of the molecule. Preferred C(O) haloalkyl groups include, without limitation, $-(CO)CH_2Cl$, $-C(O)CHCl_2$, and the like.

**[00058]** The term "$SO_2$ haloalkyl" refers to an haloalkyl group as defined above attached via sulfonyl linkage to the rest of the molecule. For example, $SO_2C_{1-6}$ haloalkyl refers to an haloalkyl group having from 1 – 6 carbon atoms, or 1 – 3 carbon atoms attached via sulfonyl linkage to the rest of the molecule. Preferred $SO_2$ haloalkyl groups include, without limitation, $-SO_2CH_2Cl$, $-SO_2CHCl_2$, and the like.

**[00059]** The term "haloalkoxy" refers to an alkoxy group as defined above attached via oxygen linkage of the haloalkoxy group to the rest of the molecule. For example, $C_{1-6}$ haloalkoxy refers to an alkoxy group having from 1 – 6 carbon atoms, or 1 – 3 carbon atoms attached via oxygen linkage to the rest of the molecule. Preferred haloalkoxy groups include, without limitation, $-OCH_2Cl$, $-OCHCl_2$, and the like.

**[00060]** The term "halogen" refers to a halogen radical, for example, fluoro, chloro, bromo, or iodo. "Haloalkyl" refers to an alkyl group, as herein before defined, in which at least one of the hydrogen atoms has been replaced with a halogen radical. "$C_{1-6}$ haloalkyl" refers to a $C_{1-6}$ alkyl group in which at least one of the hydrogen atoms has been replaced with a halogen radical. An example of 'haloalkyl' is trifluoromethyl or 2,2,2-trifluoroethyl.

**[00061]** The term "cycloalkyl" refers to a saturated hydrocarbon ring having a specified number of carbon atoms. For example, which are not limited, $C_{3-6}$ cycloalkyl refers to a cycloalkyl group having from 3 to 6 member atoms, or 3 member atoms. Preferred cycloalkyl groups include, without limitation, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, groups and the like.

**[00062]** The term "$SO_2C_{3-6}$ cycloalkyl" refers to a cycloalkyl group as defined above attached via sulfonyl linkage to the rest of the molecule. For example, $SO_2C_{3-6}$ cycloalkyl refers to a cycloalkyl group having from 3 – 6 carbon atoms attached via sulfonyl linkage to the rest of the molecule. Preferred $SO_2$ cycloalkyl groups include, without limitation, $-SO_2C_3$ cycloalkyl, and the like.

**[00063]** The term "aryl" refers to aromatic ring having a specified number of carbon atoms. For example, $C_{5-6}$ aryl refers to a aryl group having 5 or 6 member atoms, or 6 member atoms. Preferred aryl groups include, without limitation, phenyl, and the like.

**[00064]** The term "C(O) aryl" refers to an aryl group as defined above attached via carbonyl linkage to the rest of the molecule. For example, $C(O)C_{5-6}$ aryl refers to an aryl group having from 5 – 6 carbon atoms attached via carbonyl linkage to the rest of the molecule. Preferred C(O) aryl groups include, without limitation, -C(O) $C_6H_5$, -C(O) $C_5H_5$, and the like.

**[00065]** The term "$SO_2$ aryl" refers to an aryl group as defined above attached via sulfonyl linkage to the rest of the molecule. For example, $SO_2C_{5-6}$ aryl refers to an aryl group having from 5 – 6 carbon atoms attached via sulfonyl linkage to the rest of the molecule. Preferred $SO_2$ aryl groups include, without limitation, -$SO_2$ $C_6H_5$, -$SO_2$ $C_5H_5$, and the like.

**[00066]** The term "heteroaryl" refers to aromatic rings containing from 1 to 5 heteroatoms in the ring. "Heteroaryl" groups may be substituted with one or one or more substituents if so defined herein. The "$C_{1-6}$ heteroaryl" rings having 1 or 6 carbon as member atoms. The "heteroaryl" includes pyridinyl, tetrazolyl and pyrazolyl. "Heteroatom" refers to a nitrogen, sulfur, or oxygen atom, for example a nitrogen atom or an oxygen atom.

**[00067]** The term "C(O) heteroaryl" refers to an heteroaryl group as defined above attached via carbonyl linkage to the rest of the molecule. For example, $C(O)C_{1-6}$ heteroaryl refers to an alkyl group having from 1 – 6 carbon atoms attached via carbonyl linkage to the rest of the molecule. Preferred C(O) heteroaryl groups include, without limitation, -C(O) pyridinyl, -C(O) pyrazolyl, and the like.

**[00068]** The term "$SO_2$ heteroaryl" refers to an aryl group as defined above attached via sulfonyl linkage to the rest of the molecule. For example, $SO_2C_{1-6}$ heteroaryl refers to an aryl group having from 1 – 6 carbon atoms attached via sulfonyl linkage to the rest of the molecule. Preferred $SO_2$ heteroaryl groups include, without limitation, -$SO_2$ pyridinyl, -$SO_2$ pyrazolyl, and the like.

**[00069]** The term "heterocyclic" and "heterocyclyl" refer to saturated or unsaturated monocyclic aliphatic rings containing 5, 6, or 7 ring members including 1-5 heteroatoms or to saturated or unsaturated bicyclic aliphatic rings containing 5, 6 or 7 ring members each including 1-5 heteroatoms. In certain embodiments, 'heterocyclyl' groups are saturated. In other embodiments, 'heterocyclyl' groups are unsaturated. 'Heterocyclyl' groups containing more than one heteroatom may contain different heteroatoms. 'Heterocyclyl' groups may be substituted with one or more substituents as defined herein.

'Heterocyclyl' includes piperidinyl, tetrahydropyranyl, azepinyl, oxazepinyl, azabicyclo[3.1.0]hexanyl.

**[00070]** The phrase "pharmaceutically acceptable" refers to those compounds, materials, compositions, and dosage forms which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of human beings and animals without excessive toxicity, irritation, or other problem or complication, commensurate with a reasonable benefit/risk ratio.

**[00071]** As used herein, the term "pharmaceutically acceptable salts" refers to salts that retain the desired biological activity of the subject compound and exhibit minimal undesired toxicological effects. These pharmaceutically acceptable salts may be prepared in situ during the final isolation and purification of the compound, or by separately reacting the purified compound in its free base form with a suitable acid. The pharmaceutically acceptable salt selected derived from inorganic bases such as like Li, Na, K, Ca, Mg, Fe, Cu, Zn and Mn; salts of organic bases such as N, N'-diacetylethylenediamine, glucamine, triethylamine, choline, dicyclohexylamine, benzylamine, trialkylamine, thiamine, guanidine, diethanolamine, α-phenylethylamine, piperidine, morpholine, pyridine, hydroxyethylpyrrolidine, hydroxyethylpiperidine, ammonium, substituted ammonium salts, aluminum salts and the like. Salts also include amino acid salts such as glycine, alanine, cystine, cysteine, lysine, arginine, phenylalanine, and guanidine. Salts may include acid addition salts where appropriate which are sulphates, nitrates, phosphates, perchlorates, borates, hydrohalides, acetates, tartrates, maleates, citrates, succinates, palmoates, methanesulphonates, tosylates, benzoates, salicylates, hydroxynaphthoates, benzenesulfonates, ascorbates, glycerophosphates, ketoglutarates.

**[00072]** Salts and solvates having non-pharmaceutically acceptable counter-ions or associated solvents are within the scope of the present disclosure, for example, for use as intermediates in the preparation of other compounds of Formula (I), Formula (II), and Formula (III) and their pharmaceutically acceptable salts. Thus, one embodiment of the disclosure embraces compounds of Formula (I), Formula (II), and Formula (III) and salts thereof. Compounds according to Formula (I), Formula (II), and Formula (III) contain a basic functional group and are therefore capable of forming pharmaceutically acceptable acid addition salts by treatment with a suitable acid. Suitable acids include pharmaceutically acceptable inorganic acids and pharmaceutically acceptable organic acids. Representative pharmaceutically acceptable acid addition salts include

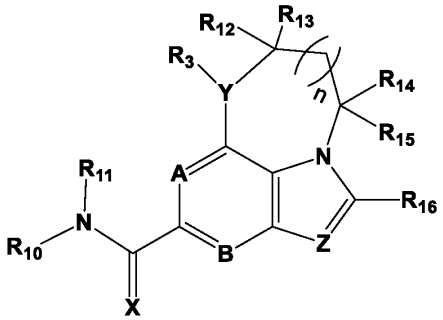
hydrochloride, hydrobromide, nitrate, methylnitrate, sulfate, bisulfate, sulfamate, phosphate, acetate, hydroxyacetate, phenyl acetate, propionate, butyrate, iso-butyrate, valerate, maleate, hydroxymaleate, acrylate, fumarate, malate, tartrate, citrate, salicylate, glycollate, lactate, heptanoate, phthalate, oxalate, succinate, benzoate, o-acetoxybenzoate, chlorobenzoate, methylbenzoate, dinitrobenzoate, hydroxybenzoate, methoxybenzoate, naphthoate, hydroxynaphthoate, mandelate, tannate, formate, stearate, ascorbate, palmitate, oleate, pyruvate, pamoate, malonate, laurate, glutarate, glutamate, estolate, methanesulfonate (mesylate), ethanesulfonate (esylate), 2-hydroxyethanesulfonate, benzenesulfonate (besylate), aminobenzenesulfonate, p-toluenesulfonate (tosylate), and naphthalene-2-sulfonate.

**[00073]** The term "PAD inhibitor" or "inhibitor of PAD" is used to identify a compound, which is capable of interacting with neutrophil extracellular traps (NETs) and more specifically in the histone citrullination that occurs during NETosis. Inhibiting PAD4 enzymatic activity means reducing the ability of PAD4 enzyme so as to inhibit the formation of citrulline through citrullination process. Preferably, such inhibition is specific to PAD4 enzyme.

**[00074]** A term once described, the same meaning applies for it, throughout the patent.

**[00075]** The utility of PAD4 inhibitors is vast as described in the background section. However, the identification and development of PAD4 inhibitor compounds still remains a problem, despite of their vast utility. Therefore, new PAD4 inhibitor compounds treating PAD4 mediated disorders are required.

**[00076]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) their polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof, wherein




Formula (I)

X is selected from O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -$NHC(NH)CH_2Cl$, $NHC(O)CH{=}CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-}$

$_6$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00077]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, C(O)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, C(O)$NR_{18}$, C(O)$C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, C(O)$C_{5-6}$ aryl, C(O)$C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, (CO)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, C(O)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, C(O)$NR_{18}$, C(O)$C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, C(O)$C_{5-6}$ aryl, C(O)$C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, (CO)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-

10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -NHC(NH)$CH_2$Cl, NHC(O)CH=$CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00078]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$

alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$

heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00079]**

**[00080]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O or N; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10

membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -NHC(NH)$CH_2Cl$, NHC(O)CH=$CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00081]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is O; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$

haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$

haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00082]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is N; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$

and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00083]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is N; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, C(O)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, C(O)$NR_{18}$, C(O)$C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, C(O)$C_{5-6}$ aryl, C(O)$C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, (CO)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen,

$C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, -COOH, and cyano; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00084]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy,

is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of

the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00085]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -

$NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00086]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl,

$C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from

hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00087]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 1; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from

the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00088]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, and $C_{1-4}$ alkyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, C(O)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, C(O)$NR_{18}$, C(O)$C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, C(O)$C_{5-6}$ aryl, C(O)$C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, (CO)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, C(O)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, C(O)$NR_{18}$, C(O)$C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, C(O)$C_{5-6}$ aryl, C(O)$C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, (CO)$C_{1-6}$ alkyl,

$C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -$NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00089]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from hydrogen; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$

alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$

haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00090]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-4}$ alkyl, $C_{3-5}$ cycloalkyl, $C_{1-4}$ alkylamino, $C_{1-4}$ haloalkyl, $C(O)C_{1-4}$ alkyl, $C(O)C_{1-4}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-4}$ alkylamino, $SO_2C_{1-4}$ alkyl, $SO_2C_{1-4}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-4}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-4}$ alkyl, $(CO)C_{1-4}$ alkyl, $C(O)C_{1-4}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-4}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH{=}CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$

alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00091]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O or S; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$

alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -$NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00092]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$

alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is selected from the group consisting of hydrogen, $C_{1-4}$ alkyl, $C_{3-5}$ cycloalkyl, $C_{1-4}$ alkylamino, $C_{1-4}$ haloalkyl, $C(O)C_{1-4}$ alkyl, $C(O)C_{1-4}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-4}$ alkylamino, $SO_2C_{1-4}$ alkyl, $SO_2C_{1-4}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-4}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-4}$ alkyl, $(CO)C_{1-4}$ alkyl, $C(O)C_{1-4}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-4}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$

heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00093]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ and $R_{11}$ are taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -$NHC(NH)CH_2Cl$, -$NHC(O)CH{=}CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or

O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00094]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl,

$SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -$NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-4}$ alkyl, $C_{1-4}$ haloalkyl, $C_{1-4}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00095]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of

hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from hydrogen, and $C_{1-4}$ alkyl; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl

is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00096]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally

substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -NHC(NH)$CH_2Cl$, NHC(O)CH=$CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from hydrogen; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00097]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, C(O)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, C(O)$NR_{18}$, C(O)$C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, C(O)$C_{5-6}$ aryl, C(O)$C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, (CO)$C_{1-6}$

alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered bicyclic aryl, and 5-10 membered bicyclic heteroaryl with 1-2 heteroatoms selected from N or S, wherein 5-10 membered bicyclic aryl, and 5-10 membered bicyclic heteroaryl are optionally substituted with 1-3 substituents selected from the group consisting of halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl- $C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl- $C_{1-6}$ heterocyclyl,$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{5-6}$ aryl, $C_{1-6}$ alkyl- $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00098]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O; Y is O or N; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -$NHC(NH)CH_2Cl$, $NHC(O)CH{=}CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted

with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[00099]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is S; Y is O or N; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, C(O)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, C(O)$NR_{18}$, C(O)$C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, C(O)$C_{5-6}$ aryl, C(O)$C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, (CO)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, C(O)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, C(O)$NR_{18}$, C(O)$C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, C(O)$C_{5-6}$ aryl, C(O)$C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, (CO)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$

alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -$NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000100]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O or N; Z is N; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally

substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of

the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000101]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O; Y is selected from O or N; Z is N; A is $CR_1$; B is $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -$NHC(NH)CH_2Cl$, $NHC(O)CH{=}CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10

membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000102]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O or N; Z is N; A is $CR_1$; B is $CR_2$; n is 0-1; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered

monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -NHC(NH)$CH_2Cl$, NHC(O)CH=$CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000103]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O; Y is selected from O or N; Z is N; A is $CR_1$; B is $CR_2$; n is 0; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, C(O)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, C(O)$NR_{18}$, C(O)$C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, C(O)$C_{5-6}$ aryl, C(O)$C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, (CO)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with

$C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, -COOH, and cyano; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000104]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O; Y is O or N; Z is N; A is $CR_1$; B is $CR_2$; n is 1; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$

acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl,

$C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000105]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is O or N; Z is N; A is $CR_1$; B is $CR_2$; n is 0-1; $R_1$, and $R_2$ are independently selected from hydrogen; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -$NHC(NH)CH_2Cl$, $NHC(O)CH{=}CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted

with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000106]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is O or N; Z is N; A is $CR_1$; B is $CR_2$; n is 0-1; $R_1$, and $R_2$ are independently selected from hydrogen; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-4}$ alkyl, $C(O)C_{1-4}$ alkyl, $C_{3-6}$ cycloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, wherein $C_{1-4}$ alkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -$NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; and $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10

membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano.

**[000107]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is O or N; Z is N; A is $CR_1$; B is $CR_2$; n is 0-1; $R_1$, and $R_2$ are independently selected from hydrogen; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-4}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-4}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, wherein $C_{1-4}$ alkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ and $R_{11}$ are taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, and $NHC(O)CH=CHCH_2N(CH_3)_2$; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; and $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups

selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano.

**[000108]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is O or N; Z is N; A is $CR_1$; B is $CR_2$; n is 0-1; $R_1$, and $R_2$ are independently selected from hydrogen; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-4}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-4}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, wherein $C_{1-4}$ alkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ and $R_{11}$ is taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, and $NHC(O)CH=CHCH_2N(CH_3)_2$,; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from hydrogen, and $C_{1-6}$ alkyl; and $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano.

**[000109]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O; Y is O or N; Z is N; A is $CR_1$; B is $CR_2$; n is 0-1; $R_1$, and $R_2$ are independently selected from hydrogen; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-4}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, wherein $C_{1-4}$ alkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ and $R_{11}$ is taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$

alkylamino, and $NHC(O)CH=CHCH_2N(CH_3)_2$; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from hydrogen, and $C_{1-6}$ alkyl; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered bicyclic aryl, and 5-10 membered bicyclic heteroaryl with 1-2 heteroatoms selected from N or S, wherein 5-10 membered bicyclic aryl, and 5-10 membered bicyclic heteroaryl are optionally substituted with 1-3 substituents selected from the group consisting of halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl- $C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl- $C_{1-6}$ heterocyclyl,$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{5-6}$ aryl, $C_{1-6}$ alkyl- $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -COOH, and cyano.

**[000110]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is selected from O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-1; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, and $C_{1-6}$ haloalkoxy, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form

a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -$NHC(NH)CH_2Cl$, -$NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S;

$R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000111]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is selected from O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano,

and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C(O)C_{1-6}$ alkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ and $R_{11}$ are taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{2-4}$ alkylamino, $C_{2-4}$ acylamino, $-NHC(NH)CH_2Cl$, $-NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{2-4}$ alkyl, halogen, $C_{2-4}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

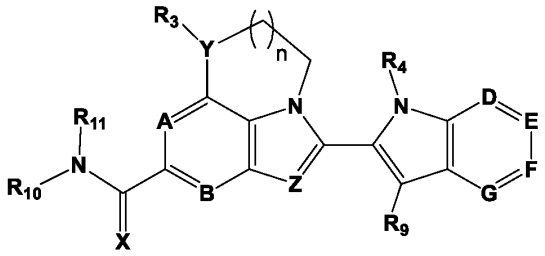
**[000112]** In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is selected from O or S; Y is selected from O,

N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-1; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, and $C_{1-6}$ haloalkoxy, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ and $R_{11}$ are taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{2-4}$ alkylamino, $C_{2-4}$ acylamino, $-NHC(NH)CH_2Cl$, $-NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{2-4}$ alkyl, halogen, $C_{2-4}$ alkoxy, and hydroxyl; $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, and $C_{1-6}$ haloalkoxy, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$

alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000113]**.In an embodiment of the present disclosure, there is provided a compound of Formula (I) as described herein, wherein X is O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is $CR_1$; B is $CR_2$; n is 0-1; $R_1$, and $R_2$ are independently selected from hydrogen; $R_3$ is absent or is selected from hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, wherein $SO_2C_{1-6}$ alkyl is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ and $R_{11}$ is taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from amino, $NHC(O)CH=CHCH_2N(CH_3)_2$, or $C_{1-6}$ alkylamino; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from hydrogen or $C_{1-6}$ alkyl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered bicyclic aryl, and 5-10 membered bicyclic heteroaryl with 1-2 heteroatoms selected from N or S, wherein 5-10 membered bicyclic aryl, and 5-10 membered bicyclic heteroaryl are optionally substituted with 1-3 substituents selected from the group consisting of halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl- $C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl- $C_{1-6}$ heterocyclyl,$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{5-6}$ aryl, $C_{1-6}$ alkyl- $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -COOH, and cyano; $R_{17}$ is selected from hydrogen, or $C_{1-6}$ alkyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000114]**In an embodiment of the present disclosure, there is provided a compound of Formula (II) their polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof, wherein



Formula (II)

X is selected from O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; D is selected from N or $CR_5$; E is selected from N or $CR_6$; F is selected from N or $CR_7$; G is selected from N or $CR_8$; n is 0-2; $R_1$, $R_2$, $R_5$, $R_6$, $R_7$, $R_8$, and $R_9$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_4$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, -COOH, and cyano; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of $C_{1-6}$

alkylamino, and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -$NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000115]** In an embodiment of the present disclosure, there is provided a compound of Formula (II) as described herein, wherein X is selected from O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; D is selected from N or $CR_5$; E is selected from N or $CR_6$; F is selected from N or $CR_7$; G is selected from N or $CR_8$; n is 1-2; $R_1$, $R_2$, $R_8$, and $R_9$ are independently selected from the group consisting of hydrogen, halogen, hydroxyl, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, and $C_{1-6}$ haloalkoxy, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_5$, $R_6$, and $R_7$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{2-6}$ alkenyl-$C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_4$ is selected from the group

consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, COOH, and cyano; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000116]** In an embodiment of the present disclosure, there is provided a compound of Formula (II) as described herein, wherein X is selected from O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; D is selected from N or $CR_5$; E is selected from N or $CR_6$; F is selected from N or $CR_7$; G is selected from N or $CR_8$; n is 0-2; $R_1$, $R_2$, $R_8$, and $R_9$ are

independently selected from the group consisting of hydrogen, halogen, hydroxyl, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, and $C_{1-6}$ haloalkoxy, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_5$, $R_6$, and $R_7$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{2-6}$ alkenyl-$C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_4$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, COOH, and cyano; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered

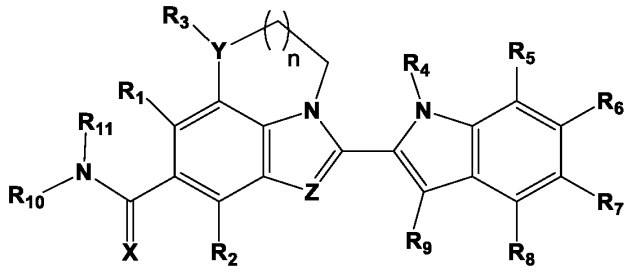
monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, -NHC(NH)$CH_2Cl$, NHC(O)CH=$CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000117]** In an embodiment of the present disclosure, there is provided a compound of Formula (II) as described herein, wherein X is selected from O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is $CR_1$; B is $CR_2$; D is selected from N or $CR_5$; E is $CR_6$; F is $CR_7$; G is $CR_8$; n is 0-2; $R_1$, $R_2$, $R_5$, $R_6$, $R_7$, $R_8$, and $R_9$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{2-6}$ alkenyl-$C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_4$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, and $SO_2C_{1-6}$

$_6$ alkyl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, COOH, and cyano; $R_{10}$ and $R_{11}$ are taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{2-4}$ alkylamino, $C_{2-4}$ acylamino, -$NHC(NH)CH_2Cl$, $NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{2-4}$ alkyl, halogen, $C_{2-4}$ alkoxy, and hydroxyl; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000118]** In an embodiment of the present disclosure, there is provided a compound of Formula (II) as described herein, wherein X is O; Y is selected from O, or N; Z is N; A is $CR_1$; B is $CR_2$; D is selected from N or $CR_5$; E is $CR_6$; F is $CR_7$; G is $CR_8$; n is 1-2; $R_1$, $R_2$, $R_8$, and $R_9$ are independently selected from hydrogen or halogen; $R_5$, $R_6$, and $R_7$ are independently selected from the group consisting of hydrogen, halogen, $C_1$ alkyl, $C_1$ alkoxy, , $C_{2-6}$ alkenyl-$C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_3$ is absent or is selected from hydrogen, $C_{1-6}$ alkyl, $C(O)C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, $C_{3-6}$ cycloalkyl, and $SO_2C_{1-6}$ alkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, wherein $SO_2C_{1-6}$ alkyl, and $SO_2C_{5-6}$ aryl is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_4$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, is optionally substituted with one or more groups selected from hydrogen, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, hydroxyl, -$CH_2OH$, COOH, and halogen; $R_{10}$ and $R_{11}$ are taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from amino, $C_{1-6}$ alkylamino or $NHC(O)CH=CHCH_2N(CH3)_2$; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000119]** In an embodiment of the present disclosure, there is provided a compound of Formula (III) their polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof, wherein




Formula (III)

X is selected from O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; n is 0-2; $R_1$, $R_2$, $R_5$, $R_6$, $R_7$, $R_8$, and $R_9$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_4$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $CH_2OH$, COOH, and cyano; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$

alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $-NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000120]** In an embodiment of the the present disclosure there is provided compound of Formula (I) or its polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof, which is selected from a group consisting of:

**1)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**2)** (R)-(3-aminopyrrolidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**3)** (R)-(3-aminopiperidin-1-yl)(2-(1-ethyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**4)** (2-(aminomethyl)piperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**5)** (R)-(3-aminopiperidin-1-yl)(2-(1-ethyl-1H-pyrrolo[2,3-b]pyridin-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**6)** (R)-(3-aminopiperidin-1-yl)(1-(1-(cyclopropylmethyl)-1H-indol-2-yl)-8,9-dihydro-7H-6-oxa-2,9a-diazabenzo[cd]azulen-4-yl)methanone,

**7)** (R)-(3-aminopyrrolidin-1-yl)(1-(1-(cyclopropylmethyl)-1H-indol-2-yl)-8,9-dihydro-7H-6-oxa-2,9a-diazabenzo[cd]azulen-4-yl)methanone,

**8)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-methyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**9)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**10)** (R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-4-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**11)** (R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-2-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**12)** (R)-(3-aminopiperidin-1-yl)(2-(3-ethylbenzo[b]thiophen-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**13)** (R)-(3-aminopiperidin-1-yl)(2-(1-(4-chlorobenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**14)** (R)-(3-aminopiperidin-1-yl)(2-(1-(2-fluorobenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**15)** (R)-(3-aminopiperidin-1-yl)(2-(1-(4-fluorobenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**16)** (R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-3-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**17)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5,6-dimethoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**18)** (R)-(3-aminopiperidin-1-yl)(2-(1-benzyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**19)** (R)-(3-aminopiperidin-1-yl)(2-(1-(4-methoxybenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**20)** (R)-(3-aminopiperidin-1-yl)(2-(1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**21)** (R)-(3-aminopiperidin-1-yl)(2-(6-methoxy-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**22)** (R)-(3-aminopiperidin-1-yl)(2-(1-(2-hydroxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**23)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-methoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**24)** (R)-(3-aminopiperidin-1-yl)(2-(1-((3-fluoropyridin-4-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**25)** (R)-(3-aminopiperidin-1-yl)(2-(1-(pyrazin-2-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**26)** (R)-(3-aminopiperidin-1-yl)(2-(1-((3-fluoropyridin-2-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**27)** (R)-(3-aminopiperidin-1-yl)(2-(1-(pyrimidin-2-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**28)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**29)** (R)-(3-aminopiperidin-1-yl)(2-(1-(pyrimidin-5-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**30)** (R)-(3-aminopiperidin-1-yl)(2-(1-(pyridazin-3-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**31)** (R)-(3-aminopiperidin-1-yl)(2-(1-isobutyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**32)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5,6-difluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**33)** (R)-(3-aminopiperidin-1-yl)(2-(1-((3-fluoropyridin-2-yl)methyl)-6-methoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**34)** (R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-((3-fluoropyridin-2-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**35)** (R)-(3-aminopiperidin-1-yl)(2-(6-fluoro-1-((3-fluoropyridin-2-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**36)** (*R*)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**37)** (R)-(3-aminopiperidin-1-yl)(2-(1-(4-(hydroxymethyl)benzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone trifluoroacetic acid salt,

**38)** (R,E)-N-(1-(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)-4-(dimethylamino)but-2-enamide trifluoroacetic acid salt,

**39)** (R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(4-methoxybenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**40)** (R)-(3-aminopiperidin-1-yl)(2-(1-((tetrahydro-2H-pyran-4-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**41)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclobutylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**42)** (R)-2-(2-(7-(3-aminopiperidine-1-carbonyl)-3,4-dihydro-5-ox1,2adiazaacenaphthylen-2-yl)-1H-indol-1-yl)acetic acid,

**43)** (R)- (3-aminopiperidin-1-yl)(2-(1-(piperidin-4-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**44)** (R)-(3-aminopiperidin-1-yl)(2-(1-(oxetan-3-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**45)** (R)-(3-aminopiperidin-1-yl)(2-(1-((1-methylpiperidin-4-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**46)** (*R*)-(3-aminopiperidin-1-yl)(2-(5-fluoro-1-(4-methoxybenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**47)** (R)-(3-aminopiperidin-1-yl)(2-(1-(2,2-difluoroethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**48)** (*R*)-(3-aminopiperidin-1-yl)(2-(5-fluoro-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**49)** (R)-(3-aminopiperidin-1-yl)(2-(6-fluoro-1-(4-fluorobenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**50)** (*R*)-(3-aminopiperidin-1-yl)(2-(6-fluoro-1-(4-methoxybenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**51)** (R)-(3-aminopiperidin-1-yl)(2-(1-(4-fluorobenzyl)-6-methoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**52)** 3-aminopiperidin-1-yl)(2-(6-fluoro-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**53)** (*R*)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(cyclobutylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**54)** (R)-(3-aminopiperidin-1-yl)(2-(5,6-difluoro-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**55)** (R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-isobutyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**56)** (R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(2,2-difluoroethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**57)** (R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**58)** (R,E)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-styryl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**59)** (R)-(3-aminopiperidin-1-yl)(2-(1-((4-methylthiazol-2-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**60)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-methoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**61)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-(hydroxymethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**62)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,3-dimethyl-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone,

**63)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**64)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**65)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**66)** (R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-3-ylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**67)** (R)-(3-aminopiperidin-1-yl)(2-(5-bromo-1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**68)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-(pyridin-3-yl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**69)** (R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-2-ylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**70)** (R)-(3-aminopiperidin-1-yl)(2-(1-(2-fluorobenzyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**71)** (R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-4-ylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**72)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-methyl-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**73)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-methoxy-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone

**74)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-methoxy-1H-indol-2-yl)-6-methyl-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**75)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-6-methyl-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**76)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(methylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**77)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5,6-difluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**78)** (R)-(3-aminopiperidin-1-yl)(6-cyclopropyl-2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**79)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(phenethylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**80)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-4-fluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**81)** (R)-(3-aminopiperidin-1-yl)(6-((4-chlorophenyl)sulfonyl)-2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**82)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(cyclopropylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**83)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-((2-ethoxyethyl)sulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**84)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-methyl-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,

**85)** (R)-1-(8-(3-aminopiperidine-1-carbonyl)-2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-4,5-dihydro-6H-imidazo[1,5,4-de]quinoxalin-6-yl)ethan-1-one,

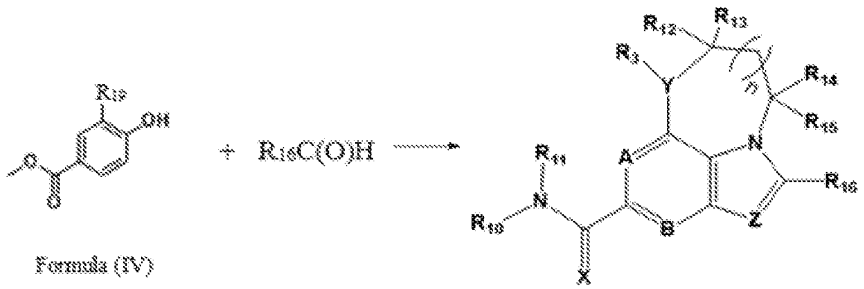
**86)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanethione.

**87)** (R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone, and

**88)** (R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(pyrimidin-5-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone

**[000121]** In an embodiment, the present disclosure relates to a process of preparation of compounds of Formula (I), Formula (II), and Formula (III) or its polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof.

**[000122]** In an embodiment, the disclosure relates to a process of preparation of compounds of Formula (I), or its polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof, the process comprising reacting Formula (IV) and $R_{16}C(O)H$




Formula (IV) Formula (I)

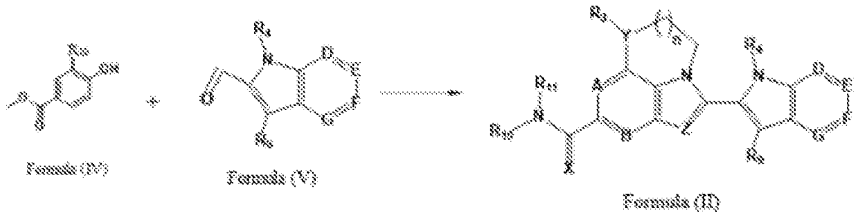
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wherein $R_{19}$ of Formula (IV) is selected from nitro, and $C_{1-6}$ alkoxy; $R_{16}$ of $R_{16}C(O)H$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, -COOH, and cyano; X of Formula (I) is selected from O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; n is 0-2; $R_1$, and $R_2$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one

or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $-NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; or $R_{12}$ and $R_{13}$ can be taken together to form =O or =S; or $R_{14}$ and $R_{15}$ can be taken together to form =O or =S; $R_{16}$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups

selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, -COOH, and cyano; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000123]** In an embodiment, the present disclosure relates to a process of preparation of compounds of Formula (II), or its polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof, the process comprising reacting Formula (IV) and Formula (V)



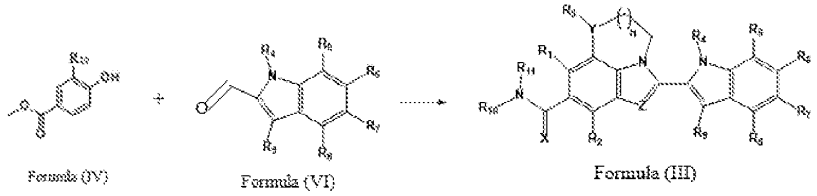
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wherein $R_{19}$ of Formula (IV) is selected from nitro, and $C_{1-6}$ alkoxy; X of Formula (II) is selected from O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; A is selected from N or $CR_1$; B is selected from N or $CR_2$; D is selected from N or $CR_5$; E is selected from N or $CR_6$; F is selected from N or $CR_7$; G is selected from N or $CR_8$; n is 0-2; $R_1$, $R_2$, $R_5$, $R_6$, $R_7$, $R_8$, and $R_9$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_4$ is

selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, -COOH, and cyano; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $-NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof; D of Formula (V) is selected from N or $CR_5$; E is selected from N or $CR_6$; F is selected from N or $CR_7$; G is selected from N or $CR_8$, $R_9$ is H; and $R_4$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl,

$C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, -COOH, and cyano.

**[000124]** In an embodiment, the present disclosure relates to a process of preparation of compounds of Formula (III), or its polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof, the process comprising reacting Formula (IV) and Formula (VI)




,

wherein $R_{19}$ of Formula (IV) is selected from nitro, and $C_{1-6}$ alkoxy; X of Formula (III) is selected from O or S; Y is selected from O, N, S, S(O), $SO_2$ or C; Z is selected from N or $CR_{17}$; n is 0-2; $R_1$, $R_2$, $R_5$, $R_6$, $R_7$, $R_8$, and $R_9$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; $R_4$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl,

wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl,$C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, $-CH_2OH$, COOH, and cyano; $R_{10}$ is hydrogen; $R_{11}$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C_{1-6}$ alkylamino, $C_{1-6}$ haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or $R_{10}$ and $R_{11}$ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, $C_{1-6}$ acylamino, $-NHC(NH)CH_2Cl$, $-NHC(O)CH=CHCH_2N(CH_3)_2$, $C_{1-6}$ alkyl, halogen, $C_{1-6}$ alkoxy, and hydroxyl; $R_{17}$ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof; and $R_5$, $R_6$, $R_7$, $R_8$, and $R_9$ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ haloalkoxy, $C_{1-6}$ acylamino, $C_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{2-6}$ alkenyl- $C_{5-6}$ aryl, and $C_{1-6}$ heteroaryl, wherein $C_{1-6}$ alkoxy, and $C_{1-6}$ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkylhydroxy, cyano, and hydroxyl; $R_4$ is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, $SO_2C_{1-6}$ alkyl, $SO_2C_{1-6}$ haloalkyl, $SO_2NR_{18}$, $SO_2NC_{1-6}$ alkylamino, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, $SO_2C_{5-6}$ aryl, and $SO_2C_{1-6}$

heteroaryl, wherein $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-6}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ alkyl-$C_{5-6}$ aryl, $C_{1-6}$ heterocyclyl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl,$C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, (CO)$C_{1-6}$ alkyl, C(O)$C_{1-6}$ haloalkyl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, $C_{5-6}$ aryl, $C_{1-6}$ heteroaryl, halogen, hydroxyl, -$CH_2OH$, COOH, and cyano; and $R_{18}$ is independently selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, and combinations thereof.

**[000125]** In another embodiment, the present disclosure relates to a pharmaceutical composition comprising a compound of Formula (I), Formula (II), and Formula (III) or a pharmaceutically acceptable salt thereof together with a pharmaceutically acceptable carrier, optionally in combination with one or more other pharmaceutical compositions.

**[000126]** In yet another embodiment, the present disclosure relates to the pharmaceutical composition as described herein, wherein the composition is in the form selected from the group consisting of a tablet, capsule, powder, syrup, solution, aerosol, and suspension.

**[000127]** In an embodiment of the present disclosure, there is provided compounds of Formula (I), Formula (II), and Formula (III) or a pharmaceutically acceptable salt thereof as described herein, wherein the pharmaceutically acceptable salt selected derived from inorganic bases such as like Li, Na, K, Ca, Mg, Fe, Cu, Zn and Mn; salts of organic bases such as N, N'-diacetylethylenediamine, glucamine, triethylamine, choline, dicyclohexylamine, benzylamine, trialkylamine, thiamine, guanidine, diethanolamine, α-phenylethylamine, piperidine, morpholine, pyridine, hydroxyethylpyrrolidine, hydroxyethylpiperidine, ammonium, substituted ammonium salts, aluminum salts and the like. Salts also include amino acid salts such as glycine, alanine, cystine, cysteine, lysine, arginine, phenylalanine, and guanidine. Salts may include acid addition salts where appropriate which are sulphates, nitrates, phosphates, perchlorates, borates, hydrohalides, acetates, tartrates, maleates, citrates, succinates, palmoates, methanesulphonates, tosylates, benzoates, salicylates, hydroxynaphthoates, benzenesulfonates, ascorbates, glycerophosphates, ketoglutarates.

**[000128]** In an embodiment of the present disclosure, there is provided compounds of Formula (I), Formula (II), and Formula (III) or a pharmaceutically acceptable salt thereof as described herein, wherein the pharmaceutically acceptable salt thereof for use in the manufacture of a medicament for inhibiting one or more PADs in a cell.

**[000129]** In an embodiment, the present disclosure relates to a method for inhibiting one or more PAD family in a cell with an effective amount of the compounds of Formula (I), Formula (II), and Formula (III) or a pharmaceutically acceptable salt thereof together

with a pharmaceutically acceptable carrier, optionally in combination with one or more other pharmaceutical compositions.

**[000130]** In an embodiment, the present disclosure relates to a method of treating a condition mediated by one or more PADs, comprising administering to a subject suffering from a condition mediated by one or more PAD family, a therapeutically effective amount of the compounds of Formula (I), Formula (II), and Formula (III) or a pharmaceutically acceptable salt thereof together with a pharmaceutically acceptable carrier, optionally in combination with one or more other pharmaceutical compositions.

**[000131]** In an embodiment, the present disclosure relates to a method for the treatment and/or prevention of PAD mediated disorder or disorders associated with PAD activity, comprising administering to a subject suffering from PAD mediated disorder or disorders associated with PAD activity a therapeutically effective amount of the compounds of Formula (I), Formula (II), and Formula (III) or a pharmaceutically acceptable salt thereof together with a pharmaceutically acceptable carrier, optionally in combination with one or more other pharmaceutical compositions.

**[000132]** In an embodiment, the present disclosure relates to a method for the treatment and/or prevention of PAD mediated disorder or disorders associated with PAD, is selected from the group consisting of rheumatoid arthritis, vasculitis, systemic lupus erythematosus, ulcerative colitis, cancer, cystic fibrosis, asthma, cutaneous lupus erythematosis, and psoriasis.

**[000133]** In an embodiment, the present disclosure relates to a method for the treatment of PAD mediated disorder, said method comprising administering a combination of compounds of Formula (I), Formula (II), and Formula (III) or a pharmaceutically acceptable salts thereof together with a pharmaceutically acceptable carrier, optionally in combination with one or more other pharmaceutical compositions, and/or with other clinically relevant agents or biological agents to a subject in need thereof.

**[000134]** In an embodiment, the present disclosure relates to a method for the treatment and/or prevention of PAD mediated disorder or disorders associated with PAD, is selected from the group consisting of acid-induced lung injury, respiratory distress syndrome, allergen induced asthma, allergic bronchopulmonary, aspergillosis, allergic conjunctivitis, alopecia, amyotropic lateral sclerosis, inflammation, arthritis, asthma, atherosclerosis, atopic dermatitis, autoimmune diseases, bone pain, bronchiolitis, chronic lung disease of prematurity, chronic obstructive pulmonary disease, colitis, complex regional pain syndrome, crohn's disease, cystic fibrosis, familial cold urticarial, gout,

gouty arthritis, graftversus- host disease, gut diseases, inflammatory bowel disease, inflammatory lung disease, inflammatory neuropathy, inflammatory pain, insect bite-induced inflammation, irritant-induced inflammation, juvenile rheumatoid arthritis, kidney disease, kidney injury caused by parasitic infections, kidney transplant rejection prophylaxis, lung injury, lupus, lupus nephritis, multiple sclerosis, muscle wasting, muscular dystrophy, non-allergen induced asthma, osterarthritis, periodontitis, peritoneal endometriosis, plant irritant-induced inflammation, psoriasis, pulmonary disease, pulmonary fibrosis, pyogenic sterile arthritis, renal disease, rheumatic carditis, rheumatic disease, rheumatoid arthritis, sepsis, severe pain and ulcerative colitis.

**[000135]** In an embodiment, the present disclosure relates to the use of compounds of Formula (I), Formula (II), and Formula (III) or a pharmaceutically acceptable salts thereof together with a pharmaceutically acceptable carrier, optionally in combination with one or more other pharmaceutical compositions for treatment of a condition mediated by one or more PAD family; or treatment and/or prevention of PAD mediated disorder; or treatment of PAD mediated disorder together with other clinically relevant agents or biological agents.

**[000136]** In an embodiment, the present disclosure relates to a method for the treatment and/or prevention of a condition mediated by one or more PAD family or a proliferative disorder or cancer, comprising administering to a subject suffering from the condition mediated by one or more PAD family or PAD mediated disorder, a therapeutically effective amount of the compound of the present disclosure or the pharmaceutical composition of the present disclosure.

**[000137]** In an embodiment, the present disclosure relates to a method comprising administering a combination of the compounds of Formula (I), Formula (II), and Formula (III) or the pharmaceutical composition with other clinically relevant agents or biologicalagents to a subject in need thereof.

**[000138]** In an embodiment, the present disclosure relates to a method for the treatment of cancer, said method comprising administering a combination of compounds of Formula (I), Formula (II), and Formula (III) or a pharmaceutically acceptable salt thereof together with a pharmaceutically acceptable carrier, optionally in combination with one or more other pharmaceutical compositions, with other clinically relevant immune modulators agents to a subject in need of thereof.

**EXAMPLES**

**[000139]** As used herein the symbols and conventions used in these processes, schemes and examples are consistent with those used in the contemporary scientific literature, for example, the Journal of the American Chemical Society. Unless otherwise noted, all starting materials were obtained from commercial suppliers and used without further purification. Specifically, the following abbreviations may be used in the examples and throughout the specification:

**Abbreviations:**

| | |
|---|---|
| AcOH | Acetic acid |
| $BOC_2O$ | Di-tert-butyl dicarbonate |
| nBuLi | n-Butyllithium |
| BuOH | Butanol |
| Bz | Benzyl |
| Cbz | Carboxybenzyl |
| cHex | Cyclohexane |
| $Cs_2CO_3$ | Caesium carbonate |
| DCM / $CH_2Cl_2$ | Dichloromethane |
| DIAD | Diisopropyl azodicarboxylate |
| Dioxane | 1,4-dioxane |
| DIPEA | N, N-diisopropylethylamine |
| DMSO | Dimethylsulfoxide |
| DMF | N,N-dimethylformamide |
| $Et_3N$ | Tri ethyl amine |
| Ether | Diethyl ether |
| EtOAc | Ethyl acetate |
| HATU | o-(7-Azabenzotriazol- 1 -yl)-N,N,N' ,N' -tetramethyluronium hexafluorophosphate |
| HPLC | High performance liquid chromatography |
| IPA | Isopropyl alcohol |
| $K_2CO_3$ | Potassium carbonate |
| KOH | Potassium hydroxide |
| LiOH | Lithium hydroxide |
| LCMS or LC/MS | Liquid chromatography- mass spectroscopy |
| MeOH | Methanol |
| min | Minutes |

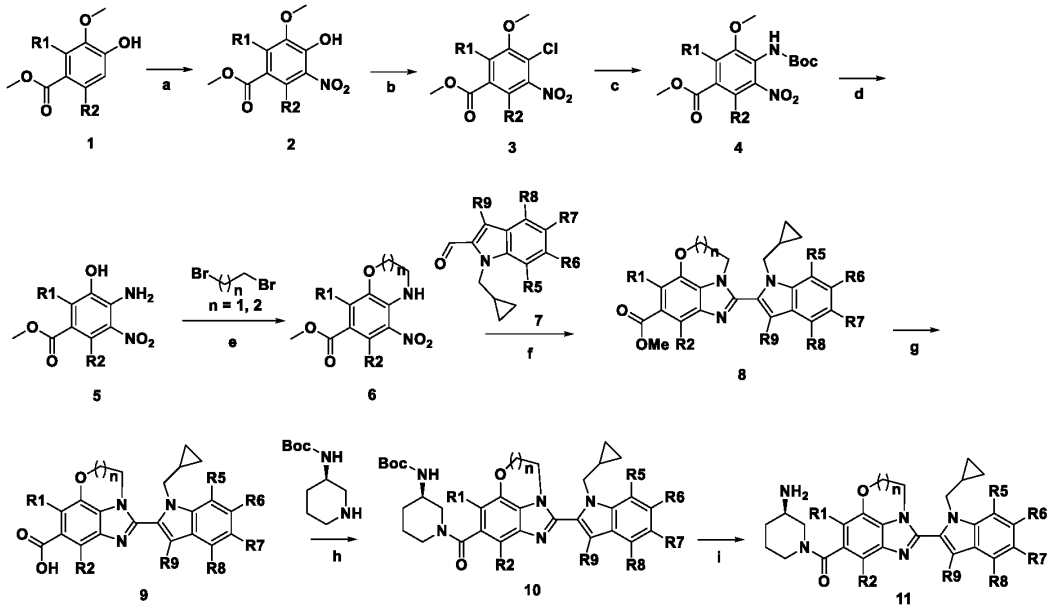
| | |
|---|---|
| $Na_2SO_4$ | Sodium sulfate |
| $NaHCO_3$ | Sodium bicarbonate |
| $NH_4Cl$ | Ammonium chloride |
| Palladium tetrakis | palladium tetrakistriphenylphosphine |
| Pd/C | Palladium on carbon |
| PTSA | p-Toluenesulfonic acid |
| rb | round-bottomed (flask) |
| r.t / rt. | Room temperature |
| Rt | Retention time |
| TFA | Trifluoroacetic acid |
| TFAA | Trifluoroacetic anhydride |
| THF / thf | Tetrahydrofuran |
| TLC / tic | Thin layer chromatography |
| TMEDA | Tetramethyl ethyl enediamine |

**[000140]** The following examples provide the details about the synthesis, activities, and applications of the compounds of the present disclosure. It should be understood the following is representative only, and that the present disclosure is not limited by the details set forth in these examples.

**[000141]** The compounds of the present disclosure may be made by a variety of methods, including standard chemistry. Any previously defined variable will continue to have the previously defined meaning unless otherwise indicated. Illustrative general synthetic methods are set out in the following schemes and can be readily adapted to prepare other compounds of the disclosure.

**[000142]** There is also provided a general process as shown in the following Scheme-1, for the preparation of compounds of the Formula (I, II, and III), wherein all the groups are as defined earlier.

**Scheme 1**




The said process for the preparation of the compounds of Formula (I, II, and III) comprises of the following steps:

**Step 1**: Compound **1** was converted to compound **2** under standard conditions using $CH_3COOH$ and $HNO_3$ (reaction condition **a**).

**Step** 2: Treatment of compound **2** with oxalyl chloride (reaction condition **b**) gave intermediate **3**.

**Step 3**: Intermediate **3** was converted to compound **4** using tert-butyl carbamate, $Cs_2CO_3$ and X-Phos (reaction condition **c**).

**Step 4**: Treatment of compound **4** with $BBr_3$ (reaction condition **d**) gave intermediate **5.**

**Step 5**: Intermediate **5** was converted to compound **6** by reacting with 1, ω-dibromoalkane and $K_2CO_3$ (reaction condition **e**).

**Step 6**: Compound **6** was coupled with substituted indole-2-carbaldehyde **7** (reaction condition **f)** to give compound **8.**

**Step 7**: Compound **8** was hydrolysed (Reaction condition **g**) to give compound **9**.

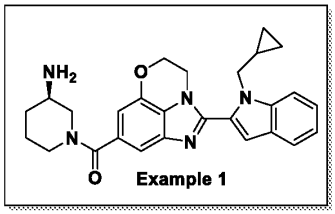
**Step 8**: Coupling of compound **9** with tert-butyl (R)-piperidin-3-ylcarbamate (reaction condition **h**) gave intermediate **10**.

**Step 9**: Compound **10** was converted to final compound **11** by Boc deprotection (reaction condition **i**).

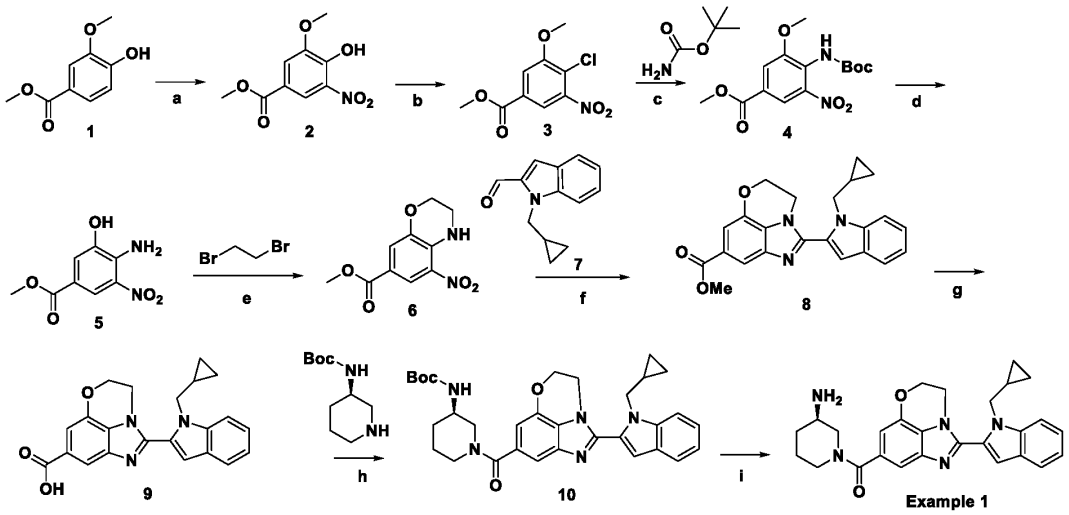
**[000143]** The examples given below are provided by the way of illustration only and therefore should not be construed to limit the scope of the disclosure.

**Example-1:**

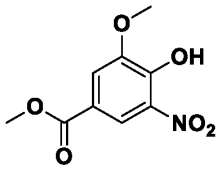
**Synthesis of ((R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone (Example -1)**




Scheme 2




**Step 1: Preparation of methyl 4-hydroxy-3-methoxy-5-nitrobenzoate (2)**

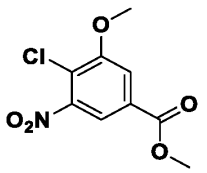


**2**

**[000144]** To a stirred solution of methyl-4-hydroxy-3-methoxybenzoate (**1**, 20 g, 109.7 mmol) in $CH_3COOH$ (100 mL) was added $HNO_3$ (5.9 mL, 94.4 mmol) under 0°C drop wise and then reaction mixture was stirred at room temperature for 4-5 h (reaction

condition **a**). To the reaction mixture ice cold water was added and the reaction mixture was filtered to obtain the precipitate which was dried using high vacuum to get the product as yellow solid (18 g, 75% yield). MS (ESI): mass calcd. for $C_9H_9NO_6$, 227.04; m/z found, 228 $[M+H]^+$.

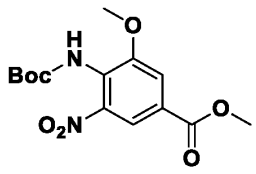
**Step 2: Preparation of methyl 4-chloro-3-methoxy-5-nitrobenzoate (3)**



**3**

**[000145]** To a stirred solution of methyl 4-hydroxy-3-methoxy-5-nitrobenzoate (**2**, 18 g, 79.29 mmol) in DMF (100 mL) was added oxalyl chloride (14.27 mL, 113.28 mmol) under 0°C slowly, then the reaction mixture was refluxed under 80°C for about 12 h (reaction condition **b**). To the reaction mixture ice cold water was added and the resulting solid was filtered. The solid was dried under high vacuum to obtain the product as brown solid (17.5 g, 90% yield). MS (ESI): mass calcd. for $C_9H_8ClNO_5$, 245.01; m/z found, 246 $[M+H]^+$.

**Step 3: Preparation of Methyl 4-((tert-butoxycarbonyl) amino)-3-methoxy-5-nitrobenzoate (4)**

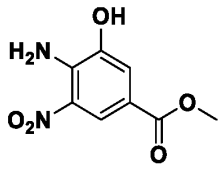


**4**

**[000146]** To a stirred solution of methyl 4-chloro-3-methoxy-5-nitrobenzoate (**3**, 6 g, 24.42 mmol) in t-butanol (50 mL) was added tert-butyl carbamate (2.86 g, 24.42 mmol), $Cs_2CO_3$ (9.5 g, 29.31 mmol) and X-Phos (1.16 g, 2.44 mmol) under $N_2$. $Pd_2(dba)_3$, (,0.44 g, 0.48 mmol) was added and stirred for about 10 min at room temperature and then resulting mixture was heated to 100 °C for 12 h (reaction condition **c**). The reaction mixture was cooled to room temperature and diluted with ethyl acetate (100 mL x 3) and the organic phase was washed with water and brine, dried over sodium sulphate and concentrated under reduced pressure to afford the crude compound which was purified by column chromatography (silica gel, 0-20% EtOAc in hexane) to afford methyl 4-((tert-

butoxycarbonyl) amino)-3-methoxy-5-nitrobenzoate (2.5 g, 75% yield) as colourless liquid. MS (ESI): Mass calcd. for $C_{14}H_{18}N_2O_7$, 325.0; m/z found, 326.3 $[M+H]^+$.

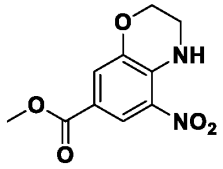
**Step 4: Preparation of Methyl 4-amino-3-hydroxy-5-nitrobenzoate (5)**



**5**

**[000147]** To a stirred solution of methyl 4-((tert-butoxycarbonyl) amino)-3-methoxy-5-nitrobenzoate (**4**, 3.5g, 10.74 mmol) in DCM (30 mL) was added $BBr_3$ (3.5 mL,) at -78°C and the resulting mixture was allowed to stir under room temperature for 3 h (reaction condition **d**). The progress of the reaction was monitored by TLC. The reaction mixture was quenched with ice and sodium bicarbonate solution (30 mL) and extracted with DCM (50 mL x 3). The combined organic extract was washed with brine, dried over sodium sulphate and concentrated under reduced pressure to afford methyl 4-amino-3-hydroxy-5-nitrobenzoate (0.7 g, 35% yield) as brown solid. MS (ESI): Mass calcd. for $C_8H_8N_2O_5$, 212.1; m/z found, 213 $[M+H]^+$.

**Step 5: Preparation of Methyl 5-nitro-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (6)**

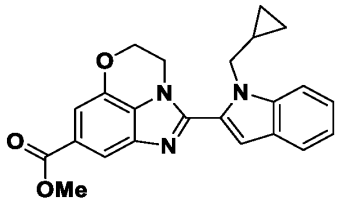


**6**

**[000148]** To a stirred solution of methyl 4-amino-3-hydroxy-5-nitrobenzoate (**5**, 1.1g, 5.12 mmol) in DMF (10 mL) was added 1,2-dibromo ethane (0.44 mL,) and $K_2CO_3$ (0.86 g, 2.38 mmol) the resulting mixture was heated to 80°C for 12 h (reaction condition **e**). The progress of the reaction was monitored by TLC. The reaction mixture was quenched with water and extracted with ethyl acetate (20 mL x 2). The combined organic extract was washed with brine, dried over sodium sulphate and concentrated under reduced pressure to afford the crude compound which was purified by column chromatography (SiO2, 0-20% EtOAc in hexane) to afford methyl 5-nitro-3,4-dihydro-

2H-benzo[b][1,4]oxazine-7-carboxylate (0.45 g, 89% yield) as brown solid. MS (ESI): Mass calcd. for $C_{10}H_{10}N_2O_5$, 238.2; m/z found, 239.1 $[M+H]^+$.

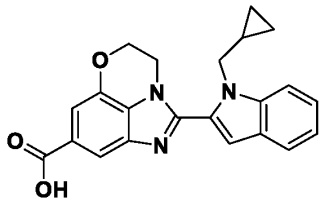
**Step 6: Preparation of Methyl 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2diazaacenaphthylene-7-carboxylate (8)**



**8**

**[000149]** To the stirred solution of mixture of methyl 5-nitro-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (**6**, 0.2 g, 0.84 mmol) and 1-(cyclopropylmethyl)-1H-indole-2-carbaldehyde (**7**, 0.18 g, 0.92 mmol) in EtOH (10 mL), was added $Na_2S_2O_4$ (0.73 g, 4.20 mmol) in water (5 mL) and stirred at 95°C for 16h (Reaction condition **f**). The reaction mixture was cooled to room temperature, water was added and compound was extracted with ethyl acetate (20 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using silica gel with eluent 15-20% ethyl acetate in hexane to afford methyl 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2diazaacenaphthylene-7-carboxylateas yellow solid (0.18 g. 12% yield). MS (ESI): Mass calcd. for $C_{23}H_{21}N_3O_3$, 387.4; m/z found, 388.1 $[M+H]^+$.

**Step 7: Preparation of 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid (9)**

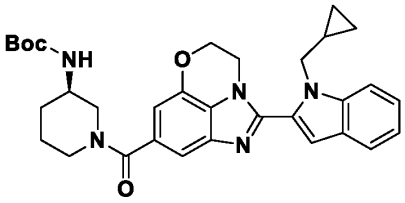


**9**

**[000150]** To the stirred solution of methyl 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2diazaacenaphthylene-7-carboxylate (**8**, 0.18 g, 0.46 mmol) in MeOH (2 mL), was added 5N NaOH solution (0.4 mL) and stirred at 75°C for 1h (reaction condition **g**). The reaction mixture was evaporated completely. The resulting crude was dissolved in water and acidified using citric acid (pH~ 4-6), extracted with DCM (20 mL x 2). Combined organic extracts were washed with brine, dried over sodium

sulfate, filtered and evaporated to get crude product as a yellow solid to afford the2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid as brown solid (0.07 g, 41% yield). MS (ESI): Mass calcd. for $C_{22}H_{19}N_3O_3$, 373.4; m/z found, 374.1 $[M+H]^+$.

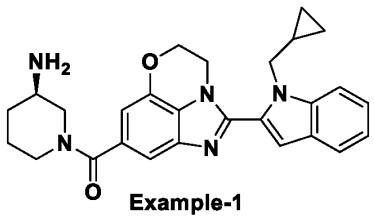
**Step 8: Preparation of tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydrooxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (10)**




**10**

**[000151]** To the stirred solution of 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3-methyl-3H-imidazo[4,5-b]pyridine-6-carboxylic acid (**9**, 0.089 g, 0.24 mmol) in DCM (2 mL), were added tert-butyl (R)-piperidin-3-ylcarbamate (0.05 g, 0.26 mmol), triethylamine (0.1 g, 0.72 mmol) followed by 50% solution of T3P in ethyl acetate (0.2 g, 0.72 mmol) and stirred at room temperature for 12 h (reaction condition **h**). To the reaction mixture was added water and compound was extracted with DCM (20 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using 5% MeOH in DCM to afford the product as yellow solid (0.07 g, 53.8% yield). MS (ESI): Mass calcd. for $C_{32}H_{37}N_5O$, 555.6; m/z found, 556.3 $[M+H]^+$.

**Step 9: Preparation of (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone (Example-1)**




**Example-1**

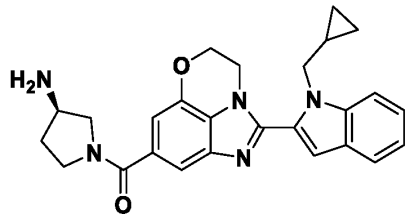
**[000152]** To the stirred solution of tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (**10**, 0.08 g, 0.14 mol) in dichloromethane (10 mL), was added trifluroacetic

acid (0.5 mL) and stirred at room temperature for 2h (reaction condition **i**). The reaction mixture was evaporated completely, dissolved in minimum volume of water (30 mL) and basified by saturated $NaHCO_3$ (20 mL) solution. The compound was extracted with ethyl acetate (50 mL x 2)). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get the product as pale yellow solid (0.044 g, 67.5% yield). $^1$HNMR (400 MHz, DMSO-d6): δ (ppm): 7.68 (t, $J$ = 4.4 Hz, 2H), 7.29 (t, $J$ = 5.2 Hz, 2H), 7.15-7.10 (m, 2H), 6.74 (s, 1H), 4.69-4.68 (m, 4H), 4.55 (s, 2H), 3.56 (m, 2H), 2.92 (s, 1H), 4.13 (s, 2H), 2.69-2.65 (m, 1H), 1.88-1844 (m, 2H), 1.64 (m, 1H), 1.43-1.41 (m, 1H), 1.23-1.22 (m, 2H), 0.32 (d, $J$ = 8 Hz, 2H), 0.28-0.27 (m, 2H). MS (ESI): mass calcd. for $C_{32}H_{37}N_5O_4$, 455.0; m/z found, 456.4 $[M+H]^+$.

**[000153]** Following compounds **(Examples 2-8)** were synthesized using the above procedure as exemplified for **Example-1** above with corresponding reactants.

**Example-2:**

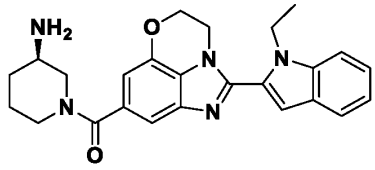
**(R)-(3-aminopyrrolidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000154]** $^1$HNMR (400 MHz, DMSO-d6): δ (ppm): 7.69 (t, $J$ =12 Hz, 2H), 7.43 (s, 1H), 7.29-7.26 (m, 1H), 7.18-7.10 (m, 2H), 6.87 (s, 1H), 4.69 (d, $J$ = 8 Hz, 2H), 4.64 (d, $J$ = 4 Hz, 2H ), 4.56-4.55 (m, 2H), 3.65-3.59 (m, 2H), 3.56-3.45 (m, 2H), 1.97 (m, 2H), 1.64 (m, 2H), 1.31-1.22 (m, 2H), 0.32 (d, $J$ = 8 Hz, 2H), 0.27-0.26 ( m, 2H). MS (ESI): mass calcd. for $C_{26}H_{27}N_5O_2$, 441.22; m/z found, 442.0 $[M+H]^+$.

**Example-3:**

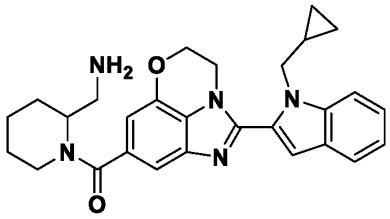
**(R)-(3-aminopiperidin-1-yl)(2-(1-ethyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000155]** $^1$HNMR (400 MHz, DMSO-d6): δ (ppm): 7.67 (d, *J* = 8 Hz, 1H), 7.62 (d, *J* = 8 Hz, 1H), 7.31-7.27 (m, 2H), 7.14-7.11 (m, 2H), 6.70 (s, 1H) , 4.80 (m, 2H), 4.77 (m, 2H), 4.75 (m, 2H) 4.00 (m, 2H), 3.60 (m, 2H), 2.94 (bs, 1H), 2.78 (bs, 2H), 1.89 (m, 1H), 1.73 (m, 1H), 1.42 (m, 1H), 1.35 (m, 3H), 1.31 (m, 1H). MS (ESI): Mass calcd. for $C_{25}H_{27}N_5O_2$, 429.52; m/z found, 430.2 $[M+H]^+$.

**Example-4:**

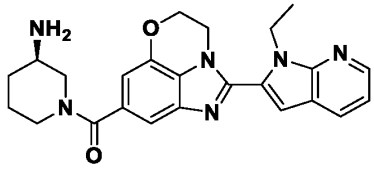
**(2-(aminomethyl)piperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**




**[000156]** $^1$HNMR (400 MHz, DMSO-d6): δ (ppm): 7.68 (t, *J* = 8 Hz, 2H), 7.50 (m, 1H), 7.29-7.26 (m, 2H), 7.14-7.05 (m, 3H), 6.74 (d, *J* = 8 Hz, 1H), 4.68 (d, *J* = 8 Hz, 2H), 4.64 (m, 2H), 4.54 (m, 2H), 3.97-3.96 (m, 2H), 2.87-2.81 (m, 1H), 1.54-1.49 (m, 2H), 1.28 (m, 1H), 1.13 (m, 6H), 0.37-0.27 (m, 4H). MS (ESI): Mass calcd. for $C_{28}H_{31}N_5O_2$, 469.59; m/z found, 470.3 $[M+H]^+$.

**Example-5:**

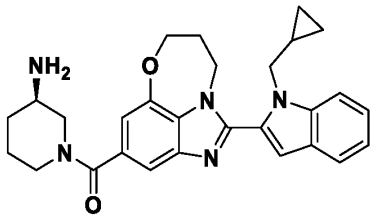
**(R)-(3-aminopiperidin-1-yl)(2-(1-ethyl-1H-pyrrolo[2,3-b]pyridin-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**




**[000157]** $^1$HNMR (400 MHz, DMSO-d6): δ (ppm): 8.42 (d, *J* = 4 Hz, 1H), 8.11 (d, *J* = 4Hz, 1H), 7.31(s, 1H), 7.22-7.19 (m, 2H), 6.75 (s, 1H), 4.89-4.86 (m, 2H), 4.68 (m, 2H), 4.56 (m, 2H), 3.51 (m, 2H), 2.91-2.87 (m,1H), 1.97 (m, 1H), 1.86-1.83 (m, 2H), 1.65 (m, 3H), 1.43-1.33 (m, 5H). MS (ESI): Mass calcd. for $C_{24}H_{26}N_6O_2$, 430.51; m/z found, 431.4 $[M+H]^+$.

**Example-6:**

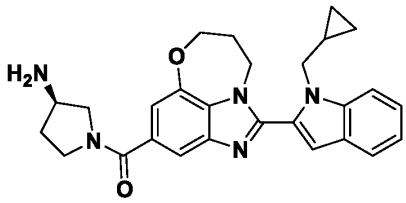
**(R)-(3-aminopiperidin-1-yl)(1-(1-(cyclopropylmethyl)-1H-indol-2-yl)-8,9-dihydro-7H-6-oxa-2,9a-diazabenzo[cd]azulen-4-yl)methanone**



**[000158]** $^1$HNMR (400 MHz, DMSO-d6): δ (ppm): 7.65 (m, 2H), 7.35 (s, 1H), 7.27 (m, 1H), 7.12 (m, 1H), 7.04 (m, 1H), 6.82 (s, 1H), 4.45-4.38 (m, 6H), 2.65 (m, 2H), 1.89 (m, 2H), 1.67 (m, 3H), 1.45-1.31 (m, 2H), 1.22 (m, 4H), 0.83 (s, 1H), 0.30 (m, 2H), 0.06 (m, 2H). MS (ESI): Mass calcd. for $C_{28}H_{31}N_5O_2$, 469.59; m/z found, 470.2 $[M+H]^+$.

**Example-7:**

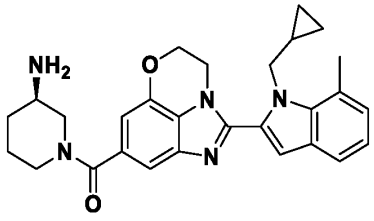
**(R)-(3-aminopyrrolidin-1-yl)(1-(1-(cyclopropylmethyl)-1H-indol-2-yl)-8,9-dihydro-7H-6-oxa-2,9a-diazabenzo[cd]azulen-4-yl)methanone**



**[000159]** $^1$HNMR (400 MHz, DMSO-d6): δ (ppm): 7.68-7.64 (m, 2H), 7.46-7.44 (m, 1H), 7.29 (t, *J* = 16 Hz, 1H), 7.14-7.10 (m, 1H) 7.04 (bs , 1H), 6.92 (s, 1H), 4.44-4.36 (m, 6H), 3.64 (m, 2H), 3.55-3.48 (m, 2H), 2.43 (m, 2H), 1.97 (m, 1H), 1.86 (m, 1H), 1.60 (m, 1H), 1.31 (m, 1H), 1.06 (m, 1H), 0.83 (m, 1H), 0.31 (m, 2H), 0.05 (m, 2H). MS (ESI): Mass calcd. for $C_{27}H_{29}N_5O_2$, 455.56; m/z found, 456.3 $[M+H]^+$.

**Example-8:**

**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-methyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**

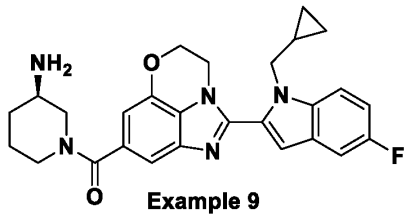


**[000160]** $^1$HNMR (400 MHz, DMSO-d6): δ (ppm): 7.51 (d , *J* = 6.0 Hz, 1H), 7.27 (s, 1H), 7.12 (s, 1H), 7.03-7.00 (m, 2H), 6.75 (s, 1H), 4.89 (d, *J* = 6.0 Hz, 2H), 4.57 (d, *J*

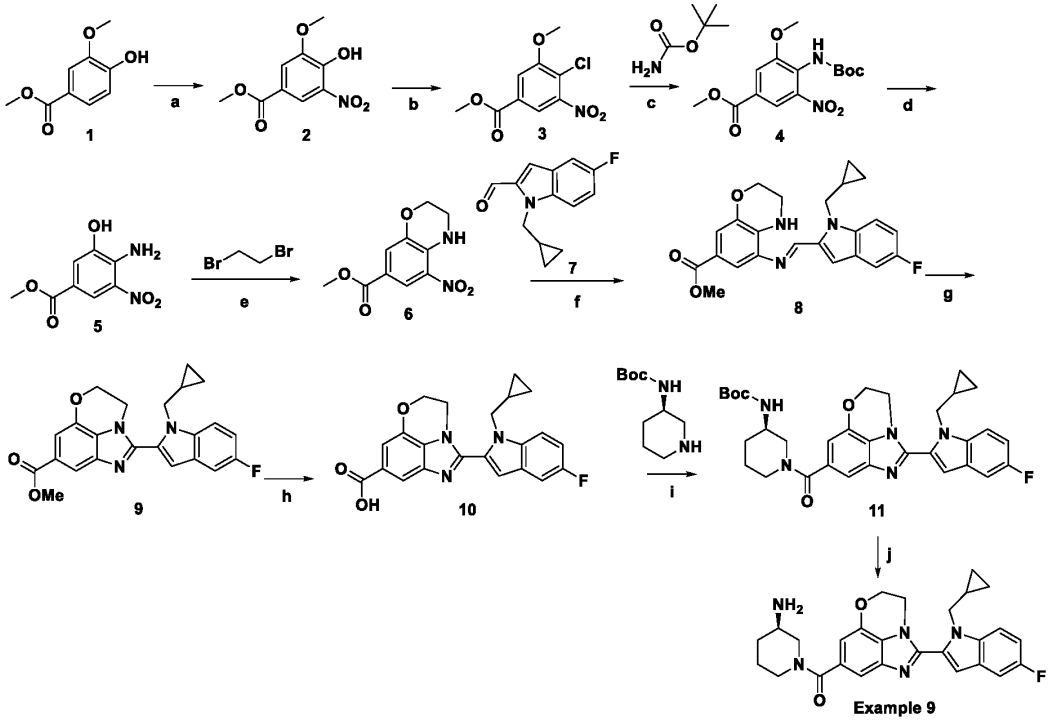
= 7.2 Hz, 4H), 4.30 (s, 1H), 3.65 (s, 1H), 2.90 (s, 1H), 2.78 ( s, 3H), 2.65 (s, 1H), 1.84-1.65 (m, 4H), 1.41 (d, *J* = 10.8 Hz, 1H), 1.22 (m, 2H), 0.94 (bs, 1H), 0.21 (d , *J* = 7.6 Hz, 2H), 0.15 (d, *J* = 4.4 Hz, 2H). MS (ESI): mass calcd. for $C_{28}H_{31}N_5O_2$, 469.5; m/z found, 470 $(M+H)^+$.

**Example-9:**

**Synthesis of (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone (Example-9)**

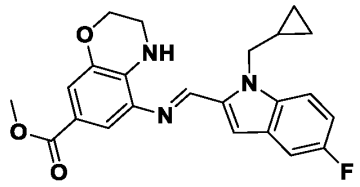



Scheme 3




**[000161]** The reaction procedure followed to obtain intermediate **(6)** was similar to the procedure outlined for the preparation of Example-1 in Scheme-2 above.

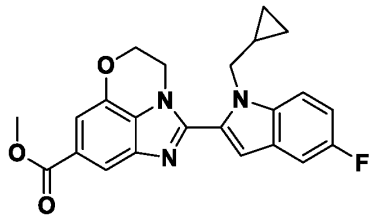
**Step 6: Preparation of methyl (E)-5-(((1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)methylene)amino)-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (8)**



**8**

**[000162]** To a stirred solution methyl 5-nitro-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (**6**, 0.25 g, 1.05 mmol) in ethanol (6 mL), were added 1-(cyclopropylmethyl)-5-fluoro-1H-indole-2-carbaldehyde (**7**, 0.27 g, 1.26 mmol), sodium dithionite (0.91 g, 5.25 mmol) and water (3 mL). Then the reaction mixture was heated to 90°C for 12 h in a sealed tube (reaction condition **f**). The reaction mixture was evaporated, diluted with water and extracted with ethyl acetate (20 mL x 2). Combined organic extracts were washed with water, brine, dried over sodium sulfate, filtered and evaporated to get crude product as a yellow solid (0.25 g, crude). MS (ESI): mass calcd. for $C_{23}H_{22}FN_3O_3$, 407.45; m/z found, 408.1 $[M+H]^+$.

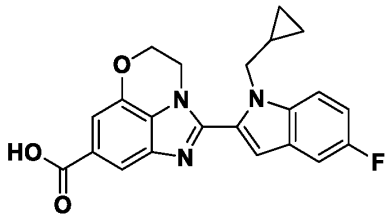
**Step 7: Preparation of methyl 2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylate (9)**



**9**

**[000163]** To a stirred solution methyl (E)-5-(((1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)methylene)amino)-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (**8,** 0.25 g, 0.61 mmol) in toluene (3 mL), was added p-toluene sulfonic acid (0.012 g, 0.0614 mmol) at room temperature. Then the reaction mixture was heated to 90°C for 12 h (reaction condition **g**). The reaction mixture was quenched with sodium bicarbonate, extracted with ethyl acetate (20 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate, filtered and evaporated to get crude product. Crude residue was purified by gradient column chromatography using silica gel and eluent 15-20% ethyl acetate in hexane to get the product as a yellow solid (0.15 g, 35% yield). MS (ESI): mass calcd. for $C_{23}H_{20}FN_3O_3$, 405.43; m/z found, 406.1 $[M+H]^+$.

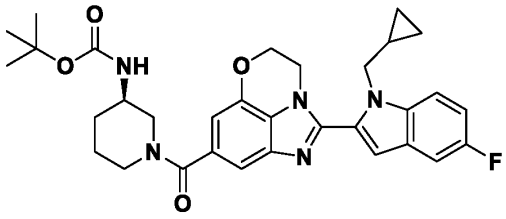
**Step 8: Preparation of 2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid (10)**



**10**

**[000164]** To a stirred solution of methyl 2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylate (**9**, 0.15 g, 0.37 mmol) in methanol (5 mL) was added 5N NaOH (0.37 mL, 1.85 mmol) solution and heated to 80°C for 1 h (reaction condition **h**). The solvent was evaporated completely and dissolved in water (10 mL) and acidified using citric acid, extracted with DCM (20 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate, filtered and evaporated to get crude product as a yellow solid (0.13 g, 90% yield). MS (ESI): mass calcd. for $C_{22}H_{18}FN_3O_3$, 391.40; m/z found, 392.1 $[M+H]^+$.

**Step 9: Preparation of Tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (11)**

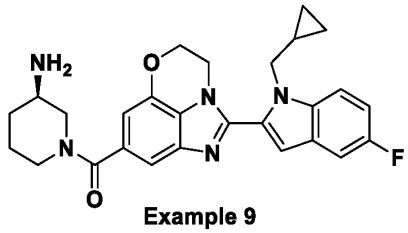


**11**

**[000165]** To a stirred solution of 2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid (**10**, 0.13 g, 0.33 mmol) in DCM (4 mL), were added tert-butyl (R)-piperidin-3-ylcarbamate (0.079 g, 0.398 mmol), triethylamine (0.09 mL, 0.66 mmol), propyl phosphonic anhydride in 50% ethyl acetate (0.316 mL, 0.498 mmol). The reaction mixture was allowed to stir at room temperature for 1h (reaction condition **i**). The reaction mixture was quenched with sodium bicarbonate solution (20 mL), extracted with ethyl acetate (20 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate, filtered and evaporated to get crude product. Crude residue was purified by gradient column

chromatography using silica gel and eluent 5-10% methanol in DCM to get the product as a yellow solid (0.13 g, 68% Yield). MS (ESI): mass calcd. for $C_{32}H_{36}FN_5O_4$, 573.67; m/z found, 574.3 $[M+H]^+$.

**Step 10: Preparation of (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone (Example-9)**



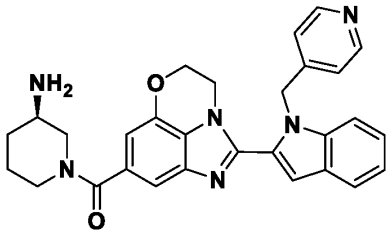

Example 9

**[000166]** To a stirred solution of Tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (**11**, 0.13 g, 0.226 mmol) in DCM (4 mL) was added trifluoro acetic acid (0.5 mL) at 0°C. Then the reaction mixture was allowed to stir at room temperature for 1 h (reaction condition **j**). Reaction mixture was evaporated under reduced pressure, washed with ether and the reaction mixture was basified using saturated sodium bicarbonate solution (20 mL) and extracted with ethyl acetate (20 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate, filtered and evaporated to get crude product. Crude residue was purified by gradient column chromatography using silica gel and eluent 5-10% methanol in DCM to get the product as off white solid (0.06 g, 57% Yield). $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): δ 7.72-7.68 (m, 1H), 7.44 (d, $J$ = 7.2 Hz, 1H), 7.29 (s, 1H), 7.13 (t, $J$ = 7.2 Hz, 2H), 6.75 (s, 1H), 4.69-4.64 (m, 4H), 4.55 (s, 2H), 4.15 (bs, 1H), 3.77 (bs, 1H), 2.91 (bs, 1H), 2.65 (bs, 2H), 1.84 (d, $J$ = 11.6 Hz, 2H), 1.64 (bs, 1H), 1.42 (d, $J$ = 10.8 Hz, 1H), 1.22 (bs, 3H), 0.34 - 0.27 (m, 4H). MS (ESI): mass calcd. for $C_{27}H_{28}FN_5O_2$, 473.55; m/z found, 474.2 $[M+H]^+$.

**[000167]** Following compounds **(Examples 10-60)** were synthesized using the above procedure as exemplified for **Example-9**.

**Example-10:**

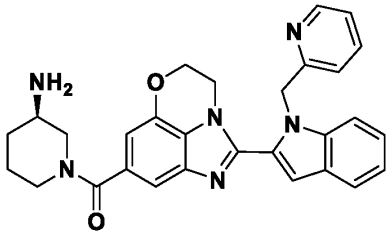
**(R)- (3-aminopiperidin-1-yl)(2-(1-(pyridin-4-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-yl)methanone**



**[000168]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 8.40-8.38 (m, 2H), 7.74-7.72 (m, 1H), 7.44-7.42 (m, 1H), 7.33 (s, 1H), 7.28 (s, 1H), 7.26-7.22 (m, 1H), 7.17-7.13 (m, 1H), 7.01-6.99 (m, 2H), 6.77 (s, 1H), 6.16 (s, 2H), 4.71 (m, 2H), 4.56-4.55 (m, 2H), 4.11(m, 2H) ,3.0 (m, 2H), 2.01-1.8 (m, 3H), 1.67 (m, 1H), 1.44 (bs, 3H). MS (ESI): mass calcd. for $C_{29}H_{28}N_6O_2$, 492.23; m/z found, 493 $[M+H]^+$.

**Example-11:**

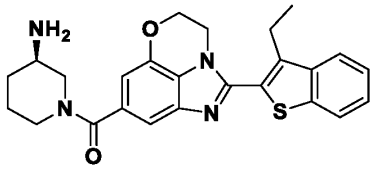
**(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridine-2-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000169]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 8.43 (d, $J$ = 4 Hz, 1H), 7.72-7.70 (m, 1H), 7.61-7.57 (m, 1H), 7.46-7.44 (m, 1H), 7.22 (s, 2H), 7.27 (s, 1H), 7.19-7.09 (m, 3H), 6.72 (s, 1H), 6.17 (s, 2H), 4.68( m, 2H), 4.55( m, 2H), 3.94 ( m, 2H), 2.87 (m, 2H), 1.84-1.81 (m, 2H), 1.62 (m, 3H), 1.40 ( bs, 2H). MS (ESI): mass calcd. for $C_{29}H_{28}N_6O_2$, 492.23; m/z found, 493.2 $[M+H]^+$.

**Example-12:**

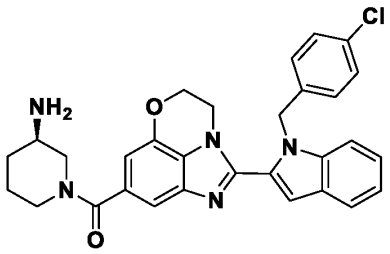
**(R)-(3-aminopiperidin-1-yl)(2-(3-ethylbenzo[b]thiophen-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone:**



**[000170]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 8.08 (m, 1H), 8.06-7.98 (m, 1H), 7.53-7.49 (m, 2H), 7.36 (s, 1H), 6.79 (s, 1H), 4.48 (d, $J$ = 8 Hz, 4H), 4.00 (bs, 2H), 3.28 (m, 2H), 3.22 (m, 3H), 1.95 (m, 1H), 1.70 (m, 1H), 1.48 (m, 2H), 1.31-1.21 (m, 5H). MS (ESI): mass calcd. for $C_{25}H_{26}N_4O_2S$, 446.57; m/z found, 447.2 $[M+H]^+$.

**Example-13:**

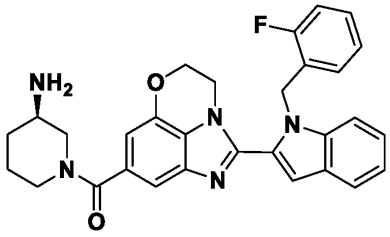
**(R)-(3-aminopiperidin-1-yl)(2-(1-(4-chlorobenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-yl)methanone**




**[000171]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.71 (d, *J* = 8 Hz, 1H), 7.47-7.45 (m, 1H), 7.28-7.21 (m, 4H), 7.15-7.09 (m, 4H), 6.74 (s, 1H), 6.09 (s, 2H), 4.68 (m, 2H), 4.55 (m, 2H), 2.92 (m, 2H), 2.73 (m, 2H), 1.97 (m, 2H), 1.88 (m, 2H), 1.62 (m, 3H). MS (ESI): mass calcd. for $C_{30}H_{28}ClN_5O_2$, 525.19; m/z found, 526.2 $[M+H]^+$.

**Example-14:**

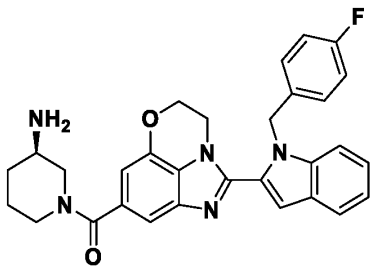
**(R)-(3-aminopiperidin-1-yl)(2-(1-(2-fluorobenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-yl)methanone**




**[000172]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.72 (d, *J* = 8 Hz, 1H), 7.46 (d, *J* = 8 Hz, 1H), 7.29-7.26 (m, 1H), 7.24-7.18 (m, 3H), 7.16-7.12 (m, 2H), 6.96-6.93 (m, 1H), 6.73 (s, 1H), 6.67-6.63 (bs, 1H), 6.17 (s, 2H), 4.66 (m, 2H), 4.55(m, 2H), 4.00 (m, 2H), 2.48 (m, 1H), 2.89 (s, 1H), 2.00 (m, 2H), 1.85 (m, 1H), 1.62 (m, 1H), 1.41-1.39 (m, 1H), 1.22 (m, 2H). MS (ESI): mass calcd. for $C_{30}H_{28}FN_5O_2$, 509.22; m/z found, 510.2$[M+H]^+$.

**Example-15:**

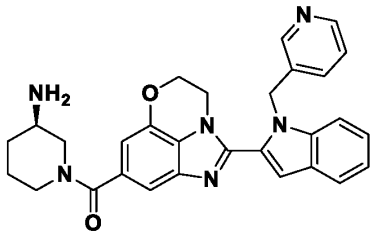
**(R)-(3-aminopiperidin-1-yl)(2-(1-(4-fluorobenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000173]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.71 (d, *J* = 8 Hz, 1H), 7.50-7.48 (d, *J* = 8 Hz, 1H), 7.25 (s, 2H), 7.22 (m, 1H), 7.16-7.10 (m, 3H), 7.05 (t, *J* = 8.8 Hz, 2H), 6.73 (s, 1H), 6.08 (s, 2H), 4.67 (m, 2H), 4.56 (m, 2H), 4.01 (m, 2H), 2.88 (m, 2H), 1.98-1.97 (m, 2H), 1.82 (m, 1H), 1.70 (m, 2H), 1.41-1.31 (m, 2H). MS (ESI): mass calcd. for $C_{30}H_{28}FN_5O_2$, 509.59; m/z found, 510.2 $[M+H]^+$.

**Example-16:**

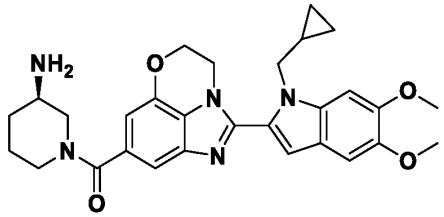
**(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-3-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000174]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 8.40 (s, 1H), 8.36 (d, *J* = 3.6 Hz, 1H), 7.70 (d, *J* = 8 Hz, 1H), 7.54 (d, *J* = 8 Hz, 1H ), 7.46 (d, *J* = 8 Hz, 1H ), 7.29-7.12 (m, 4H), 7.16-7.12 (m, 1H), 6.74 (s, 1H), 6.14 (s, 2H), 4.68-4.55 (m, 4H), 4.12 (m, 2H), 2.90 (m, 1H), 2.71-2.65 (m, 2H), 1.88-1.83 (m, 2H), 1.63 (m, 1H), 1.42-1.12 (m, 3H). MS (ESI): mass calcd. for $C_{29}H_{28}N_6O_2$, 492.58; m/z found, 493.4 $[M+H]^+$.

**Example-17:**

**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5,6-dimethoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**

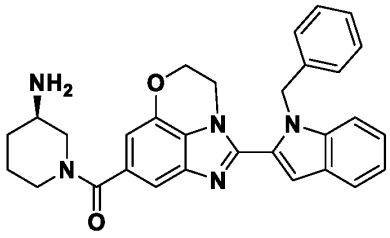


**[000175]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.25 (s, 1H), 7.18 (s, 1H), 7.13 (s, 1H), 6.99 (s, 1H), 6.72 (s, 1H), 4.68 (d, *J* = 6.4 Hz, 2H), 4.61 (s, 2H), 4.54 (s, 2H),

3.85 (s, 3H), 3.78 (s, 3H), 4.30-4.00 (s, 1H), 3.15 (d, $J$ = 4.0 Hz, 1H), 2.92 (bs, 2H), 2.70 (bs, 2H), 1.91 (bs, 1H), 1.81 (bs, 1H), 1.65 (bs, 1H), 1.44 (bs, 2H), 0.84 (s, 1H), 0.33-0.28 (m, 4H). MS (ESI): mass calcd. for $C_{29}H_{33}FN_5O_4$, 515.61; m/z found, 516.3$[M+H]^+$.

**Example-18:**

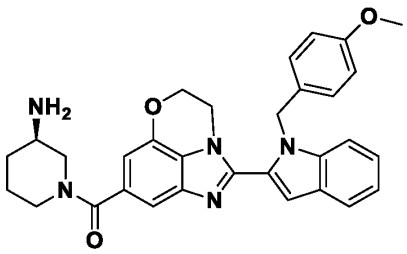
**(R)-(3-aminopiperidin-1-yl)(2-(1-benzyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000176]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.70 (d , $J$ = 8.0 Hz, 1H), 7.47 (d, $J$ = 8.0 Hz, 1H), 7.26-7.10 (m, 7H), 7.06 (d , $J$ = 7.2 Hz, 2H), 6.73 (s, 1H), 6.11 (s, 2H), 4.66 (d , $J$ = 5.0 Hz, 2H), 4.55 (d , $J$ = 5.0 Hz, 2H), 3.65 (bs, 1H), 2.88 (bs, 1H), 2.65 (bs, 1H), 1.98 (d , $J$ = 7.6 Hz, 1H), 1.83 (d, $J$ = 11.6 Hz, 1H), 1.63 (bs, 1H), 1.41-1.22 (m, 4H), 0.84 (s, 1H). MS (ESI): mass calcd. for $C_{30}H_{29}N_5O_2$, 491.6; m/z found, 492.2 $(M+H)^+$.

**Example-19:**

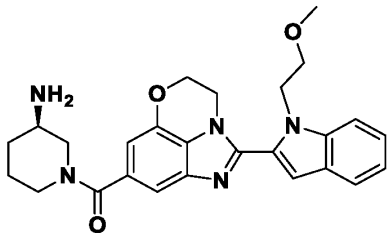
**(R)-(3-aminopiperidin-1-yl)(2-(1-(4-methoxybenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000177]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.68 (d, $J$ = 8 Hz, 1H), 7.45 (d, $J$ = 8 Hz, 1H), 7.25 (s, 1H), 7.23-7.22 (m, 2H), 7.12 (t, $J$ = 7.2 Hz, 1H), 7.03 (d , $J$ =8.4 Hz, 2H), 6.76 (s, 1H), 6.74 (s, 2H), 6.01 (bs, 2H), 4.65-4.55 (m, 2H), 4.55-4.54 (m, 2H), 4.12 (bs, 2H), 3.80 (s, 3H) 2.89 (m, 1H), 2.65 (m, 1H), 1.87 (m,1H), 1.82 (m,1H), 1.63 ( m ,1H), 1.41 (m, 1H), 1.21-1.20 ( m, 3H). MS (ESI): mass calcd. for $C_{31}H_{31}N_5O_3$, 521.62; m/z found, 522.2 $[M+H]^+$.

**Example-20:**

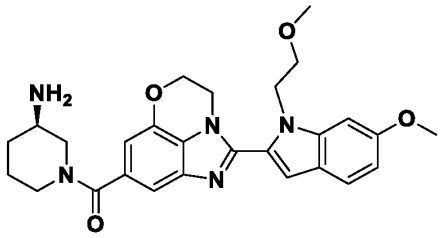
**Synthesis of (R)-(3-aminopiperidin-1-yl)(2-(1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000178]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.69-7.63 (m, 2H), 7.31-7.27 (m, 2H), 7.16-7.12 (m, 2H), 6.76 (s, 1H), 4.91 (t, *J* = 5.7 Hz, 2H), 4.64 (t, *J* = 3.44 Hz, 2H), 4.56 (t, *J* = 4.24 Hz, 2H), 4.16 (bs, 2H), 3.66 (t, *J* = 5.28 Hz, 2H), 3.41 (bs, 1H), 3.09 (s, 3H), 2.91 (bs, 1H), 2.70 (m, 1H), 2.08 (s, 1H), 1.87 (d, *J* = 12.04 Hz, 2H), 1.76-1.68 (m, 1H), 1.50-1.45 (m, 1H), 1.26-1.23 (m, 1H). MS (ESI): mass calcd for. $C_{26}H_{29}N_5O_3$ for 459.23; found *m/z* 460.10 $[M+H]^{+1}$.

**Example-21:**

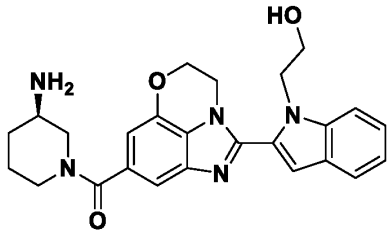
**(R)-(3-aminopiperidin-1-yl)(2-(6-methoxy-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000179]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.54 (d, *J* = 8.64 Hz, 1H), 7.34 (s, 1H), 7.07 (s, 1H), 6.98 (s, 1H), 6.82-6.81 (m, 2H), 4.83 (d, *J* = 11.12 Hz, 2H), 4.57 (s, 4H), 3.89 (s, 3H ), 3.61 (t, *J* = 5.04 Hz, 2H), 3.06 (s, 3H), 2.87 (d, *J* = 10.28 Hz, 2H), 2.04 (d, *J* = 11.80 Hz, 1H), 1.89-1.59 (m, 4H), 1.43-1.37 (m, 2H), 1.33-1.29 (m, 2H). MS (ESI): mass calcd for $C_{27}H_{31}N_5O_4$ 489.19; found m/z 490.27 $[M+1]^+$.

**Example-22:**

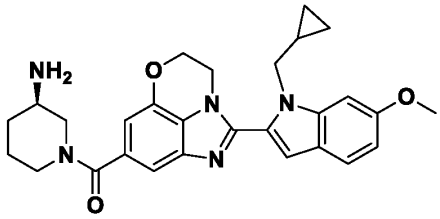
**(R)-(3-aminopiperidin-1-yl)(2-(1-(2-hydroxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000180]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.69 (d, *J* = 7.88 Hz, 1H), 7.65 (d, *J* = 7.91 Hz, 1H), 7.31-7.27 (m, 2H), 7.16-7.12 (m, 2H), 6.76 (s, 1H), 4.99 (bs, 2H), 4.77 (t, *J* = 5.36 Hz, 2H), 4.63 (d, *J* = 3.84 Hz, 2H), 4.56 (s, 2H), 3.74 (t, *J* = 5.52 Hz, 2H), 2.91 (s, 1H), 2.71-2.65 (m, 1H), 1.87 (s, 4H), 1.84 (s, 1H), 1.71-1.65 (m, 1H), 1.44-1.41 (m 1H), 1.24-1.22 (m, 1H). MS (ESI): mass calcd for $C_{25}H_{27}N_5O_3$ 445.21; found m/z 446.24 $[M+H]^{+1}$.

**Example-23:**

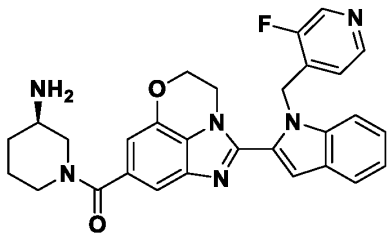
**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-methoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000181]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.56 (d, *J* = 8.64 Hz, 1H), 7.28 (s, 1H), 7.17 (s, 1H), 7.09 (s, 1H), 6.79 (d, *J* = 7.4 Hz, 1H), 6.74 (s, 1H), 4.70 (d, *J* = 6.68 Hz, 2H), 4.64 (s, 2H), 4.55 (s, 2H), 4.15 (bs, 1H), 3.85 (s, 3H), 3.38 (d, *J* = 6.92 Hz, 1H), 2.92 (bs, 2H), 2.07 (m, 2H), 1.86 (d, *J* = 9.28 Hz, 1H), 1.67 (bs, 1H), 1.45 (m, 1H), 1.23 (m, 2H), 1.09 (t, *J* = 7.00 Hz, 1H), 0.35-0.30 (m, 4H). MS (ESI): mass calcd. for $C_{28}H_{31}N_5O_3$ 485.24; found *m/z* 486.20 $[M+H]^{+1}$.

**Example-24:**

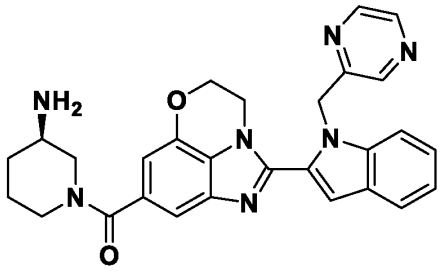
**(*R*)-(3-aminopiperidin-1-yl)(2-(1-((3-fluoropyridin-4-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000182]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 8.53 (s, 1H), 8.18 (d, *J* = 4.72 Hz, 1H), 7.77 (d, *J* = 7.84 Hz, 1H), 7.52 (d, *J* = 8.28 Hz, 1H), 7.36 (s, 1H), 7.31 (t, *J* = 7.32 Hz, 1H), 7.21-7.18 (m, 2H), 6.73 (s, 1H), 6.55 (t, *J* = 5.64 Hz, 1H), 6.25 (s, 2H), 4.71 (t, *J* = 4.16 Hz, 2H), 4.56 (t, *J* = 3.08 Hz, 2H), 2.88 (bs, 1H), 2.63-2.57 (m, 2H), 1.84 (d, *J* = 11.8 Hz, 2H), 1.64 (bs, 2H), 1.41 (m, 2H), 1.23-1.19 (m, 2H). MS (ESI): mass calcd. for $C_{29}H_{27}FN_6O_2$ 511.23; found *m/z* 511.14 $[M+H]^+$.

**Example-25:**

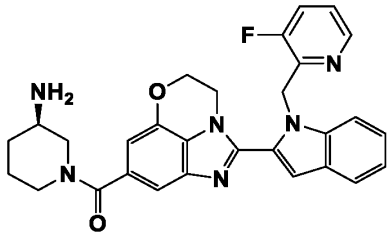
**(R)-(3-aminopiperidin-1-yl)(2-(1-(pyrazin-2-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000183]** $^1$HNMR (400 MHz, DMSO-$d_6$): δ (ppm): 8.49 (d, *J* = 13.1 Hz, 1H), 8.41 (s, 1H), 7.73 (d, *J* = 7.4 Hz, 1H), 7.57 (d, *J* = 7.1 Hz, 1H), 7.30-7.24 (m, 3H), 7.18-7.16 (m, 2H), 6.75 (s, 1H), 6.25 (s, 2H), 4.72 (bs, 2H), 4.56 (bs, 2H), 4.15 (bs, 2H), 2.90 (bs, 2H), 2.69-2.63 (m, 1H), 1.84 (bs, 2H), 1.64 (bs, 2H), 1.42 (bs, 1H), 1.23-1.22 (m, 1H). MS (ESI): mass calcd. for $C_{28}H_{27}N_7O_2$ 493.12; found *m/z* 494.10 $[M+H]^+$.

**Example-26:**

**(R)-(3-aminopiperidin-1-yl)(2-(1-((3-fluoropyridin-2-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**

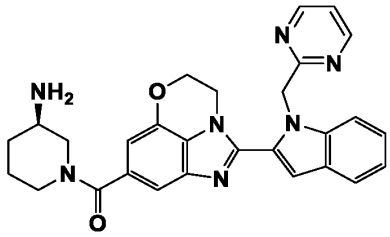


**[000184]** $^1$HNMR (400 MHz, DMSO-d6): δ (ppm): 8.12 (d, *J* = 4.16 Hz, 1H), 7.70 (d, *J* = 7.92 Hz, 1H), 7.62 (t, *J* = 9.2 Hz, 1H), 7.53 (d, *J* = 8.12 Hz, 1H), 7.28-7.20 (m, 4H), 7.13 (t, *J* = 7.16 Hz, 1H), 6.72 (s, 1H), 6.28 (s, 2H), 4.65 (t, *J* = 4.20 Hz, 2H ), 4.55 (t, *J* = 5.52 Hz, 2H ), 4.18 (bs, 2H), 2.87 (bs, 1H), 2.61 (m, 2H), 1.84 (d, *J* = 10.1 Hz,

2H), 1.75-1.66 (m, 1H), 1.45-1.41 (m, 1H), 1.23-1.19 (m, 2H). MS (ESI): mass calcd. for $C_{29}H_{27}FN_6O_2$ 510.22; found *m/z* 511.18 $[M+H]^+$.

**Example-27:**

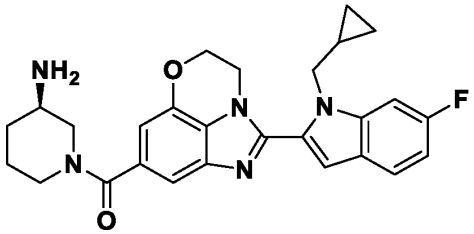
**(R)-(3-aminopiperidin-1-yl)(2-(1-(pyrimidin-2-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000185]** $^1$HNMR (400 MHz, DMSO-d6): δ (ppm): 8.62 (d, *J* = 4.84 Hz, 2H), 7.20 (d, *J* = 7.7 Hz, 1H), 7.43 (d, *J* = 8.2 Hz, 1H), 7.29-7.26 (m, 2H), 7.23-7.20 (t, *J* = 7.28 Hz, 1H), 7.16-7.12 (m, 2H), 6.71 (s, 1H), 6.33 (s, 2H), 4.69 (t, *J* = 6.24 Hz, 2H), 4.55 (t, *J* = 4.88 Hz, 2H), 4.17 (bs, 1H), 3.54 (bs, 1H), 2.87 (bs, 1H), 2.61 (m, 1H), 1.83 (d, *J* = 10.96 Hz, 3H), 1.63 (s, 1H), 1.41-1.38 (m, 1H), 1.23-1.19 (m, 2H). MS (ESI): ): mass calcd. for $C_{28}H_{27}N_7O_2$ 493.22; found *m/z* 494.23 $[M+H]^+$.

**Example-28:**

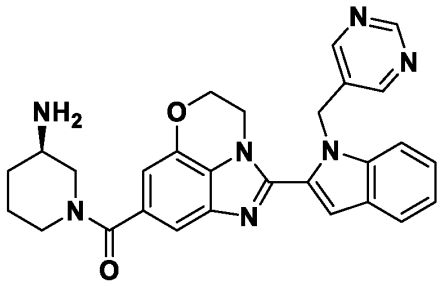
**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000186]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.71-7.68 (m, 1H), 7.58 (d, *J* = 7.9 Hz, 1H), 7.29 (s, 1H), 7.19 (s, 1H), 7.01 (t, *J* = 9.2 Hz, 1H), 6.75 (s, 1H), 4.68-4.65 (m, 4H), 4.51 (s, 2H), 4.21 (bs, 1H), 3.61 (bs, 1H), 2.91 (bs, 1H), 2.63-2.61 (m, 1H), 1.86-1.84 (m, 2H), 1.66 (bs, 1H), 1.64-1.42 (m, 3H), 1.25-1.23 (m, 2H), 0.34-0.28 (m, 4H). MS (ESI): $C_{27}H_{28}FN_5O_2$ 473.12; found *m/z* 474.20 $[M+H]^+$.

**Example-29:**

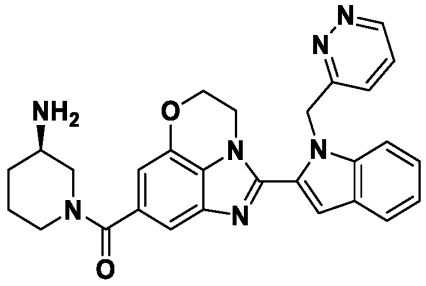
**(R)-(3-aminopiperidin-1-yl)(2-(1-(pyrimidin-5-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000187]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 9.03 (s, 1H), 8.65 (s, 2H), 7.75 (d, *J* = 7.8 Hz, 1H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.33-7.26 (m, 3H), 7.18 (t, *J* = 7.7 Hz, 1H), 6.76 (s, 1H), 6.17 (s, 2H), 4.72 (bs, 2H), 4.57 (bs, 2H), 4.18 (bs, 2H), 3.60 (bs, 2H), 3.17 (d, *J* = 4.8 Hz, 1H), 2.88 (bs, 1H), 2.66-2.62 (m, 1H), 1.83 (bs, 1H), 1.65 (bs, 1H), 1.39-1.33 (bs, 1H), 1.23-1.22 (m, 1H). MS (ESI): mass calcd. for $C_{28}H_{27}N_7O_2$ 493.12; found *m/z* 494.27 $[M+H]^+$.

**Example-30:**

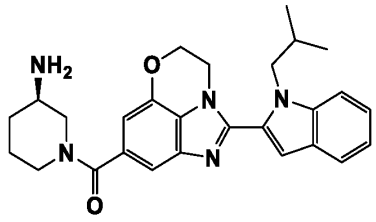
**(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridazin-3-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000188]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 9.07 (d, *J* = 3.9 Hz, 1H), 7.74 (d, *J* = 7.9 Hz, 1H), 7.58-7.52 (m, 2H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.32 (s, 1H), 7.27 (d, *J* = 7.1 Hz, 1H), 7.23 (s, 1H), 7.16 (t, *J* = 7.7 Hz, 1H), 6.77 (s, 1H), 6.37 (s, 2H), 4.71 (bs, 2H), 4.57 (bs, 2H), 4.15 (bs, 1H), 3.54 (bs, 1H), 2.88 (bs, 1H), 2.66-2.62 (m, 2H), 1.96 (bs, 2H), 1.85-1.82 (m, 1H), 1.64 (bs, 1H), 1.41-1.39 (m, 1H), 1.25-1.20 (m, 1H). MS (ESI): mass calcd. for $C_{28}H_{27}N_7O_2$ 493.12; found *m/z* 494.24 $[M+H]^+$.

**Example-31:**

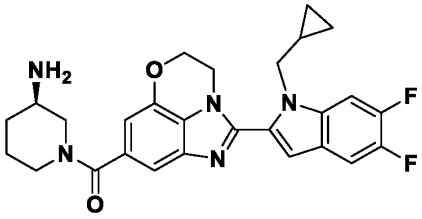
**(R)-(3-aminopiperidin-1-yl)(2-(1-isobutyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000189]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.68 (d, *J* = 8.1 Hz, 1H), 7.64 (d, *J* = 7.9 Hz, 1H), 7.30-7.26 (m, 2H), 7.16-7.11 (m, 2H), 6.75 (s, 1H), 4.64 (m, 4H), 4.56 (s, 2H), 4.17 (bs, 1H), 3.62 (bs, 1H), 2.90 (bs, 1H), 2.66 (m, 1H), 2.1-2.04 (m, 1H), 1.86 (d, *J* = 9.84 Hz, 3H), 1.65 (bs, 1H), 1.43 (d, *J* = 9.68 Hz, 1H), 1.23 (m, 2H), 0.73 (d, *J* = 6.6 Hz, 6H). MS (ESI): mass calcd. for $C_{27}H_{31}N_5O_2$ 457.25; found *m/z* 458.28 $[M+H]^+$.

**Example-32:**

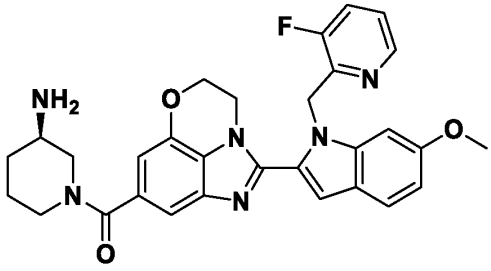
**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5,6-difluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000190]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.90-7.86 (m, 1H), 7.70 (t, *J* = 7.7 Hz, 1H), 7.30 (s, 1H), 7.17 (s, 1H), 6.76 (s, 1H), 4.68-4.62 (m, 4H), 4.56 (s, 2H), 4.24 (bs, 1H), 3.66 (bs, 1H), 2.98-2.89 (m, 2H), 2.67-2.63 (m, 1H), 1.86-1.84 (d, *J* = 9.7 Hz, 1H), 1.67 (m, 2H), 1.23 (m, 3H), 1.44 (m, 1H), 0.34 (d, *J* = 7.2 Hz, 2H), 0.29 (m, 2H). MS (ESI): mass calcd. for $C_{27}H_{27}F_2N_5O_2$ 491.12; found *m/z* 492.25 $[M+H]^+$.

**Example-33:**

**(R)-(3-aminopiperidin-1-yl)(2-(1-((3-fluoropyridin-2-yl)methyl)-6-methoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**

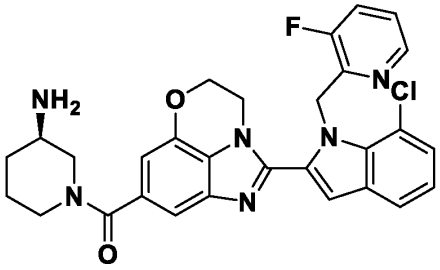


**[000191]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 8.14 (d, *J* = 4.52 Hz, 1H), 7.62 (t, *J* =9.0 Hz, 1H), 7.57 (d, *J* = 9.6 Hz, 1H), 7.30-7.28 (m, 1H), 7.17 (s, 1H), 7.08 (s, 1H),

6.81 (d, *J* = 1.9 Hz, 2H), 6.78 (s, 1H), 6.27 (s, 2H), 4.64 (d, *J* = 4.32 Hz, 2H), 4.54 (d, *J* = 4.0 Hz, 2H), 4.08 (bs, 2H), 3.76 (s, 3H), 3.20-3.10 (m, 4H), 2.00-1.97 (m, 2H), 1.72-1.71 (m, 1H), 1.55-1.53 (m, 2H). MS (ESI): mass calcd. for $C_{30}H_{29}FN_6O_3$ 540.60; found *m/z* 541.29 $[M+H]^+$.

**Example-34:**

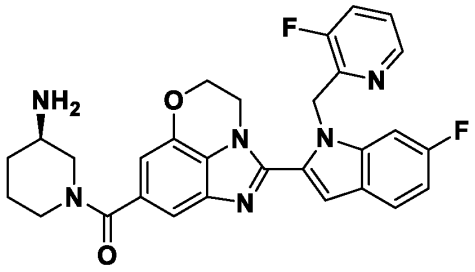
**(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-((3-fluoropyridin-2-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**




**[000192]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 8.06 (d, *J* = 4.3 Hz, 1H), 7.22-7.63 (m, 2H), 7.34 (s, 1H), 7.28-7.22 (m, 3H), 7.12 (t, *J* = 7.6 Hz, 1H), 6.74 (m, 1H), 6.62 (s, 2H), 4.63 (s, 2H), 4.53 (s, 2H), 4.01 (bs, 1H), 3.75 (bs, 1H), 2.88 (bs, 1H), 2.66 (bs, 1H), 1.83 (d, *J* = 10.2 Hz, 2H), 1.68 (m, 2H), 1.42 (s, 1H ), 1.26-1.23 (m, 2H). MS (ESI): mass calcd. for $C_{29}H_{26}ClFN_6O_2$ 544.18; found *m/z* 545.27 $[M+H]^+$.

**Example-35:**

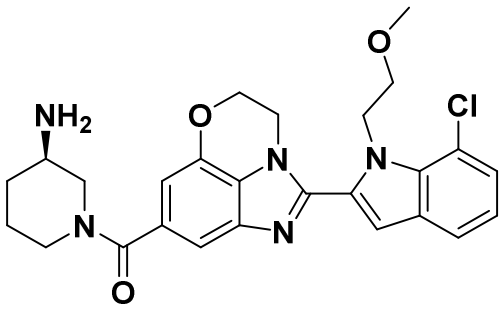
**(R)-(3-aminopiperidin-1-yl)(2-(6-fluoro-1-((3-fluoropyridin-2-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**




**[000193]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 8.12 (d, *J* = 7.7 Hz, 1H), 7.73-7.70 (m, 1H), 7.63 (t, *J* = 8.1 Hz, 1H), 7.45 (d, *J* = 9.7 Hz, 1H), 7.29-7.26 (m, 2H),7.18 (s, 1H), 7.04 (t, *J* = 9.6 Hz, 1H), 6.71 (s, 1H), 6.25 (s, 2H), 4.63 (s, 2H), 4.53 (s, 2H), 4.28 (bs, 1H), 2.88 (m, 1H), 2.72-2.62 (m, 2H), 1.85 (d, *J* = 11.1 Hz, 2H), 1.65 (bs, 2H), 1.39 (m, 1H), 1.23-1.17 (m, 2H) MS (ESI): mass calcd. for $C_{29}H_{26}F_2N_6O_2$ 528.18; found *m/z* 529.26 $[M+H]^+$.

**Example-36:**

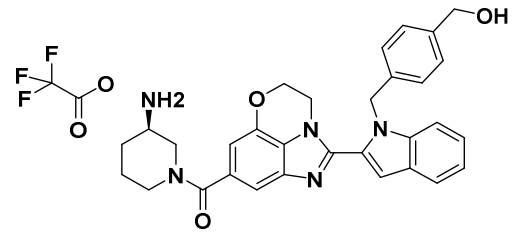
**(*R*)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000194]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.68 (d, *J* = 7.8 Hz, 1H), 7.34 (d, *J* = 7.9 Hz, 1H), 7.31 (s, 1H), 7.22 (s, 1H), 7.15 (t, *J* = 7.7 Hz, 1H), 6.77 (s, 1H), 5.23 (t, *J* = 5.4 Hz, 2H), 4.57 (s, 4H), 3.58 (t, *J* = 5.48 Hz, 2H), 2.97 (s, 3H), 2.92 (bs, 2H), 2.66 (m, 2H), 1.85 (d, *J* = 10.2 Hz, 2H), 1.66 (bs, 2H), 1.43 (m, 1H), 1.23-1.15 (m, 2H). MS (ESI): mass calcd. for $C_{26}H_{28}ClN_5O_3$ 493.1; found *m/z* 494.5 $[M+H]^+$.

**Example-37:**

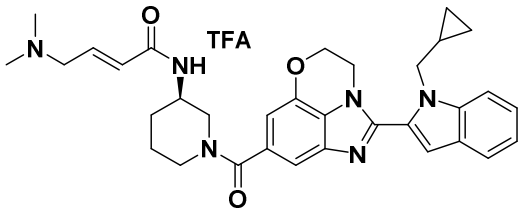
**(R)-(3-aminopiperidin-1-yl)(2-(1-(4-(hydroxymethyl)benzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone trifluoroacetic acid salt**



**[000195]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.71 (d, *J* = 7.7 Hz, 1H), 7.47 (d, *J* = 8.3 Hz, 1H), 7.27 (s, 2H), 7.23 (t, *J* = 7.5 Hz, 1H), 7.15-7.11 (m, 3H), 7.02 (d, *J* = 8.0 Hz, 2H), 6.75 (s, 1H), 6.10 (s, 2H), 5.04 (bs, 1H), 4.69 (s, 2H), 4.56 (s, 2H), 4.36 (s, 2H), 2.91 (bs, 2H), 2.69 (m, 2H), 1.90-1.83 (m, 2H), 1.64 (m, 2H) 1.39 (m, 1H), 1.25-1.23 (m, 2H). MS (ESI): mass calcd. for $C_{31}H_{31}N_5O_3$ 521.2; found *m/z* 522.2 $[M+H]^+$.

**Example-38:**

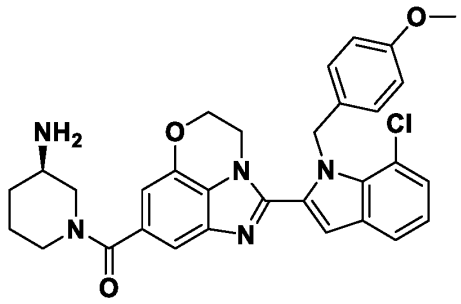
**(R,E)-N-(1-(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)-4-(dimethylamino)but-2-enamide trifluoroacetic acid salt**



**[000196]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 9.62 (bs, 1H), 8.29 (bs, 1H), 7.68 (t, *J* = 6.92 Hz, 2H), 7.33-7.28 (m, 2H), 7.17-7.12 (m, 2H), 6.77 (s, 1H), 6.28 (d, *J* = 15.1 Hz, 1H), 4.71-4.66 (m, 4H), 4.56 (s, 2H), 3.86 (m, 4H), 3.24-3.06 (m, 2H), 2.76 (s, 6H), 1.90 (bs, 1H), 1.76 (m, 2H), 1.56-1.50 (m, 2H ), 1.27-1.21 (m, 2H ), 0.35-0.28 (m, 4H). MS (ESI) ): mass calcd. for $C_{35}H_{39}N_6F_3O_4$ 566.30; *m/z* found 567.42.

**Example-39:**

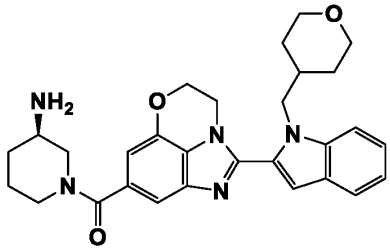
**(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(4-methoxybenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**




**[000197]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.71 (d, *J* = 7.7 Hz, 1H), 7.36 (s, 1H), 7.29 (d, *J* = 5.4 Hz, 2H), 7.14 (t, *J* = 7.7 Hz, 1H), 6.76 (s, 1H), 6.73-6.67 (m, 4H), 6.34 (s, 2H), 4.59 (t, *J* = 3.9 Hz, 2H), 4.53 (t, *J* = 3.3 Hz, 2H), 4.16 (bs, 2H), 3.61 (s, 3H), 2.89 (bs, 1H), 2.66 (bs, 2H), 1.88-1.82 (m, 2H), 1.64 (bs, 1H), 1.41-1.39 (m, 1H ), 1.25-1.20 (m, 2H). MS (ESI): mass calcd. for $C_{31}H_{30}ClN_5O_3$ 555.18; found *m/z* 556.36 $[M+H]^+$.

**Example-40:**

**(R)-(3-aminopiperidin-1-yl)(2-(1-((tetrahydro-2H-pyran-4-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**

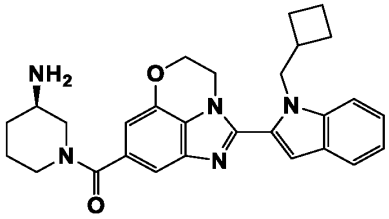



**[000198]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.69 (d, *J* = 8.32 Hz, 2H), 7.33-7.28 (m, 2H), 7.17-7.12 (m, 2H), 6.76 (s, 1H), 4.74 (d, *J* = 6.68 Hz, 2H), 4.65 (s, 2H), 4.56 (s, 2H), 4.18 (bs, 1H), 3.70 (d, *J* = 9.4 Hz, 2H), 3.40-3.39 (m, 1H), 3.09 (t, *J* = 10.88 Hz, 2H), 2.92 (bs, 1H), 2.66 (m, 1H), 2.08-2.05 (m, 1H), 1.85 (d, *J* = 10.28 Hz, 2H), 1.69

(bs, 2H), 1.44-1.41 (m, 2H), 1.28-1.17 (m, 5H). MS (ESI): mass calcd. for $C_{29}H_{33}N_5O_3$ 499.26; found *m/z* 500.30 $[M+H]^+$.

**Example-41:**

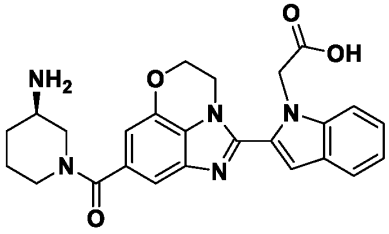
**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclobutylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000199]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.67(d, *J* = 8.1 Hz, 2H), 7.34 (s, 1H), 7.29 (t, *J* = 8.3 Hz, 1H), 7.14-7.11 (m, 2H), 6.78 (s, 1H), 4.87 (d, *J* = 7.0 Hz, 2H), 4.65 (s, 2H), 4.56 (s, 2H), 4.14 (bs, 2H), 2.97 (bs, 1H), 2.81(m, 2H), 2.72-2.65 (m, 1H), 1.88 (m, 1H), 1.77-1.66 (m, 6H), 1.63-1.57 (m, 3H), 1.51-1.45 (m, 1H), 1.23 (s, 1H). MS (ESI): mass calcd. for $C_{28}H_{31}N_5O_2$ 469.25; found *m/z* 470.31 $[M+H]^+$.

**Example-42:**

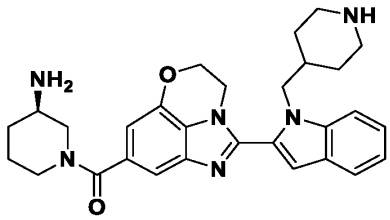
**(R)-2-(2-(7-(3-aminopiperidine-1-carbonyl)-3,4-dihydro-5-oxa1,2adiazaacenaphthylen-2-yl)-1H-indol-1-yl)acetic acid**



**[000200]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.67 (d, *J* = 7.7 Hz, 1H), 7.48 (d, *J* = 8.2 Hz, 1H), 7.31 (s, 1H), 7.24 (t, *J* = 7.4 Hz, 1H), 7.13-7.10 (m, 2H), 6.74 (s, 1H), 5.32 (s, 2H), 4.64 (s, 2H), 4.55 (s, 2H), 4.17 (bs, 2H), 2.95-2.88 (m, 4H), 1.79 (bs, 3H), 1.25-1.08 (m, 3H). MS (ESI): mass calcd. for $C_{25}H_{25}N_5O_4$ 459.18; found *m/z* 460.21 $[M+H]^+$.

**Example-43:**

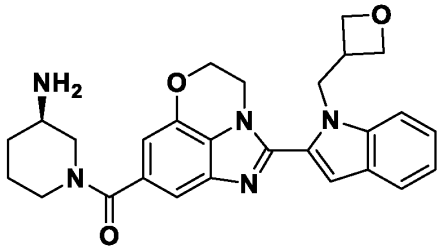
**(R)- (3-aminopiperidin-1-yl)(2-(1-(piperidin-4-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000201]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.69 (d, $J$ = 7.7 Hz, 1H), 7.64 (d, $J$ = 8.32 Hz, 1H), 7.30-7.27 (m, 2H), 7.14-7.11 (m, 2H) 6.75 (s, 1H), 4.71 (d, $J$ = 6.68 Hz, 2H), 4.64 (s, 2H), 4.56 (s, 2H ), 4.10 (bs, 1H ), 2.91 (bs, 1H ), 2.73 (d, $J$ = 11.8 Hz, 2H), 2.66-2.64 (m, 3H), 2.19 (t, $J$ = 11.3 Hz, 2H), 1.83 (bs, 2H), 1.66 (bs, 2H), 1.44-1.41 (m, 2H), 1.25-1.23 (m, 3H), 0.97-0.89 (m, 3H). MS (ESI): mass calcd. for $C_{29}H_{34}N_6O_2$ 498.1; found *m/z* 499.29 $[M+H]^+$.

**Example-44:**

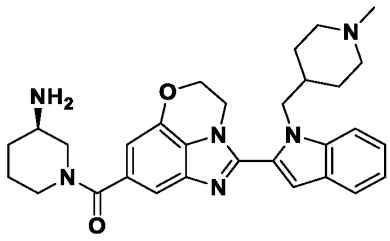
**(R)-(3-aminopiperidin-1-yl)(2-(1-(oxetan-3-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000202]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.71 (d, $J$ = 7.9 Hz, 1H), 7.51 (d, $J$ = 8.4 Hz, 1H), 7.32 (s, 1H), 7.28 (t, $J$ = 7.7 Hz, 1H), 7.22 (s, 1H), 7.15 (t, $J$ = 7.9 Hz, 1H), 6.78 (s, 1H), 5.47 (s, 2H), 5.01-5.05 (m, 1H), 4.91 (s, 1H), 4.66 (s, 2H), 4.56 (s, 2H), 4.36 (s, 1H), 3.80 (s, 2H), 2.98-2.87 (m, 4H), 1.90 (m, 2H), 1.69 (m, 1H), 1.46-1.37 (m, 2H). MS (ESI): mass calcd. for $C_{27}H_{29}N_5O_3$ 471.23; found *m/z* 472.27 $[M+H]^+$.

**Example-45:**

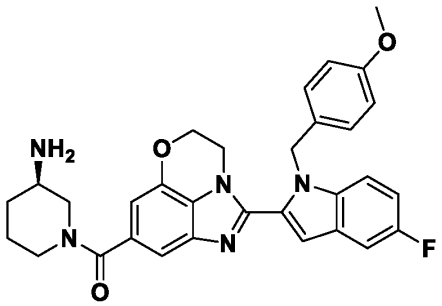
**(R)-(3-aminopiperidin-1-yl)(2-(1-((1-methylpiperidin-4-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000203]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.69-7.64 (m, 2H), 7.30-7.27 (m, 2H), 7.15-7.12 (m, 2H), 6.70 (s, 1H), 4.73 (d, *J* = 6.72 Hz, 2H), 4.65 (s, 2H), 4.56 (s, 2H ), 4.15 (bs, 1H ), 3.63 (bs, 1H ), 2.90 (bs, 1H), 2.66-2.56 (m, 4H), 2.00 (s, 3H), 1.87-1.84 (m, 2H), 1.73-1.72 (m, 2H), 1.60 (t, *J* = 11.3 Hz, 2H), 1.44-1.41 (m, 1H), 1.31-1.28 (m, 2H), 1.23-1.13 (m, 2H), 1.11-0.92 (m, 2H). MS (ESI): mass calcd. for $C_{30}H_{36}N_6O_2$ 512; found *m/z* 513.34 $[M+H]^+$.

**Example-46:**

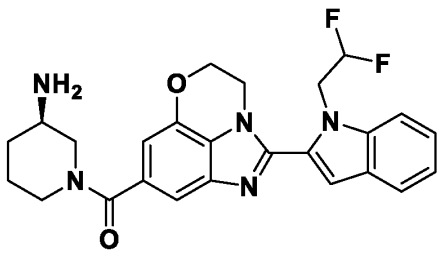
**(*R*)-(3-aminopiperidin-1-yl)(2-(5-fluoro-1-(4-methoxybenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000204]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.56-7.53 (m, 1H), 7.47 (d, *J* = 9.36 Hz, 1H), 7.28 (s, 1H), 7.22 (s, 1H), 7.10 (t, *J* = 7.81 Hz, 1H), 7.05 (d, *J* = 8.11 Hz, 2H), 6.77 (d, *J* = 8.96 Hz, 3H), 6.02 (s, 2H), 4.66 (s, 2H), 4.56 (s, 2H), 4.18 (bs, 2H), 3.64 (s, 3H), 2.89 (bs, 1H), 2.62 (m, 1H), 1.83 (d, *J* = 9.92 Hz, 2H), 1.63-1.42 (m, 3H), 1.21 (m, 2H). MS (ESI): mass calcd. for $C_{31}H_{30}FN_5O_3$ 539.23; found *m/z* 540.33 $[M+H]^+$.

**Example-47:**

**(R)-(3-aminopiperidin-1-yl)(2-(1-(2,2-difluoroethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**

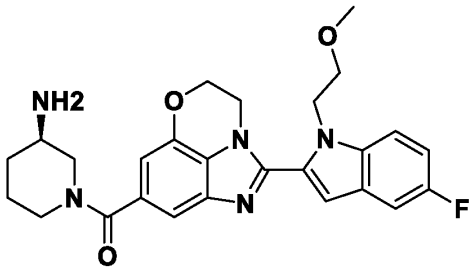


**[000205]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.71 (t, *J* = 7.2 Hz, 2H), 7.34 (t, *J* = 7.1 Hz, 1H), 7.29-7.21 (m, 2H), 7.19 (t, *J* = 7.1 Hz, 1H), 6.76 (s, 1H), 6.50 (t, *J* = 55.4 Hz, 1H), 5.27 (t, *J* = 13.1 Hz, 2H), 4.68 (s, 2H), 4.57 (s, 2H), 4.10 (bs, 1H), 3.70 (bs, 1H), 2.90 (m, 1H), 2.66 (m, 2H), 1.86 (t, *J* = 10.5 Hz, 2H), 1.66 (bs, 2H), 1.44-1.41 (m, 1H),

1.24-1.21 (m, 1H). MS (ESI): mass calcd. for $C_{25}H_{25}F_2N_5O_2$ 465.12; found *m/z* 466.26 $[M+H]^+$.

**Example-48:**

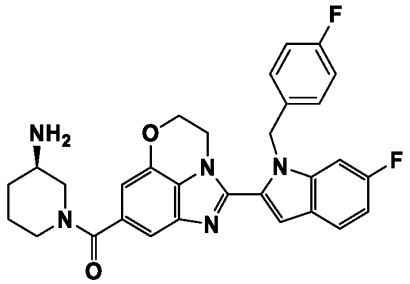
**(*R*)-(3-aminopiperidin-1-yl)(2-(5-fluoro-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**




**[000206]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.69-7.66 (m, 1H), 7.45 (d, *J* = 7.6 Hz, 1H), 7.29 (s, 1H), 7.17-7.14 (m, 2H), 6.76 (s, 1H), 4.90 (t, *J* = 5.8 Hz, 2H), 4.63 (s, 2H), 4.56 (s, 2H), 4.20 (bs, 2H), 3.66 (t, *J* = 5.1 Hz, 2H), 3.08 (s, 3H), 2.92 (bs, 1H), 2.65 (m, 2H), 1.85 (d, *J* = 10.28 Hz, 1H), 1.69 (bs, 2H), 1.43 (m, 1H), 1.23 (m, 2H). MS (ESI): $C_{26}H_{28}FN_5O_3$ 477.23; found *m/z* 478.39 $[M+H]^+$.

**Example-49:**

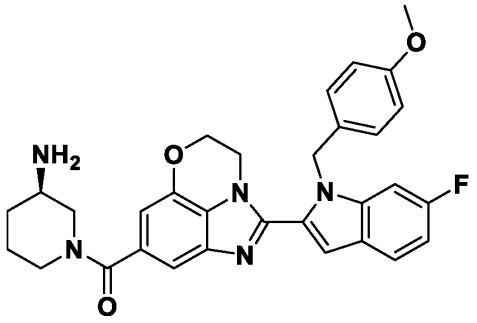
**(R)-(3-aminopiperidin-1-yl)(2-(6-fluoro-1-(4-fluorobenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**




**[000207]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.75-7.71(m, 1H), 7.41 (d, *J* = 9.76 Hz, 1H), 7.28 (d, *J* = 10.24 Hz, 2H), 7.18-7.14 (m, 2H), 7.08-7.00 (m, 3H), 6.75 (s, 1H), 6.07 (s, 2H), 4.66 (s, 2H), 4.56 (s, 2H), 4.18 (bs, 1H ), 3.60 (bs, 1H ), 2.90 (bs, 1H), 2.66 (bs, 2H ), 1.96 (bs, 1H), 1.84 (d, *J* = 9.68 Hz, 1H), 1.64 (bs, 1H), 1.42-1.39 (m, 1H), 1.23 (bs, 2H). MS (ESI): mass calcd. for $C_{30}H_{27}F_2N_5O_2$ 527.21; found *m/z* 528.36 $[M+H]^+$.

**Example-50:**

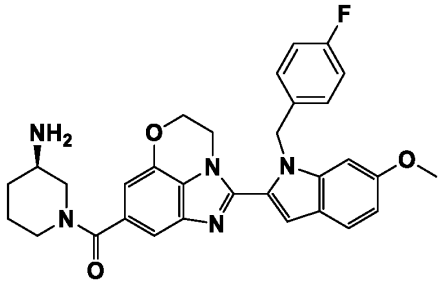
**(*R*)-(3-aminopiperidin-1-yl)(2-(6-fluoro-1-(4-methoxybenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000208]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.73-7.70 (m, 1H), 7.41 (d, *J* = 10.08 Hz, 1H), 7.27 (d, *J* = 6.76 Hz, 2H), 7.02 (d, *J* = 7.76 Hz, 2H), 6.99 (d, *J* = 6.96 Hz, 1H), 6.78-6.72 (m, 3H), 6.01 (s, 2H), 4.65 (s, 2H), 4.56 (s, 2H), 4.11 (bs, 2H), 3.64 (s, 3H), 2.89 (bs, 1H), 2.66-2.62 (m, 1H), 1.84 (d, J = 10.48 Hz, 1H), 1.64 (bs, 2H), 1.42 (m, 2H), 1.22-1.19 (m, 2H). MS (ESI): mass calcd. for $C_{31}H_{30}FN_5O_3$ 539.23; found *m/z* 540.27 $[M+H]^+$.

**Example-51:**

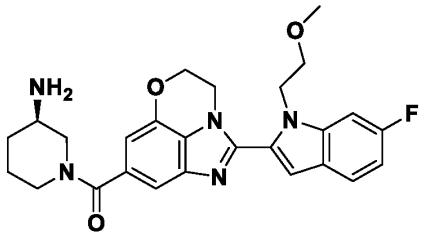
**(R)-(3-aminopiperidin-1-yl)(2-(1-(4-fluorobenzyl)-6-methoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000209]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.59 (d, *J* = 8.64 Hz, 1H), 7.24 (s, 1H), 7.19 (s, 1H), 7.18-7.14 (m, 2H), 7.07-7.04 (m, 3H), 6.80 (d, *J* = 8.52 Hz, 1H), 6.73 (s, 1H), 6.09 (s, 2H), 4.65 (s, 2H), 4.54 (s, 2H), 4.16 (bs, 1H), 3.76 (s, 3H), 3.60-3.45 (m, 1H), 2.88 (bs, 1H), 2.62 (bs, 2H), 1.83-1.65 (m, 3H), 1.39-1.33 (m, 1H), 1.23 (bs, 1H), 1.19-1.10 (m, 1H). MS (ESI): mass calcd. for $C_{31}H_{30}FN_5O_3$ 539.23; found *m/z* 540.42 $[M+H]^+$.

**Example-52**

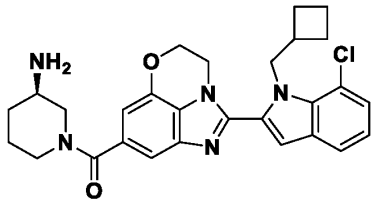
**3-aminopiperidin-1-yl)(2-(6-fluoro-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000210]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.71-7.67 (m, 1H), 7.51 (d, *J* = 9.8 Hz, 1H), 7.28 (s, 1H), 7.18 (s, 1H), 7.01 (t, *J* = 8.2 Hz, 1H), 6.75 (s, 1H), 4.88 (t, *J* = 5.16 Hz, 2H), 4.63 (s, 2H), 4.56 (s, 2H), 4.13 (bs, 2H), 3.65 (t, *J* = 4.9 Hz, 2H), 3.09 (s, 3H), 2.91-2.90 (m, 1H), 2.66 (m, 2H), 1.85 (d, *J* = 11.2 Hz, 2H), 1.66 (bs, 2H), 1.42 (d, *J* = 11.5 Hz, 1H), 1.27-1.17 (m, 1H). MS (ESI): mass calcd. for $C_{26}H_{28}FN_5O_3$ 477.12; found *m/z* 478.26 $[M+H]^+$.

**Example-53**

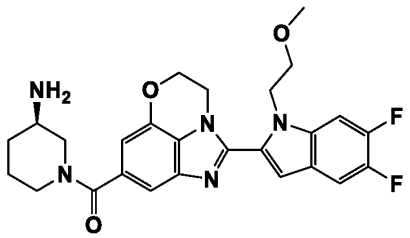
**(*R*)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(cyclobutylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000211]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.68 (d, *J* = 7.8 Hz, 1H), 7.35-7.33 (m, 2H), 7.23 (s, 1H), 7.13 (t, *J* = 7.7 Hz, 1H), 6.78 (s, 1H), 5.21 (d, *J* = 6.9 Hz, 2H), 4.60-4.56 (m, 4H), 4.18 (bs, 1H), 3.64 (bs, 1H), 2.92 (bs, 1H), 2.68 (m, 1H), 2.62-2.55 (m, 1H), 1.86 (d, *J* = 10.6 Hz, 2H), 1.69-1.52 (m, 6H), 1.42-1.38 (m, 4H), 1.23 (bs, 1H). MS (ESI): mass calcd. for $C_{28}H_{30}ClN_5O_2$ 503.26; found *m/z* 504.44 $[M+H]^+$.

**Example-54**

**(R)-(3-aminopiperidin-1-yl)(2-(5,6-difluoro-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**

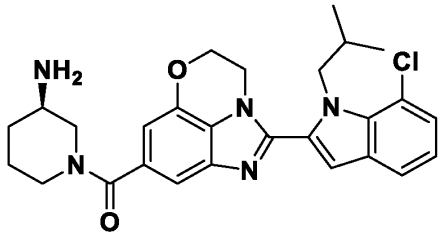


**[000212]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.81-7.76 (m, 1H), 7.71-7.66 (m, 1H), 7.28 (s, 1H), 7.16 (s, 1H), 6.75 (s, 1H), 4.88 (t, *J* = 5.08 Hz, 2H), 4.61 (d, *J* = 4.44

Hz, 2H), 4.56 (d, *J* = 4.16 Hz, 2H), 4.16 (bs, 1H), 3.65 (t, *J* = 5.28 Hz, 2H), 3.07 (s, 3H), 2.90 (bs, 1H), 2.67-2.64 (m, 3H), 1.85 (d, *J* = 11.04 Hz, 1H), 1.66 (bs, 2H), 1.42 (d, *J* = 9.44 Hz, 1H), 1.26-1.20 (m, 2H). MS (ESI): $C_{26}H_{27}F_2N_5O_3$ 495.21; found *m/z* 496.15 $[M+H]^+$.

**Example-55**

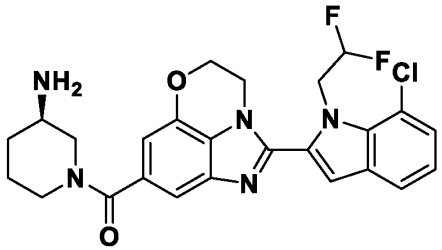
**(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-isobutyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**




**[000213]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.69 (d, *J* = 8.9 Hz, 1H), 7.35-7.33 (m, 2H), 7.24 (s, 1H), 7.14 (t, *J* = 7.8 Hz, 1H), 6.78 (s, 1H), 4.95 (d, *J* = 7.24 Hz, 2H), 4.60 (s, 2H), 4.56 (s, 2H), 4.16 (bs, 1H), 3.68 (bs, 1H), 2.92 (bs, 1H), 2.67-2.62 (m, 1H), 2.08-1.91(m, 1H), 1.87-1.71 (m, 4H), 1.44-1.41 (m, 1H), 1.23 (s, 2H), 0.60 (s, 6H) MS (ESI): mass calcd. for $C_{27}H_{30}ClN_5O_2$ 492.02; found *m/z* 492.41 $[M+H]^+$.

**Example-56**

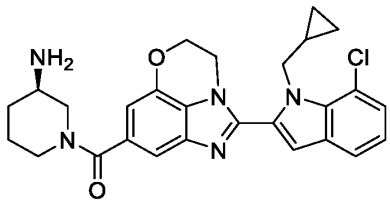
**(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(2,2-difluoroethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**




**[000214]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.70 (d, *J* = 7.5 Hz, 1H), 7.39 (s, 2H), 7.32 (s, 1H), 7.21-7.19 (m, 1H), 6.78 (s, 1H), 6.39 (t, *J* = 55.2 Hz, 1H), 5.71 (t, *J* = 12.2 Hz, 2H), 4.64 (s, 2H), 4.57 (s, 2H), 4.13 (bs, 1H), 3.71 (bs, 1H), 2.92 (m, 1H), 2.66 (m, 1H), 1.84 (m, 1H), 1.65 (bs, 2H), 1.44 (m, 2H), 1.23 (m, 2H) MS (ESI): mass calcd. for $C_{25}H_{24}ClF_2N_5O_2$ 499.16; found *m/z* 500.35 $[M+H]^+$.

**Example-57**

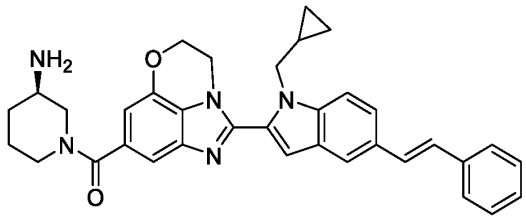
**(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000215]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.69 (d , *J* = 8.0 Hz, 1H), 7.36-7.33 (m, 2H), 7.26 (s, 1H), 7.16-7.12 (t, *J* = 8.0Hz, 1H), 6.81 (s, 1H), 6.0-5.9 (bs, 2H), 5.05 (d , *J* = 7.2 Hz, 2H), 4.61-4.56 (m, 4H), 4.11 (d , *J* = 4.0 Hz, 1H), 2.96-2.94 (m, 2H), 1.94-1.46 (m, 4H), 1.11 (s, 1H), 0.88-0.84 (m, 2H),0.27-0.25 (m, 2H), 0.04-0.03 (m, 2H). MS (ESI): mass calcd. For $C_{27}H_{28}ClN_5O_2$, 490.0 m/z found, 490.2 (M+H).

**Example-58**

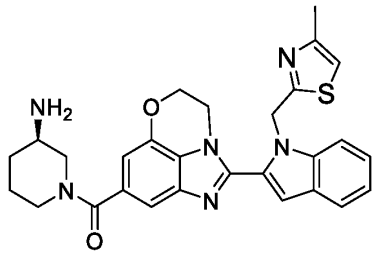
**(R,E)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-styryl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000216]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.84 (s, 1H), 7.70-7.59 (m, 4H), 7.39-7.35(m, 3H), 7.31 (s, 1H), 7.25-7.17 (m, 3H), 6.77 (s, 1H), 4.71-4.66 (m, 4H), 4.57 (s, 2H), 4.0-3.9 (bs, 2H), 2.95 (s, 2H), 2.77 (s, 2H), 1.89-1.22 (m, 5H), 0.88-0.84 (m, 1H). 0.33-0.26 (m,4H). MS (ESI): mass calcd. For $C_{35}H_{35}N_5O_2$, 557.0 m/z found, 558.6 $(M+H)^+$.

**Example-59**

**(R)-(3-aminopiperidin-1-yl)(2-(1-((4-methylthiazol-2-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**

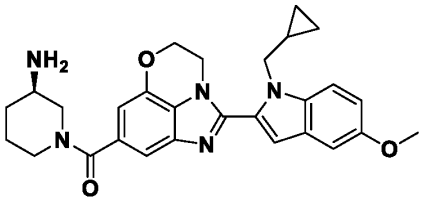


**[000217]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.77-7.64 (m, 2H), 7.31-7.30 (m, 2H), 7.19 (s, 1H), 7.023 (s, 2H), 6.78 (s, 1H), 6.34 (s, 1H), 4.68 (m, 2H), 4.56 (m, 2H), 3.05-2.9 (m, 3H), 2.25 (s, 3H), 1.90-1.87 (m, 2H), 1.70-1.67 (m, 2H), 1.49-1.45 (m, 1H),

1.37-1.33 (m, 2H), 1.26-1.21 (m, 2H). MS (ESI): mass calcd.for $C_{27}H_{28}N_6OS$ , 484.20; *m/z* found 485.1 $(M+H)^+$.

**Example-60**

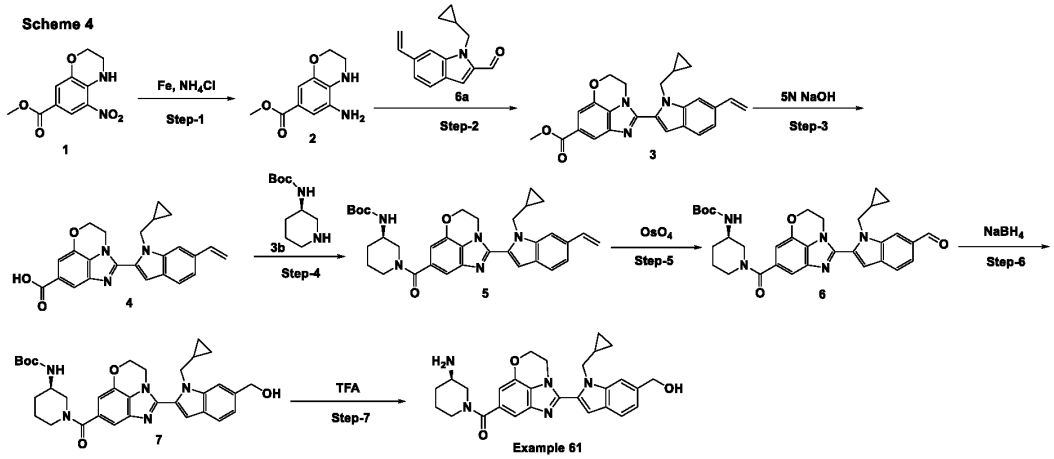
**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-methoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



**[000218]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.56 (d , *J* = 9.2 Hz, 1H), 7.30 (s, 1H), 7.14 (s, 1H), 7.04 (s, 1H), 6.94-6.91 (m, 1H), 6.75 (s, 1H), 4.65-4.63 (m, 4H), 4.55 (s, 2H), 3.96-3.9 (bs, 2H), 3.79 (s, 3H), 2.95 (s, 1H), 2.79 (d , *J* = 7.2 Hz, 2H), 1.89-1.26 (m, 6H), 0.88-0.84 (m, 1H), 0.33-0.26 (m, 4H). MS (ESI): mass calcd. For $C_{28}H_{31}N_5O_3$, 485.5 m/z found, 486.5 $(M+H)^+$.

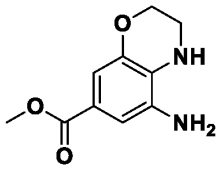
**Example-61**

**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-(hydroxymethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**




**[000219]** Intermediate 1 was synthesized using the procedure described in Scheme-3.

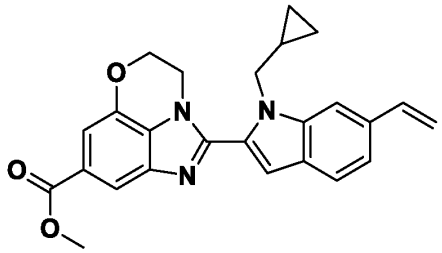
**Step 1: Synthesis of methyl 5-amino-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (2).**



**[000220]** To a stirred solution of methyl 5-nitro-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (**1**, 11.0 g, 46.18 mmol) in mixture of ethanol (110 mL, 10 vol) and water (33 mL, 3 vol) were added ammonium chloride (37.0 g, 692.0 mmol) and iron powder (38.6 g, 692.0 mmol) at room temperature and the resulting mixture was stirred at 80 °C for 3 h. The progress of the reaction was monitored by TLC. After completion of reaction, the reaction mixture was evaporated, filtered through celite and celite bed washed with ethyl acetate (200 mL × 3). The combined ethyl acetate layer was washed with water and brine. Obtained organic layer was dried over anhydrous sodium sulphate and concentrated under reduced pressure to afford methyl 5-amino-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (**2**) as brown solid. Yield: 9.0 g (93%).

**[000221]** $^1$HNMR (400 MHz, DMSO-$d_6$), δ (ppm): 6.86 (d, $J$ = 1.6 Hz, 1H), 6.67 (d, $J$ = 1.6 Hz, 1H), 5.39 (s, 2H), 4.73 (s, 1H), 4.06 (s, 2H), 3.70 (s, 3H), 3.35 (s, 2H). MS (ESI): 208.12, *m/z* found 209.20 $[M+H]^{+1}$.

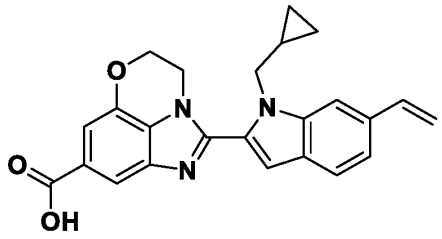
**Step-2: Synthesis of methyl-2-(1-(cyclopropylmethyl)-6-vinyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylate (3)**



**[000222]** To a stirred solution of methyl-5-amino-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (**2**, 1.0 g, 4.80 mmol) and 1-(cyclopropylmethyl)-6-vinyl-1H-indole-2-carbaldehyde (**6a**, 1.2 g, 5.70 mmol) in *N, N*-dimethylformamide (10.0 mL) and water (3.0 mL), potassium peroxomonosulfate (0.88 g, 5.76 mmol) was added at room temperature. The reaction mixture was stirred at room temperature for 16 h. After completion of reaction, the reaction mixture was cooled to room temperature and water was added. Precipitated solid was filtered and washed with water (20 mL × 2) and methanol (10 mL × 2). The compound obtained was dried under vacuum to afford methyl 2-(1-(cyclopropylmethyl)-6-vinyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-

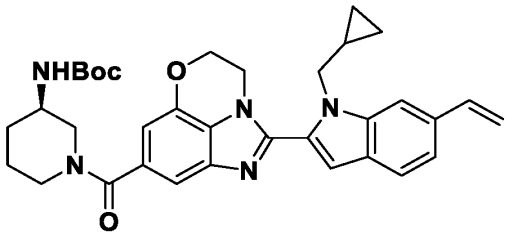
diazaacenaphthylene-7-carboxylate (**3**) as yellow solid. Yield: 0.550 g (crude). MS (ESI) 413.17; *m/z* found 414.26 $[M+H]^{+1}$.

**Step-3: Synthesis of 2-(1-(cyclopropylmethyl)-6-vinyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid (4)**



**[000223]** To a stirred solution of afford methyl 2-(1-(cyclopropylmethyl)-6-vinyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylate (**3**, 0.55 g, 1.3 mmol) in tetrahydrofuran (5.0 mL) and methanol (3.0 mL) 5N sodium hydroxide solution (3.0 mL) was added and reaction mixture was stirred at 60 °C for 2 h. After completion of reaction, the reaction mixture was concentrated under reduced pressure. The resulting crude was dissolved in minimum volume of water and acidified with saturated citric acid solution at 0 °C up to pH 2~3. The precipitated solid was filtered, washed with water (10 mL × 2). The compound obtained was dried under vacuum to afford 2-(1-(cyclopropylmethyl)-6-vinyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid (**4**) as white solid. Yield: 0.440 g (Crude). MS (ESI) 399.16; *m/z* found 400.16 $[M+H]^{+1}$.

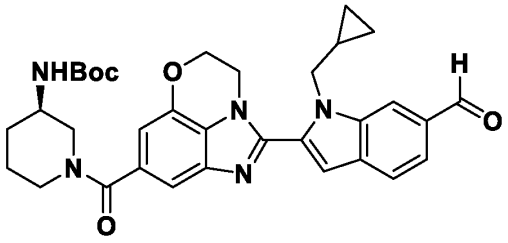
**Step-4: Synthesis of tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-6-vinyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (5)**



**[000224]** To a stirred solution of 2-(1-(cyclopropylmethyl)-6-vinyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid (**4**, 0.44 g, 1.10 mmol) in dichloromethane (10.0 mL), *tert*-butyl-(*R*)-piperidin-3-ylcarbamate (**3b**, 0.26 g, 1.29 mmol) and triethylamine (0.4 mL, 3.31 mmol) were added, followed by addition of propylphosphonic anhydride (50% solution in ethyl acetate, 0.8 mL, 3.37 mmol). The reaction mixture was stirred at room temperature for 2 h. After completion of reaction,

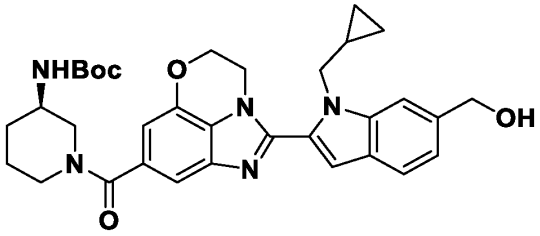
the reaction mixture was diluted with water and extracted with dichloromethane (10 mL × 2). The combined organic layers were washed with water and brine solution, further dried over anhydrous sodium sulfate, filtered and concentrated to get crude product. The crude was purified by CombiFlash using 12.0 g, RediSep and 70% ethyl acetate in hexane as eluent to afford tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-6-vinyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (**5**) as brown solid. Yield: 0.250 g (44%). MS (ESI) 581.30; *m/z* found 582.41 $[M+1]^+$.

**Step-5: preparation of tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-6-formyl-1H-indol-2-yl)-3, 4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (6)**



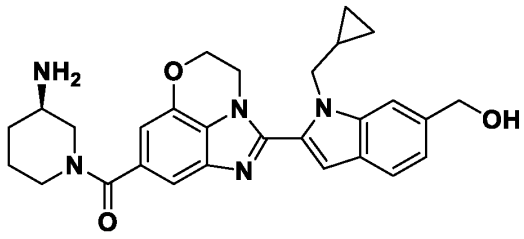

**[000225]** To a stirred solution of tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-6-vinyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl) piperidin-3-yl)carbamate (**5**, 0.25 g, 0.43 mmol) in tetrahydrofuran (10.0 mL) and water (3.0 mL), osmium tetroxide ( 0.6 ml , 0.08 mmol) and sodium per iodate (0.29 g, 1.37 mmol) were added at 0 °C . The reaction mixture was stirred at room temperature for 20 min. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (10 mL × 2). The combined organic layers were washed with water and brine solution, further dried over anhydrous sodium sulfate, filtered and concentrated to get crude product. The crude was purified by CombiFlash using 12.0 g, RediSep and 70% ethyl acetate in hexane as eluent to afford tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-6-formyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (**6**) as white solid. Yield: 0.200 g (80%). MS (ESI) 583.28; *m/z* found 584.30 $[M+1]^+$.

**Step-6: preparation of tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-6-(hydroxymethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl) carbamate (7)**




**[000226]** To a stirred solution of tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-6-formyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl) piperidin-3-yl)carbamate (**6**, 0.2 g, 0.34 mmol) in methanol (10.0 mL), sodium borohydride ( 0.014 g, 0.34 mmol) was added at 0 °C. The reaction mixture was stirred at room temperature for 1 h. After completion of reaction, the reaction mixture was diluted with water and extracted with dichloromethane (10 mL × 2). The combined organic layers were washed with water and brine solution, further dried over anhydrous sodium sulfate, filtered and concentrated to get crude product. The crude was purified by CombiFlash using 12.0 g, RediSep and 70% ethyl acetate in hexane as eluent to afford tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-6-(hydroxymethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (**7**) as yellow solid. Yield: 0.100 g (51%). MS (ESI) 585.30; *m/z* found 586.30 $[M+1]^+$.

**Step-7: prepararion of (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-(hydroxymethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl) methanone (Example-61)**



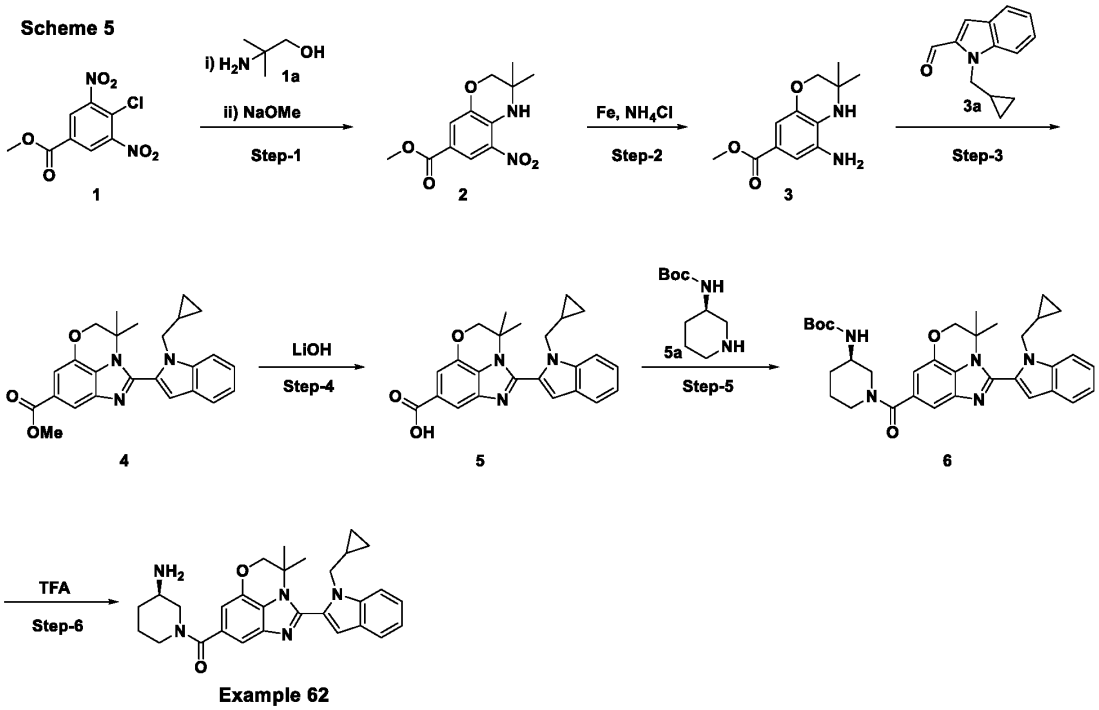

**[000227]** To a stirred solution tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-6-(hydroxymethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (**6**, 0.1 g, 0.17 mmol) in dichloromethane (10.0 mL), trifluoroacetic acid (1.0 mL) was added at 0 °C and stirred at room temperature for 2 h. After completion of reaction, the reaction mixture was concentrated completely, basified by saturated sodium bicarbonate solution (10 mL). The compound was extracted with dichloromethane (10 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated to get crude product. The crude was purified by reverse prep HPLC to afford ((R)-(3-aminopiperidin-1-yl)(2-(1-

(cyclopropylmethyl)-6-(hydroxymethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone as off white solid. Yield: 0.0023 g (0.02%).

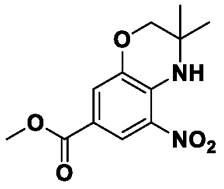
**[000228]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.63 (d, *J* = 8.1 Hz, 1H), 7.59 (s, 1H), 7.29 (s, 1H), 7.13 (s, 1H), 7.11 (d, *J* = 8.2 Hz, 1H), 6.75 (s, 1H), 5.22 (s, 2H), 4.70-4.65 (m, 6H), 4.56 (s, 2H), 4.15 (s, 1H), 2.92 (s, 1H), 2.66 (m, 2H), 1.88-1.84 (m, 3H), 1.66 (s, 1H), 1.43 (m, 1H), 1.24 (m, 2H), 0.35-0.29-(m, 4H). MS (ESI): mass calcd. for $C_{28}H_{31}N_5O_3$ 485.24; found *m/z* 486.32 $[M+H]^+$.

**Example-62**

**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,3-dimethyl-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**

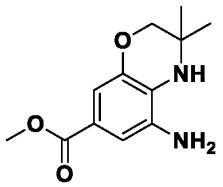



**Step-1: Synthesis of methyl 3,3-dimethyl-5-nitro-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (2)**



**[000229]** To the stirred solution of methyl-4-chloro-3,5-dinitrobenzoate (**1**, 5.0 g, 19.19 mmol) in methanol (30.0 mL), 2-amino-2-methylpropan-1-ol (**1a**, 2.6 g, 28.7 mmol) was added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After 3 h, 25% sodium methoxide solution in methanol (12.5 mL, 57.6 mmol) was added in the reaction mixture at 0 °C. The reaction mixture subjected to 80 °C for 3 h. After completion of reaction, the reaction mixture was diluted with water. Precipitated solid was filtered and washed with water. The crude was dried under reduced pressure to afford methyl 3,3-dimethyl-5-nitro-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (**2**) as yellow solid. Yield: 1.8 g (35%). MS (ESI): 266.0, *m/z* found 267.1 $[M+H]^{+1}$.

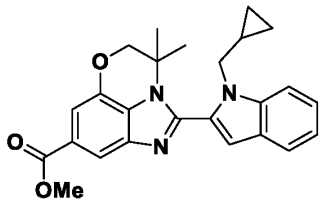
**Step-2: Synthesis of methyl 5-amino-3,3-dimethyl-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (3)**



**[000230]** To a stirred solution of methyl 3,3-dimethyl-5-nitro-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (**2**, 1.8 g, 6.76 mmol) in ethanol (20 mL) - water (10 mL) were added ammonium chloride (5.4 g, 101.4 mmol) and iron powder (5.6 g, 101.4 mmol) at room temperature and the resulting mixture was stirred at 60 °C for 3 h. The progress of the reaction was monitored by TLC. After completion of reaction, the reaction mixture was evaporated, filtered through celite and washed with ethyl acetate (50 mL × 3). The combined ethyl acetate layer was washed with water and brine. The organic layer was dried over anhydrous sodium sulphate and concentrated under reduced pressure to afford methyl 5-amino-3,3-dimethyl-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (**3**) as yellow solid.

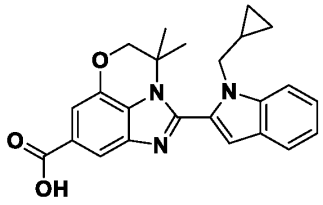
**[000231]** Yield: 1.0 g (55%). MS (ESI): 236.11, *m/z* found 237.20 $[M+H]^{+1}$.

**Step-3: Synthesis of methyl 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,3-dimethyl-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylate (4)**



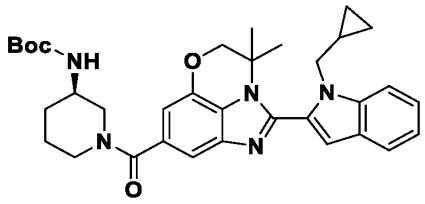
**[000232]** To a stirred solution of methyl-5-amino-3,3-dimethyl-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (**3**, 0.5 g, 2.12 mmol) and 1-(cyclopropylmethyl)-1H-indole-2-carbaldehyde (**3a**, 0.46 g, 2.33 mmol) in *N, N*-dimethylformamide (5.0 mL) and water (0.5 mL), potassium peroxomonosulfate (Oxone, 0.39 g, 2.54 mmol) was added at room temperature. The reaction mixture was stirred at room temperature for 16 h. After completion of reaction, the reaction mixture was cooled to room temperature and water was added. The precipitated solid was filtered and washed with water (10 mL × 2) and methanol (5 mL × 2). The compound obtained was dried under vacuum to afford methyl 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,3-dimethyl-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylate (**4**) as yellow solid. Yield: 0.50 g, crude, MS (ESI) 415.19; *m/z* found 416.27 $[M+H]^{+1}$.

**Step-4: Synthesis of 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,3-dimethyl-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid (5)**



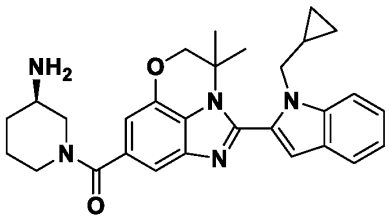
**[000233]** To a stirred solution of afford methyl 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,3-dimethyl-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylate (**4**, 0.5 g, 1.2 mmol) in tetrahydrofuran (10.0 mL) and methanol (5.0 mL) 5N sodium hydroxide solution (5.0 mL) was added and reaction mixture was stirred at 60 °C for 3 h. After completion of reaction, the reaction mixture was concentrated under reduced pressure completely. The resulting crude was dissolved in minimum volume of water and acidified with saturated citric acid solution at 0 °C up to pH 2~3. The precipitated solid was filtered, washed with water (10 mL × 2). The compound obtained was dried under vacuum to afford 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,3-dimethyl-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid (**5**) as orange solid. Yield: 0.50 g (Crude). MS (ESI) 401.17; *m/z* found 402.27 $[M+H]^{+1}$.

**Step-5: Synthesis of tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,3-dimethyl-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (6)**




**[000234]** To a stirred solution of 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,3-dimethyl-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid (**5**, 0.5 g, 1.25 mmol) in dichloromethane (20.0 mL), *tert*-butyl-(*R*)-piperidin-3-ylcarbamate (**5a**, 0.3 g, 1.49 mmol) and triethylamine (0.6 mL, 3.99 mmol) were added, followed by addition of propylphosphonic anhydride (50% solution in ethyl acetate, 2.5 mL, 3.99 mmol). The reaction mixture was stirred at room temperature for 12 h. After completion of reaction, the reaction mixture was diluted with water and extracted with dichloromethane (40 mL × 2). The combined organic layers were washed with water and brine solution, further dried over anhydrous sodium sulfate, filtered and concentrated to get crude product. The crude was purified by CombiFlash using 12.0 g, RediSep and 70% ethyl acetate in hexane as eluent to afford tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,3-dimethyl-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl) carbamate (**6**) as yellow solid. Yield: 0.25 g (34%). MS (ESI) 583.32; *m/z* found 584.37 $[M+1]^+$.

**Step-6: preparation of (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,3-dimethyl-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone (Example 62)**

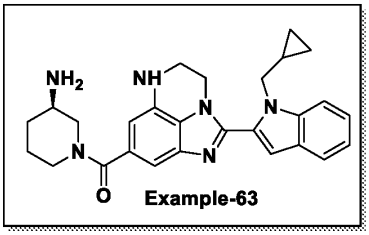


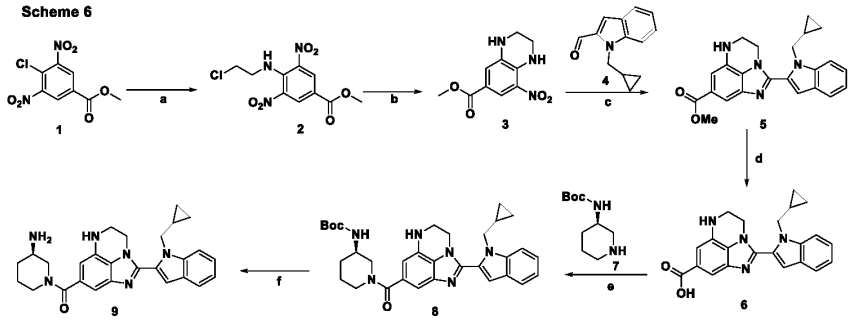

**[000235]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.71-7.65 (m, 2H), 7.32 (s, 1H), 7.28 (t, *J* = 7.7 Hz, 2H), 7.14 (t, *J* = 7.8 Hz, 1H), 7.00 (s, 1H), 6.82 (s, 1H), 4.21 (s, 2H), 4.18 (d, *J* = 6.8 Hz, 2H), 3.67 (bs, 2H), 2.92 (bs, 1H), 2.66-2.64 (m, 2H), 1.87-1.84 (m, 1H), 1.64-1.55 (m, 3H), 1.43 (s, 6H), 1.25-1.21 (m, 1H), 1.10-1.07 (m, 1H), 0.32 (d, *J* =

5.0 Hz, 2H), 0.31 (d, $J$ = 4.3 Hz, 2H). MS (ESI): mass calcd. for $C_{29}H_{33}N_5O_2$ 483.2; found $m/z$ 484.37 $[M+H]^+$.

**Example-63:**

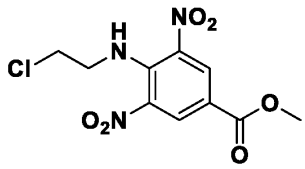
**Synthesis of (R)-(3-aminopiperidin-1-yl) (2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5, 6-dihydro-4H-imidazo [1, 5, 4-de]quinoxalin-8-yl) methanone (Example-63)**




**[000236]** The intermediate **(1)** used for the preparation of **Example-61** was purchased commercially (from Reddy N Reddy Pharmaceuticals). The intermediate **(1)** mentioned in Scheme-4 is equivalent to intermediate **(3)** of Scheme-2 above.

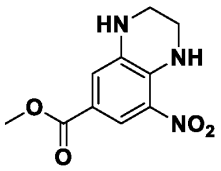
**Step 3: Preparation of methyl 4-((2-chloroethyl) amino)-3, 5-dinitrobenzoate (2)**




**2**

**[000237]** To a stirred solution of (**1**, 0.5g 1.92 mmol) in MeOH (50 mL) was added 2-Chloro-ethylamine hydrochloride (0.46 g, 4.03 mmol), followed by triethylamine (0.7 ml, 4.031 mmol) then resulting mixture was heated to 80 °C for 1h (Reaction condition **a**). The reaction mixture was cooled to room temperature and diluted with ethyl acetate (100 mL x 2) and the organic phase was evaporated through vacuum and crude carried to next step without purification to give yellow color solid (0.9g, 100% yield). MS (ESI): mass calcd. for $C_{10}H_{10}ClN_3O_6$, 303.66; m/z found, 304.0 $[M+H]^+$.

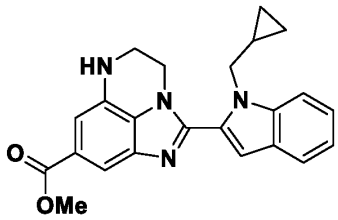
**Step 4: Preparation of methyl 8-nitro-1, 2, 3, 4-tetrahydroquinoxaline-6-carboxylate (3)**



3

**[000238]** To a stirred solution of methyl 4-((2-chloroethyl)amino)-3,5-dinitrobenzoate (**2**, 0.3g, 0.99 mmol) in AcOH (30 mL) was added iron powder (0.27 g, 4.95 mmol) at room temperature and the resulting mixture was allowed to stir under room temperature for 12 h (Reaction condition **b**). The progress of the reaction was monitored by TLC. Then reaction mixture was evaporated, filtered through celite and extracted with ethyl acetate (50 mL x 3). The combined organic extract was washed $NaHCO_3$ solution with brine, dried over sodium sulphate and concentrated under reduced pressure to afford crude compound which was purified by column chromatography (silica gel, 0-20% EtOAc in hexane) to give dark brown solid (0.23 g, 99% yield). MS (ESI): mass calcd. for $C_{10}H_{11}N_3O_4$ 237.22; m/z found, 238.1 $[M+H]^+$.

**Step 5: Preparation of methyl 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylate (5)**

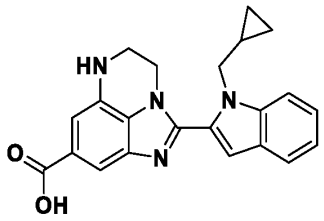


5

**[000239]** To the stirred solution of mixture of methyl 5-nitro-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (**3**, 0.1g, 0.42mmol) and 1-(cyclopropylmethyl)-1H-indole-2-carbaldehyde (**4**, 0.09 g, 0.46 mmol) in EtOH (10 mL), was added $Na_2S_2O_4$ (0.4 g, 2.32 mmol) in water (5 mL) and the reaction mixture was stirred at 80°C for 16h (reaction condition **c**). The reaction mixture was cooled to room temperature, water was added and the compound was extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using silica

gel and eluent 15-20% ethyl acetate in hexane to afford yellow solid (0.08 g, 62% Yield). MS (ESI): mass calcd. for, $C_{23}H_{22}N_4O_2$ 386.46; m/z found, 387.2 $[M+H]^+$.

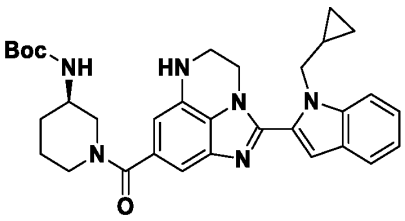
**Step 6: Preparation of 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylic acid (6)**




**6**

**[000240]** To the stirred solution of methyl 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylat**e** (**5**, 0.1 g, 0.25 mmol) in MeOH (2 mL), was added 5N NaOH solution (0.4 mL) and stirred at 75°C for 1h (reaction condition **d**). The reaction mixture was evaporated completely. The resulting crude was dissolved in minimum volume of water and acidified with saturated citric acid solution. Compound was extracted with DCM (50 mL x 2), washed with brine, dried over sodium sulfate and evaporated to get crude product as pale yellow color solid (0.07g, 72% Yield). MS (ESI): mass calcd. for, $C_{22}H_{20}N_4O_2$ 372.43; m/z found, 373 $[M+H]^+$.

**Step 7: Preparation of tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carbonyl)piperidin-3-yl)carbamate (8)**

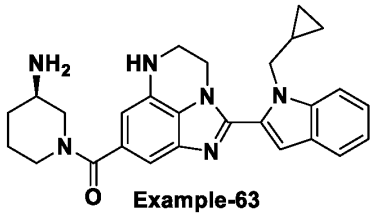



**8**

**[000241]** To the stirred solution of 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylic acid (**6**, 0.07 g, 0.18 mmol) in DCM (5 mL), were added tert-butyl-(R)-piperidin-3-ylcarbamate (**7**, 0.041 g, 0.206 mmol), triethylamine (0.07 mL, 0.56 mmol) followed by 50% solution of T3P in ethyl acetate (0.17 g, 0.565 mmol) and stirred at room temperature for 12 h (reaction condition **e**). To the reaction mixture was added water and compound was extracted with DCM (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate

and evaporated to get crude product. The crude residue was purified by gradient column chromatography using silica gel and eluent 5% MeOH in DCM to afford the product as yellow solid (0.1g.71% Yield). MS (ESI): mass calcd. for $C_{32}H_{38}N_6O_3$, 554.7; m/z found, 555.3 $[M+H]^+$.

**Step 8: Preparation of (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone (Example-63)**



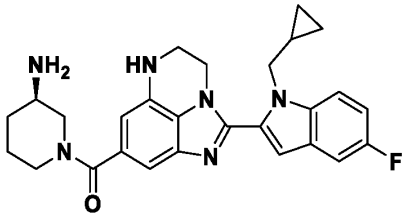
Example-63

**[000242]** To the stirred solution Tert-butyl (R)-(1-(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H- imidazo[1,5,4-de]quinoxaline-8-carbonyl)piperidin-3-yl)carbamate) (**8**, 0.05 g, 0.09 mmol) in dichloromethane (10 mL), was added trifluroacetic acid (0.5 mL) stirred at room temperature for 2 h (reaction condition **f**). The reaction mixture was evaporated completely, dissolved in minimum volume of water and basified by saturated $NaHCO_3$ solution (20 mL). The compound was extracted with DCM (20 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get the product as pale yellow solid (0.025g, 62.5% yield). $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.67 (t , $J$ = 8 Hz, 2H), 7.28 (t, $J$ = 8 Hz, 1H), 7.13-7.07 (m, 2H), 6.94 ( s, 1H), 6.40 (s, 1H) 6.37 (s, 1H), 4.65 (d, $J$ = 8 Hz, 2H), 4.48 (t , $J$ = 4 Hz, 2H ), 3.93-3.88 (m, 2H), 3.53 (m, 2H), 2.87 (m, 1H), 2.66-2.65 (m, 2H), 1.88-1.85 (m, 2H), 1.64 (m, 1H), 1.42-1.17 (m, 4H), 0.33-0.199 (m, 4H). MS (ESI): mass calcd. for, $C_{27}H_{30}N_6O$ 455.58; m/z found, 456.2 $[M+H]^+$.

**[000243]** Following compounds **(Examples 64-80)** were synthesized using procedure as exemplified for **Example-63**.

**Example-64**

**R-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**

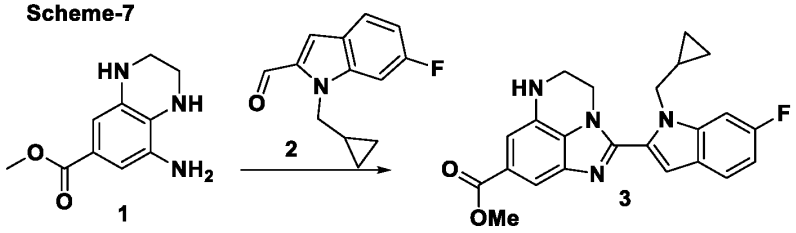


**[000244]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.70-7.66 (m ,1H), 7.43-7.40 (m, 1H), 7.13-7.09 (m, 1H), 7.05 ( s, 1H), 6.94 (s, 1H), 6.41 (s, 1H), 6.38 (s, 1H), 4.63 (d , *J* = 6.8 Hz, 2H ), 4.46 (m, 2H), 4.00 (s, 2H), 3.52 (m, 2H), 2.88 (m, 2H), 2.68 (m, 2H), 1.64 (m, 1H), 1.89-1.85 (m, 1H), 1.64 (m, 1H), 1.42-1.39 (m , 1H), 1.26-1.22 (m, 2H), 0.32 (d, *J* = 7.6 Hz, 2H), 0.21 (m, 2H). MS (ESI): mass calcd. for $C_{27}H_{29}FN_6O$, 472.57; m/z found, 473.58 $[M+H]^+$.

**Example-65**

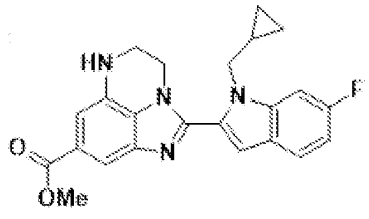
**Synthesis of (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone (Example-65)**

**Scheme-7**



**[000245]** Intermediate **(1)** was synthesized from intermediate **(3)** of Scheme-6 under reduction conditions.

**Step 5: Preparation of methyl 2-(1-(cyclopropylmethyl)-6-fluro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylate (3)**



3

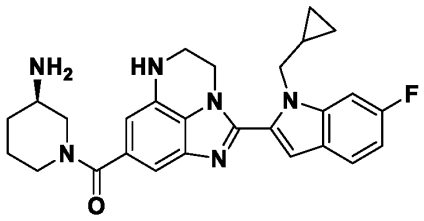
**[000246]** To the stirred solution of methyl 8-amino-1, 2, 3, 4-tetrahydroquinoxaline-6-carboxylate (**1**, 0.1 g, 0.48 mmol) and 1-(cyclopropylmethyl)-6-fluoro-1H-indole-2-carbaldehyde (**2**, 0.11 g, 0.53 mmol) in DMF (3 mL), was added water (0.1 mL) and finally added oxone (0.09 g, 0.31 mmol). Then reaction mixture was allowed to stir under

room temperature for about 1 h. The reaction mixture was quenched with potassium carbonate (0.005g), extracted with ethyl acetate (20 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate, filtered and evaporated to get crude product. Crude residue was purified by gradient column chromatography using silica gel and eluent 20-30% ethyl acetate in hexane to get the product as a yellow solid (0.15 g, 65.2% yield). MS (ESI): mass calcd. for $C_{23}H_{21}FN_4O_2$, 404.16; m/z found, 405.2 $[M+H]^+$.

**[000247]** Following compounds **(Examples 65-71)** were synthesized using the above intermediate **(3)**, and the procedure as exemplified for **Example-63**.

**Example-65:**

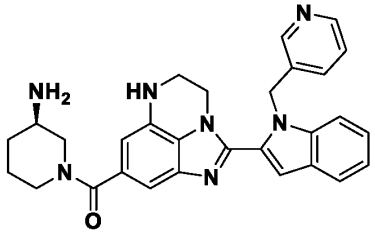
**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**




**[000248]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.68-7.64 (m, 1H), 7.54 (d, *J* = 8 Hz, 1H), 7.09 (s, 1H), 7.0 (s, 1H), 6.96 (d, *J* = 12 Hz, 1H), 6.4-6.38 (m, 2H), 4.63-4.61 (m, 2H), 4.46 (m, 2H), 4.0 (m, 2H), 3.52 (m, 2H), 2.91 (m, 1H), 2.76 (m, 2H), 1.89 (m, 2H), 1.65 (m, 1H), 1.43 (m, 1H), 1.41 (m, 1H), 1.17 (m, 2H), 0.31-0.24 (m, 2H), 0.24-0.20 (m, 2H). MS (ESI): mass calcd. for $C_{27}H_{29}FN_6O$, 472.24; m/z found, 473.3 $[M+H]^+$.

**Example-66**

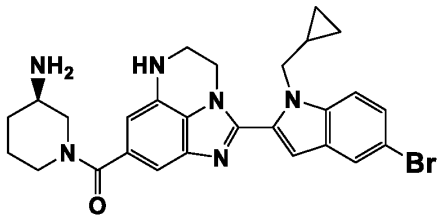
**(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-3-ylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**




**[000249]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 8.36 (bs, 2H), 7.70-7.69 (m, 1H), 7.54-7.52 (m, 1H), 7.44-7.52 (m, 1H), 7.24-7.23 (m, 3H), 7.15-7.11 (m, 1H), 6.99 (bs, 1H), 6.77 (s, 1H), 6.39-6.37 (m, 1H), 6.10 (bs, 2H), 4.50 (m, 2H), 4.00 (m, 2H), 3.51 (m, 2H), 2.65-2.55 (m, 2H), 1.88-1.82 (m, 2H), 1.56 (m, 1H), 1.44 (m, 2H), 1.22 ( m, 2H). MS (ESI): mass calcd. for $C_{29}H_{29}N_7O$, 491.60; m/z found, 492.4 $[M+H]^+$.

**Example-67**

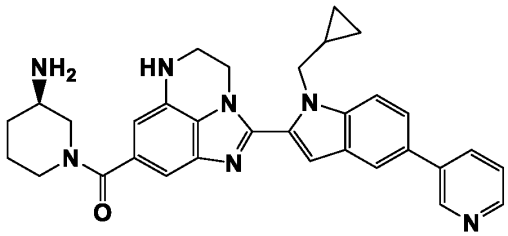
**(R)-(3-aminopiperidin-1-yl)(2-(5-bromo-1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**



**[000250]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.85 (s, 1H), 7.65 (d, *J* = 8.8 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.06 (s, 1H), 6.98 (s, 1H), 6.42-6.40 (m, 2H), 5.40-5.30 (bs. 2H), 4.64 (d, *J* = 7.2 Hz, 2H), 4.46 (s, 2H), 3.53 (s, 2H), 2.87-2.84 (m, 3H), 1.93-1.88 (m, 1H), 1.67 (s, 1H), 1.45-1.17 (m, 4H), 0.88-0.84 (m, 1H), 0.32-0.20 (m,4H). MS (ESI): mass calcd. For, $C_{27}H_{29}BrN_6O$ 533.47; m/z found, 497 [M+H]+.

**Example-68**

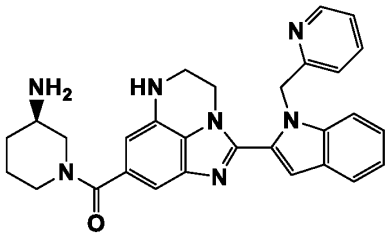
**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-(pyridin-3-yl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**



**[000251]** $^1$HNMR (400 MHz, DMSO-$d_6$ δ(ppm): 8.93 (s, 1H), 8.52 (d , *J* = 4.8 Hz, 1H), 8.09 (d , *J* = 8.4 Hz, 1H), 7.99 (s, 1H), 7.78 (d, *J* = 8.8 Hz, 1H), 7.61 (d, *J* = 8.8 Hz, 1H), 7.48-7.45 (m, 1H), 7.14 (s, 1H), 6.96 (s, 1H), 6.41-6.39 (m, 2H), 4.68 (d, *J* = 7.2 Hz, 2H), 4.49 (s, 2H), 4.12-3.80 (bs, 2H), 3.54 (s, 2H), 2.95 (s, 1H), 2.75 (s, 2H), 1.96-1.31 (m, 6H), 0.87-0.81 (m, 1H). 0.33-0.22 (m,4H). MS (ESI): mass calcd. For, $C_{32}H_{33}N_7O$ 531.6; m/z found, 533.2 [M+H]+.

**Example-69**

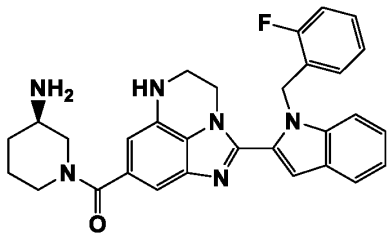
**(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-2-ylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**



**[000252]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 8.43 (d , *J* = 4.6 Hz, 1H), 7.70 (d, *J* = 7.7 Hz, 1H), 7.62-7.58 (m, 1H), 7.44 (d, *J* = 7.7 Hz, 1H), 7.23-7.11 (m, 4H) 6.91 (s, 1H), 6.84 (d, *J* = 7.68 Hz, 1H), 6.40 (s, 2H), 6.15 (s, 1H), 4.53 (bs, 2H ), 3.53 (bs, 2H), 3.53 (m, 2H), 2.89 (m, 1H), 2.73-2.66 (m, 2H), 1.90-1.86 (m, 2H), 1.64 (bs, 1H), 1.44-1.08 (m, 4H). MS (ESI): mass calcd. For, $C_{29}H_{29}N_7O$ 491.02; m/z found, 492.09 $[M+H]^+$.

**Example-70**

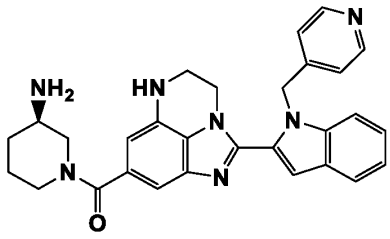
**(R)-(3-aminopiperidin-1-yl)(2-(1-(2-fluorobenzyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**



**[000253]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.71 (d, *J* = 7.3 Hz, 1H), 7.47 (t, *J* = 7.8 Hz, 1H), 7.26-7.12 (m, 4H), 7.01-6.86 (m, 3H), 6.40 (s, 2H), 6.10 (s, 2H), 4.52 (d, *J* = 3.36 Hz, 2H), 4.17 (bs, 2H), 3.53 (s, 2H), 2.83 (bs, 2H), 2.67 (bs, 2H ), 1.84 (d, *J* = 9.24 Hz, 2H), 1.64 (bs, 2H), 1.39 (bs,2H). MS (ESI): mass calcd. for $C_{30}H_{29}FN_6O$ 508.2; found *m/z* 509.16 $[M+H]^+$.

**Example-71**

**(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-4-ylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**



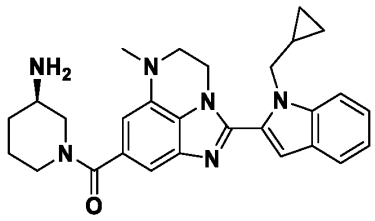
**[000254]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 8.39 (d, J = 5.7 Hz, 1H), 7.73 (d, J = 7.9 Hz, 1H), 7.43 (d, J =7.5 Hz, 1H), 7.25-7.21 (m, 2H), 7.15 (t, J = 7.5 Hz, 1H), 6.98

(d, J = 5.3 Hz, 2H), 6.87 (s, 2H), 6.39 (s, 2H), 6.15 (s, 2H), 4.54 (s, 2H), 4.34 (m, 2H), 3.53 (s, 2H), 2.89 (bs, 1H), 2.66 (m, 1H), 1.85 (d, J =12.8 Hz, 2H), 1.63-1.62 (m, 2H), 1.38-1.33 (m, 1H), 1.23-1.17 (m, 2H). MS (ESI): mass calcd. for $C_{29}H_{29}N_7O$ 491.12; found m/z 492.22 $[M+H]^+$.

**[000255]** Following compound was synthesized using the above intermediate **3**, and the procedure as exemplified for Example 63.

**Example-72**

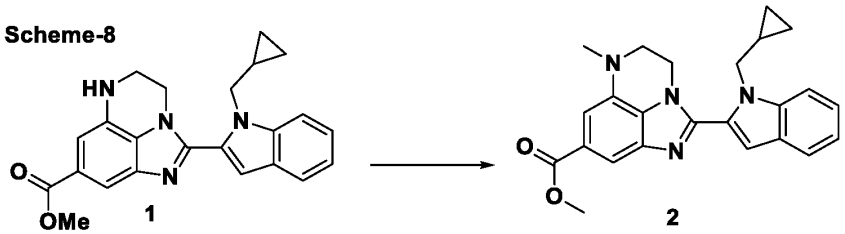
**R-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-methyl-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone (Example-72)**



**Preparation of methyl2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-methyl-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylate (2)**

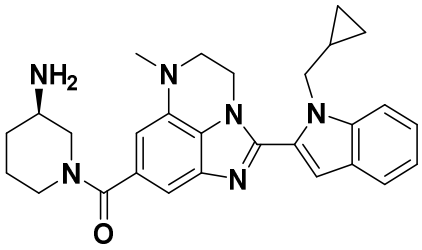
**[000256]** The intermediate **(3)** obtained from the Scheme-6 above was methylated to obtain intermediate **(2)** as given below. Rest of the reaction steps were the same as exemplified for **Example-63**.

**Scheme-8**



**[000257]** To a stirred solution of methyl 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylate (**1** 0.1 g, 0.25 mmol) in DMF(10 mL) was added potassium carbonate (0.07g, 0.51mmol) followed by methyl iodide (0.01 mL, 0.28 mmol) at room temperature and the resulting mixture was allowed to stir under room temperature for 12 h. The progress of the reaction was monitored by TLC. Then reaction mixture was evaporated, and extracted with ethyl acetate (50 mL x 3), dried over sodium sulphate and concentrated under reduced pressure to afford crude compound which was purified by column chromatography (silica gel, 0-20% EtOAc in hexane) to give pale yellow solid (0.05g, 50% yield). MS (ESI): mass calcd. for $C_{24}H_{24}N_4O_2$, 400.48; m/z found, 401.2 $[M+H]^+$.

**R-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-methyl-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone (Example-72)**

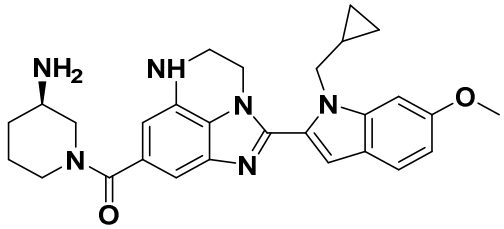


**[000258]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.67 (t , *J* = 8 Hz, 2H), 7.28 (t, *J* = 8 Hz, 1H), 7.13-7.05 (m, 3H), 6.45 ( s, 1H), 4.65 (d, *J* = 8 Hz, 2H), 4.47 ( m, 2H ), 4.12 (m, 2H), 3.46 (m, 2H) 2.96 (s, 4H), 2.80 (m, 2H), 1.99 (m, 2H), 1.66 (m, 1H), 1.46-1.44 (m, 1H) ,1.33-1.18 (m, 3H), 0.31-133 (m, 4H). MS (ESI): mass calcd. for $C_{28}H_{32}N_6O$, 468.61; m/z found, 469.3 $[M+H]^+$.

**[000259]** Following compounds **(Examples 73, 77 and 80)** were synthesized using the procedure as exemplified for **Example-63**.

**Example-73**

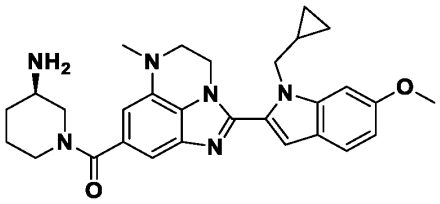
**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-methoxy-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**



**[000260]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.60 (m, 1H), 7.14 (bs, 1H), 6.98 (s, 1H), 6.91 (m, 1H), 6.74 (m, 1H), 6.38 (m, 2H), 4.65 (d, *J* = 8 Hz, 2H), 4.45 (m, 2H), 3.83 (bs, 4H), 2.91 (bs, 1H), 2.53 (m, 3H), 1.88 (m, 2H), 1.64 (m,2H), 1.41 (m, 2H), 1.22-1.17 (m, 3H), 0.21-0.20 (m, 2H), 0.01 (m, 2H). MS (ESI): mass calcd. for $C_{28}H_{32}N_6O_2$, 484.26; m/z found, 485.3 $[M+H]^+$.

**Example-74**

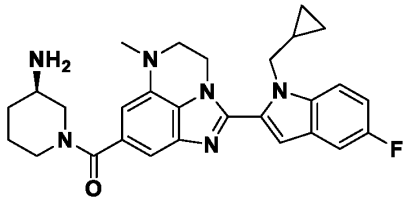
**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-methoxy-1H-indol-2-yl)-6-methyl-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**



**[000261]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.56 (d , *J* = 9.2 Hz, 1H), 7.30 (s, 1H), 7.14 (s, 1H), 7.04 (s, 1H), 6.94-6.91 (m, 1H), 6.75 (s, 1H), 4.65-4.63 (m , 4H), 4.55 (s, 2H), 3.96-3.9 (bs, 2H), 3.79 (s, 3H), 2.95 (s, 3H), 2.79 (d , *J* = 7.2 Hz, 2H), 1.89-1.26 (m, 4H), 0.88-0.84 (m, 1H). 0.33-0.26 (m,4H). MS (ESI): mass calcd. For $C_{28}H_{31}N_5O_3$, 485.5 m/z found, 486.5 $(M+H)^+$.

**Example-75**

**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-6-methyl-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**

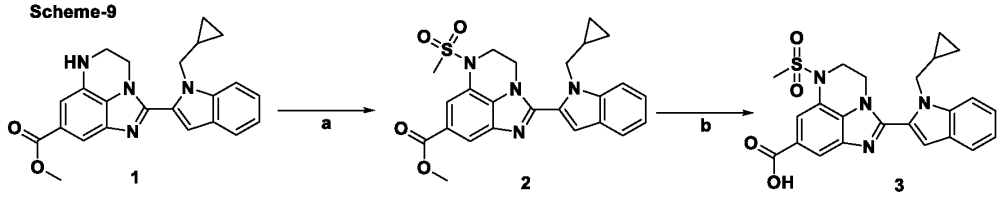


**[000262]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.70 – 7.63 (m, 1H), 7.43 - 7.40 (m, 1H), 7.14 – 7.02 (m, 3H), 6.44 (s, 1H), 4.64 (d, *J* = 6.8 Hz, 2H), 4.58 - 4.56 (m, 2H), 3.45 – 3.44 (m, 2H), 2.96 (s, 3H), 2.89 - 2.79 (bs, 1H), 2.65 (bs, 2H), 2.01 – 1.97 (m, 2H),1.88 - 1.84 (m, 2H), 1.43 -1.37 (m, 2H), 1.35 – 1.26 (m, 2H), 0.87 – 0.84 (bs, 1H), 0.33 – 0.29 (m, 2H), 0.25 - 0.20 (m, 2H). MS (ESI) calculated for $C_{28}H_{31}FN_6O$ *m/z* 486.25 found $(M+H)^+$. 487.3.

**Example-76**

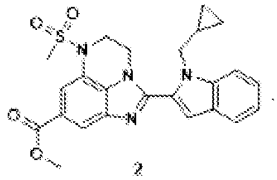
**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(methylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**

Scheme-9




**[000263]** Intermediate **(1)** of the above Scheme-9 was obtained by a similar procedure as exemplified for **Example-63** (Scheme 6).

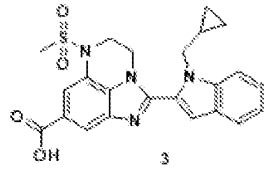
**Step 6: Preparation of methyl 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(methylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylate (2)**



2

**[000264]** To a stirred solution of methyl 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylate (**1,** 0.15 g, 0.39 mmol) in DCM (10 mL) was added pyridine (0.061 g, 0.77 mmol) followed by methanesulfonyl chloride (0.03 ml, 0.39 mmol) at 0° C and the resulting mixture was allowed to stir under room temperature for 1 h. The progress of the reaction was monitored by TLC. Then reaction mixture was evaporated, and extracted with DCM (50 mL x 3), dried over sodium sulphate and concentrated under reduced pressure to give brown solid (0.18 g, crude ). LC-MS m/z calcd for $C_{24}H_{24}N_4O_4S$, 464.5; m/z found, 465.1 $[M+H]^+$.

**Step 7: Preparation of 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(methylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylic acid-(3)**

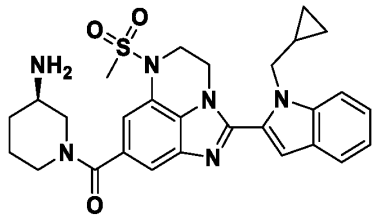


3

**[000265]** To the stirred solution of methyl 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(methylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylate (**2**, 0.18 g, 0.39 mmol) in MeOH (5 mL) and Water (0.5 mL) was added $LiOH.H_2O$ (0.027 g, 0.12 mmol) and stirred at 60°C for 2 h. The reaction mixture was evaporated completely. The resulting crude was dissolved in minimum volume of water and acidified with saturated citric acid solution. Compound was extracted with DCM (30 mL x 2), washed with brine, dried over sodium sulfate and evaporated to give crude product as a pale yellow solid (0.15 g, crude). MS (ESI): Mass calcd. for, $C_{23}H_{22}N_4O_4S$, 450.51; m/z found, 451.1 $[M+H]^+$. Further steps for **Example-76** were carried using the similar procedure as exemplified for **Example-63**.

**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(methylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**

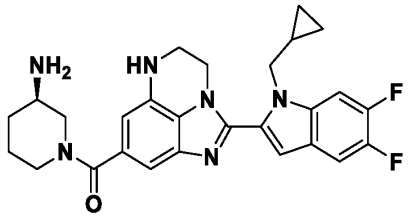
**(Example-76)**



**[000266]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.68 (d , *J* = 6.4 Hz, 2H), 7.52 (s, 1H), 7.31 (d, *J* = 18 Hz, 2H), 7.15 (s, 2H), 4.66 (bs, 4H), 4.12 (s, 2H), 3.60 (bs, 1H), 3.21 (s, 3H), 2.95 (s, 1H), 2.68 (s, 2H), 1.86-1.68 (m, 4H), 1.44 (s, 1H), 1.23 (s, 3H), 0.33-0.27 (m ,4H). MS (ESI): mass calcd. For $C_{28}H_{32}N_6O_3S$ 532.6; m/z found 533 $[M+H]^+$.

**Example-77**

**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5,6-difluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**

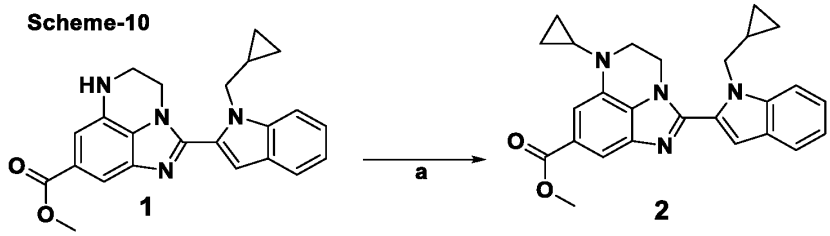


**[000267]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.84 (m, 1H), 7.68-7.63 (m, 1H), 7.08 (s, 1H), 6.97 (s, 1H), 6.42-6.40 (m, 2H), 4.63-4.62 (m, 2H), 4.46 (m, 2H), 3.97 (m, 2H), 3.52 (m, 3H), 2.94 (m, 3H), 1.89 (m, 1H), 1.67 (m, 1H), 1.42-1.34 (m, 2H), 1.22-1.16 (m, 2H), 0.31 (m, 2H), 0.20 (m, 2H). MS (ESI): Mass calcd. for $C_{27}H_{28}F_2N_6O$, 490.23; m/z found, 491.2 $[M+H]^+$.

**Example-78**

**<u>(R)-(3-aminopiperidin-1-yl)(6-cyclopropyl-2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone</u> (Example-78)**

**Scheme-10**

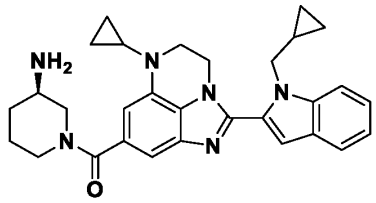



**<u>Step 6: Preparation of methyl 6-cyclopropyl-2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylate (2)</u>**

**[000268]** To a stirred solution of methyl 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylate (**1,** 0.2 g, 0.52 mmol) and cyclopropyl boronic acid (0.088 g, 1.04 mmol) in DCM (10 mL) was added copper (II) acetate (0.164 g, 1.036 mmol) followed by pyridine (0.1 mL, 1.04 mmol) at room temperature and the resulting mixture was allowed to stir under room temperature in the presence of air for 24 h. The progress of the reaction was monitored by TLC. Then reaction mixture was quenched with dilute HCl, extracted with DCM (50 mL x 3), dried over sodium sulphate and concentrated under reduced pressure to afford crude compound. This was purified by column chromatography (silica gel, 0-20% EtOAc in hexane) to give pale yellow solid (0.11g, 50% yield). MS (ESI): Mass calcd. for $C_{26}H_{26}N_4O_2$, 426.2; m/z found, 427 $[M+H]^+$.

**[000269]** Further steps for **Example-78** were carried using the similar procedure as exemplified for **Example-63**.

**(R)-(3-aminopiperidin-1-yl)(6-cyclopropyl-2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone (Example-78)**

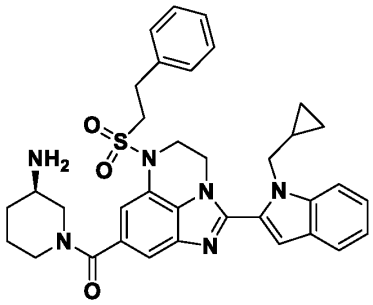



**[000270]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.65 (t , *J* = 6.8 Hz, 2H), 7.26 (t, *J* = 7.6 Hz, 1H), 7.13-7.09 (m, 2H), 7.054 (s, 1H), 6.74 (s, 1H), 4.65 - 4.64 (m, 2H), 4.52 ( m, 2H ), 4.00 (m, 2H), 3.54 (bs, 2H), 2.74 (m, 1H), 2.65 (bs, 2H), 1.88 (m, 2H), 1.69 (bs, 2H), 1.46-1.44 (m, 2H), 1.17 (m, 3H), 0.87- 0.86 (m, 2H), 0.66 (s, 1H), 0.31 - 0.29 (m, 2H), 0.20 - 0.19 (m, 2H). MS (ESI): Mass calcd. for $C_{30}H_{34}N_6O$, 494.64; m/z found, 495.5 $[M+H]^+$.

**[000271]** **Example 79** was synthesized using the above procedure as exemplified for **Example-76**.

**Example 79**

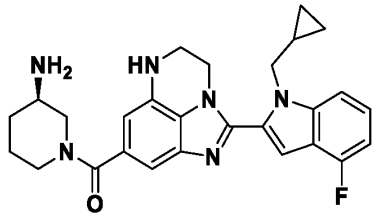
**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(phenethylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**



**[000272]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.67 (d, *J* = 7.2 Hz, 2H), 7.49 (s, 1H), 7.35 (s, 1H), 7.28 (d, *J* = 7.6 Hz, 1H), 7.23-7.20 (m, 4H), 7.17-7.13 (m, 3H), 4.65-4.64 (m, 2H), 4.59-4.57 (m, 2H), 4.14-4.11 (m, 3H), 3.72-3.36 (m, 3H), 3.05 (t, *J* = 8.0 Hz, 2H), 2.95-2.93 (m, 2H), 2.71-2.69 (m, 2H), 1.88-1.85 (m, 1H), 1.66-1.64 (m, 1H), 1.45-1.43 (m, 1H), 1.27-1.22 (m, 3H), 0.31 (d, *J* = 8.0 Hz, 2H), 0.25 (d, *J* = 3.6 Hz, 2H). MS (ESI): Mass calcd. for $C_{35}H_{38}N_6O_3S$ , 622.27; m/z found 623.2 $(M+H)^+$.

**Example-80**

**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-4-fluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**

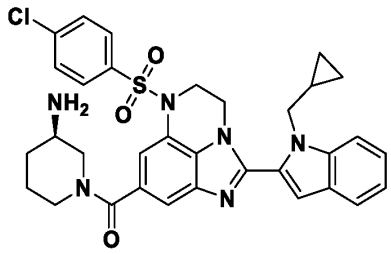


**[000273]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.52 (d , *J* = 8.4 Hz, 1H), 7.27-7.21 (m, 1H), 7.13 (s, 1H), 6.95 (s, 1H), 6.92-6.88 (m, 1H), 6.41-6.38 (m, 2H), 4.66 (d, *J* = 6.8 Hz, 2H), 4.49 (bs, 2H), 4.00 (m, 2H), 3.93 (m, 3H), 2.88 (m, 1H), 2.69 (m, 1H), 1.88 (m, 2H), 1.64 (m, 1H), 1.39 (m, 1H), 1.24-1.17 (m, 3H), 0.32 (d, *J* =7.6 Hz, 2H), 0.21 (m, 2H). MS (ESI): Mass calcd. for $C_{27}H_{29}FN6O$, 472.57; m/z found, 473.2 $[M+H]^+$.

**[000274]** **Examples 81-83** were synthesized using the above procedure as exemplified for **Example-76. Example 84** was synthesized using the above procedure as exemplified for **Example-63.**

**Example-81**

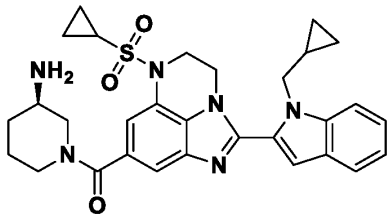
**(R)-(3-aminopiperidin-1-yl)(6-((4-chlorophenyl)sulfonyl)-2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**



**[000275]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.82 (d, *J* = 8.4 Hz, 2H), 7.67 - 7.63 (m, 4H), 7.51 (s, 1H), 7.42 (s, 1H), 7.27 (t , *J* = 7.2 Hz, 1H), 7.12 (t, *J* = 7.6 Hz, 1H), 7.03 (s, 1H), 4.57 (d, *J* = 6.4 Hz, 2H), 4.30 – 4.24 (m, 4H), 3.09 – 2.97 (bs, 2H), 2.74 – 2.65 (m, 1H), 1.88 – 1.86 (m, 2H), 1.70 (bs, 1H), 1.43 - 1.31 (m, 2H), 1.28 – 1.21 (m, 3H), 1.10 (bs, 2H), 0.25 - 0.23 (m, 2H), 0.13 – 0.12 (m, 2H). MS (ESI): mass calcd. for $C_{30}H_{34}N_6O_3S$, 629.18; m/z found, 629.2 $[M+H]^+$ .

**Example-82**

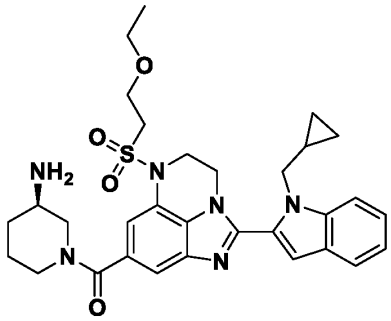
**(R)- (3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(cyclopropylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**



**[000276]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.68 (t , *J* = 7.2 Hz, 2H), 7.53 (s, 1H), 7.35 (s, 1H), 7.29 (t, *J* = 7.2 Hz, 1H), 7.16 - 7.12 (m, 2H), 4.67 - 4.63 (m, 4H), 4.12 (bs, 2H), 2.96 – 2.87 (bs, 2H), 2.73 – 2.65 (m, 3H), 1.89 (m, 2H), 1.67 (bs, 1H), 1.43 - 1.31 (m, 1H), 1.28 – 1.22 (m, 4H), 1.03 – 1.01 (m, 4H), 0.33 - 0.31 (m, 2H), 0.26 (bs, 2H). MS (ESI): mass calcd. for $C_{30}H_{34}N_6O_3S$, 558.7; m/z found, 559.2 $[M+H]^+$.

**Example-83**

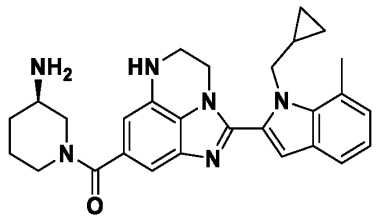
**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-((2-ethoxyethyl)sulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**



**[000277]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.68 (d, *J* = 7.2 Hz, 2H), 7.49 (s, 1H), 7.33-7.27 (m, 2H), 7.15-7.10 (m, 2H), 4.68-4.65 (m, 2H), 4.60-4.58 (m, 2H), 4.14-4.11 (m, 3H), 3.67-3.65 (m, 3H), 3.62-3.60 (m, 2H), 3.12-3.10 (m, 1H), 2.91-2.89 (m, 3H), 2.71-2.69 (m, 2H), 1.88-1.85 (m, 2H), 1.66-1.64 (m, 2H), 1.45-1.43 (m, 1H), 1.27-1.22 (m, 3H), 0.70-0.67 (m, 1H), 0.32(d, *J* = 6.8 Hz, 2H), 0.23 (d, *J* = 3.6 Hz, 2H). MS (ESI): mass calcd. for $C_{31}H_{38}N_6O_4S$, 590.27; *m/z* found, 591.3 $(M+H)^+$.

**Example-84**

**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-methyl-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone**

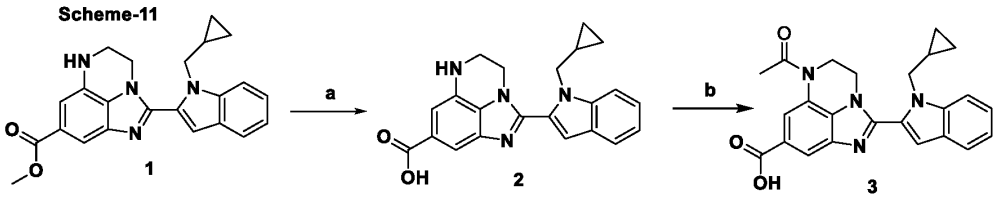


**[000278]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.56 (m, 1H), 7.08 (m, 3H), 6.97 (s, 1H), 6.45 (m, 2H), 4.89 (d, *J* = 8 Hz, 2H), 4.46 (m, 2H), 4.00 (m, 2H), 3.57 (bs, 2H), 2.83 (s, 3H), 2.70 (m, 2H), 1.93 (m, 2H), 1.80 (m, 2H), 1.30 (m,1H), 1.26 (m,1H), 0.98 (m, 2H), 0.24 (d, *J* =12 Hz, 2H), 0.19 (m, 2H). MS (ESI): mass calcd. for $C_{28}H_{32}N_6O$, 468.61; m/z found, 469.1 $[M+H]^+$.

**Example-85**

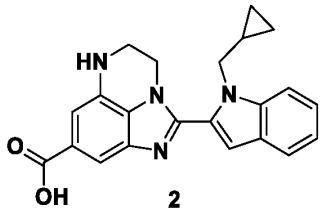
**(R)-1-(8-(3-aminopiperidine-1-carbonyl)-2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-4,5-dihydro-6H-imidazo[1,5,4-de]quinoxalin-6-yl)ethan-1-one**

Scheme-11



**[000279]** Intermediate **(1)** of the above Scheme-11 was obtained by a similar procedure as exemplified for **Example-63** (Scheme 6).

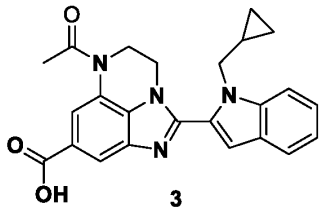
**Step 6: Preparation of 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylic acid-(2)**




2

**[000280]** To the stirred solution of methyl methyl 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylate (**1**, 0.09 g, 0.21 mmol) in MeOH (5 mL) and water (0.5 mL) was added LiOH.$H_2O$ (0.044 g, 1.05 mmol) and stirred at room temperature for 12 h. The reaction mixture was evaporated completely. The resulting crude was dissolved in minimum volume of water and acidified with saturated citric acid solution. Compound was extracted with DCM (30 mL x 2), washed with brine, dried over sodium sulfate and evaporated to give the crude product as a pale yellow solid (0.07 g, crude). MS (ESI): Mass calcd. for $C_{22}H_{20}N_4O_2$, 372.43; m/z found, 373.0 $[M+H]^+$.

**Step 7: Preparation of 6-acetyl-2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylic acid (3)**



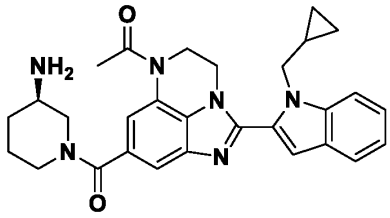

3

**[000281]** To a stirred solution of 2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxaline-8-carboxylic acid (0.07 g, 0.19 mmol) in DCM (10 mL) was added pyridine (0.03 mL, 0.37 mmol) followed by acetyl chloride (0.02 mL, 0.28 mmol) at 0°C and the resulting mixture was stirred at room temperature for 1 h. The progress of the reaction was monitored by TLC. The reaction mixture was evaporated, extracted with DCM (50 mL x 3), dried over sodium sulphate and concentrated under reduced pressure to give the brown solid (0.059 g, 76 % ). LC-MS m/z calcd for $C_{24}H_{22}N_4O_3$, 414.4, found 415.1 $[M+H]^+$.

**[000282]** The remaining steps for preparing **Example-85** were carried using the similar procedure as exemplified for **Example-63**.

**Example-85**

**(R)-1-(8-(3-aminopiperidine-1-carbonyl)-2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-4,5-dihydro-6H-imidazo[1,5,4-de]quinoxalin-6-yl)ethan-1-one**

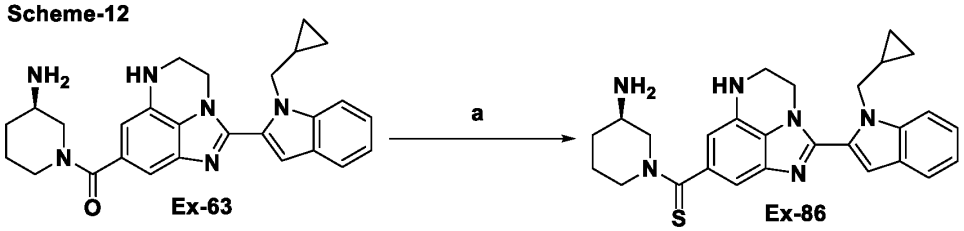


**[000283]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 7.90 (s,1H), 7.68 (t, *J* = 7.6 Hz, 2H), 7.53 (s, 1H), 7.29 (t, *J* = 7.6 Hz, 1H), 7.13 (t, *J* = 6.8 Hz, 2H), 6.00 (bs, 2H), 4.67-4.58 (m, 4H), 4.17 (s, 3H), 3.00 (bs, 3H), 2.40 (s, 3H), 1.96 (s, 1H), 1.70 (s, 1H), 1.46 (s, 2H), 1.22 (s, 2H), 0.34-0.26 (m,4H). MS (ESI): Mass calcd. for $C_{29}H_{32}N_6O_2$, 496.6; m/z found, 497.3 $[M+H]^+$.

**Example-86**

**(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanethione**

**Scheme-12**

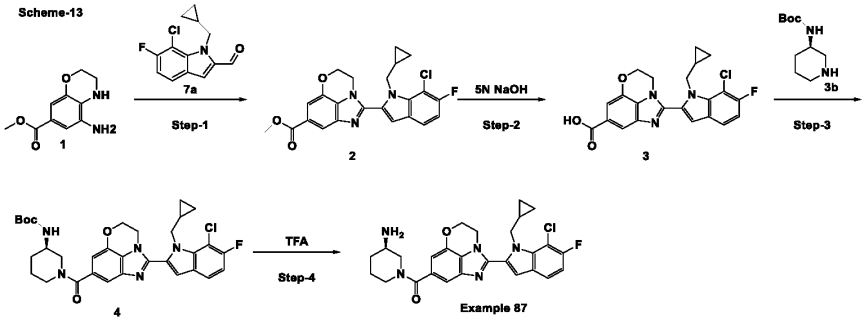



**[000284]** To the stirred solution (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone (**Example-63**, 0.07g, 0.15 mmol) in Toluene (50 mL), was added Lawessons reagent (0.12 g, 0.39 mmol) at room temperature. The reaction mixture was reflux at bath temperature of 100°C for 12 h. The reaction mixture was diluted with $NaHCO_3$ (50 mL x 2) and extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using 15-100% ethyl acetate in hexane to afford (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-

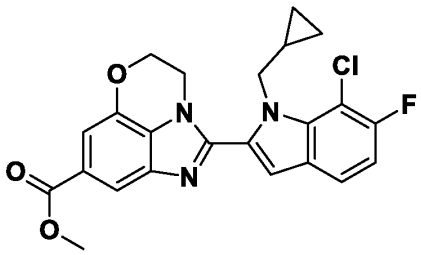
yl)methanethionen as yellow colour solid (0.007 g, 10% Yield). $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 8.06 (m, 1H), 7.79 (m, 1H), 7.67 (t, *J* = 8 Hz, 2H), 7.28 (t, *J* = 12 Hz, 1H), 7.28-7.03 (m, 2H), 6.39 (m, 1H), 5.12 (m, 1H), 4.63 (m, 2H), 4.47 (bs, 2H), 3.79 (bs, 1H), 3.48 (bs, 2H), 2.04-1.97 (m, 3H), 1.72-1.61 (m, 4H), 1.44 (m, 2H), 0.83 (s, 1H), 0.32-0.31 (d. *J* = 4 Hz, 2H), 0.21 (m, 2H). MS (ESI): Mass calcd. for $C_{27}H_{30}N_6S$, 470.64; m/z found 471.2$[M+H]^+$.

**Example-87**

**Synthesis of (R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**



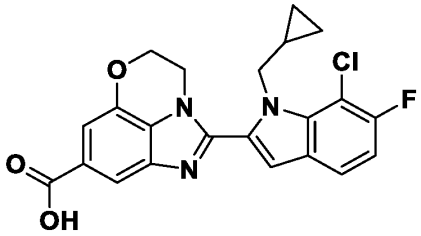

**Step-1: Synthesis of methyl-2-(7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylate (2)**



**[000285]** To a stirred solution of methyl-5-amino-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (**1**, 0.33 g, 1.31 mmol) and 7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indole-2-carbaldehyde (**7a**, 0.27 g, 1.31 mmol) in *N*, *N*-dimethylformamide (10.0 mL) and water (3.0 mL), potassium peroxomonosulfate (Oxone, 0.484 g, 1.57 mmol) was added at room temperature. The reaction mixture was stirred at room temperature for 16 h. After completion of reaction, the reaction mixture was cooled to room temperature, water was added. Precipitated solid was filtered and washed with water (20 mL × 2) and methanol (10 mL × 2). The compound obtained was dried under vacuum to afford methyl-2-(7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-

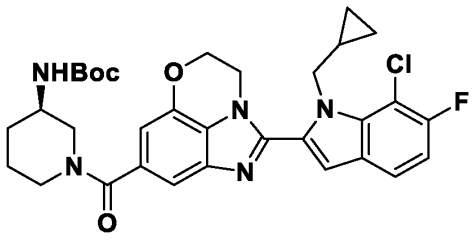
indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylate (**2**) as yellow solid. Yield: 0.12 g (22%). MS (ESI) 439.11; *m/z* found 440.28 $[M+H]^{+1}$.

**Step-2: Synthesis of 2-(7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid (3)**




**[000286]** To a stirred solution of methyl-2-(7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylate (**2**, 0.12 g, 0.29 mmol) in tetrahydrofuran (5.0 mL) and methanol (3.0 mL), 5N sodium hydroxide solution (3.0 mL) was added and reaction mixture was stirred at 60 °C for 2 h. After completion of reaction, the reaction mixture was concentrated under reduced pressure. The resulting crude was dissolved in minimum volume of water and acidified with saturated citric acid solution at 0 °C up to pH 2~3. The precipitated solid was filtered, washed with water (10 mL × 2). The compound obtained was dried under vacuum to afford 2-(7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid (**3**) as white solid. Yield: 0.11 g (89%). MS (ESI) 425.09; *m/z* found 424.13 $[M-H]^{-1}$.

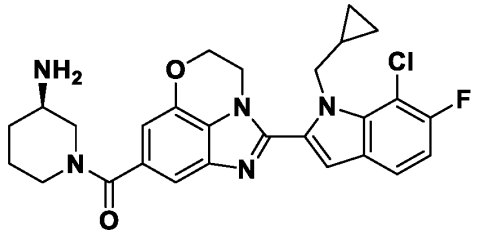
**Step-3: Synthesis of tert-butyl (R)-(1-(2-(7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (4)**




**[000287]** To a stirred solution of 2-(7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid (**3**, 0.11 g, 0.25 mmol) in dichloromethane (10.0 mL), *tert*-butyl-(*R*)-piperidin-3-ylcarbamate (**3b**, 0.06 g, 0.31 mmol) and triethylamine (0.11 mL, 0.83 mmol) were added, followed by

addition of propylphosphonic anhydride (50% solution in ethyl acetate, 0.25 mL, 0.86 mmol). The reaction mixture was stirred at room temperature for 2 h. After completion of reaction, the reaction mixture was diluted with water and extracted with dichloromethane (10 mL × 2). The combined organic layers were washed with water and brine solution, further dried over anhydrous sodium sulfate, filtered and concentrated to get crude product. The crude was purified by CombiFlash using 4.0 g, RediSep column and 70% ethyl acetate in hexane as eluent to afford tert-butyl (R)-(1-(2-(7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (**4**) as yellow solid. Yield: 0.07 g (45%). MS (ESI) 607.24; *m/z* found 608.32 $[M+1]^{+1}$.

**Step-4: Synthesis of (R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone (Example-87)**

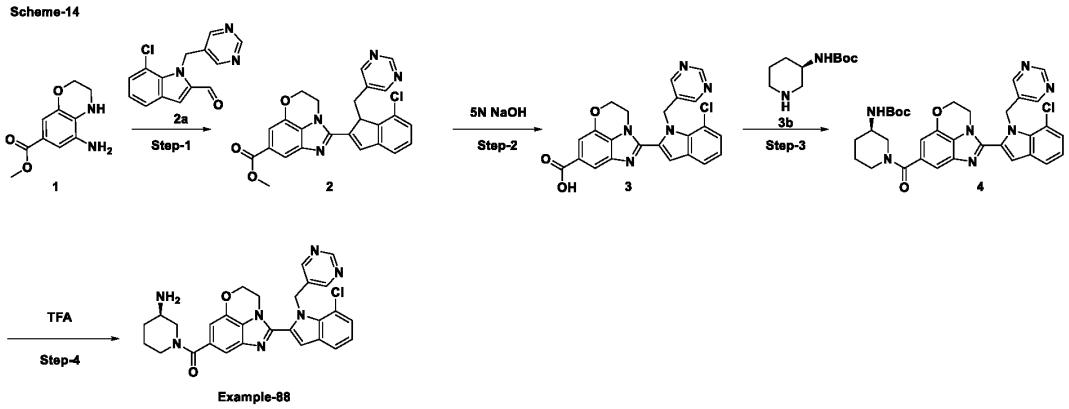



**[000288]** To a stirred solution of tert-butyl (R)-(1-(2-(7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (**4**, 0.07 g, 0.11 mmol) in dichloromethane (5.0 mL), trifluoroacetic acid (1.0 mL) was added at 0 °C and stirred at room temperature for 2 h. After completion of reaction, the reaction mixture was concentrated completely, basified by saturated sodium bicarbonate solution (10 mL). The compound was extracted with dichloromethane (10 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated to afford (R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone, as white solid. Yield: 0.042 g (72%).

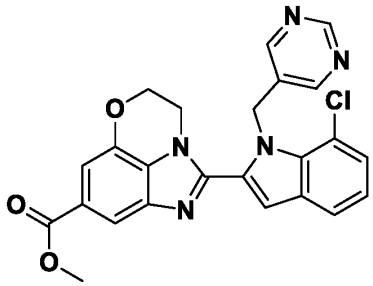
**[000289]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 7.74-7.70 (m, 1H), 7.31 (s, 1H), 7.28 (s, 1H), 7.24 (t, *J* = 9.16 Hz, 1H), 6.78 (s, 1H), 5.06 (d, *J* = 6.8 Hz, 2H), 4.60-4.58 (m, 4H), 4.17(bs, 1H), 3.60 (bs, 1H), 2.90 (bs, 2H), 2.64 (m, 1H), 1.86-1.83 (m, 1H), 1.64 (bs, 2H), 1.43 (m, 1H), 1.23-1.12 (m, 3H), 0.28 (d, *J* = 7.68 Hz, 2H), 0.06 (d, *J* = 4.36 Hz, 2H). MS (ESI): 507.18; found *m/z* 508.36 $[M+H]^+$.

**Example-88**

**Synthesis of (R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(pyrimidin-5-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone**

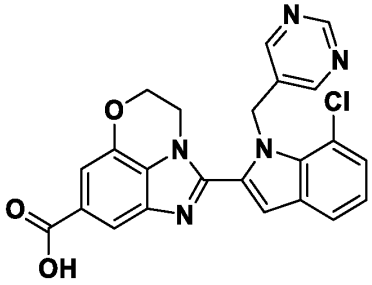



**Step-1: Synthesis of methyl-2-(7-chloro-1-(pyrimidin-5-ylmethyl)-1H-inden-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylate (2)**



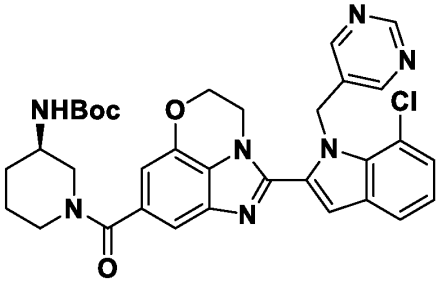
**[000290]** To a stirred solution of methyl-5-amino-3,4-dihydro-2H-benzo[b][1,4]oxazine-7-carboxylate (**1**, 0.200 g, 0.96 mmol) and 7-chloro-1-(pyrimidin-5-ylmethyl)-1H-indole-2-carbaldehyde (**2a**, 0.260 g, 1.05 mmol) in *N,N*-dimethylformamide (5.0 mL) and water (1.5 mL), potassium peroxomonosulfate (Oxone, 0.175g, 1.15 mmol) was added at room temperature. The reaction mixture was stirred at room temperature for 16 h. After completion of reaction, the reaction mixture was cooled to room temperature, water was added. Precipitated solid was filtered and washed with water (10 mL × 2) and methanol (5 mL × 2). The compound obtained was dried under vacuum to afford methyl 2-(7-chloro-1-(pyrimidin-5-ylmethyl)-1H-inden-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylate (**2**) as yellow solid. Yield: 0.30 g (crude). MS (ESI) 458.90; *m/z* found 459.80 $[M+H]^{+1}$.

**Step-2: Synthesis of 2-(7-chloro-1-(pyrimidin-5-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid (3)**



**[000291]** To a stirred solution of methyl-2-(7-chloro-1-(pyrimidin-5-ylmethyl)-1H-inden-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylate (**2**, 0.30 g, 0.65 mmol) in tetrahydrofuran (5.0 mL) and methanol (3.0 mL), 5N sodium hydroxide solution 3.0 mL) was added and reaction mixture was stirred at 60 °C for 2 h. After completion of reaction, the reaction mixture was concentrated under reduced pressure completely. The resulting crude was dissolved in minimum volume of water and acidified with saturated citric acid solution at 0 °C up to pH 2~3. The precipitated solid was filtered, washed with water (10 mL × 2). The compound obtained was dried under vacuum to afford 2-(7-chloro-1-(pyrimidin-5-ylmethyl)-1H-indol-2-yl)-3, 4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid (**3**) as white solid. Yield: 0.250 g (Crude). MS (ESI) 445.86; *m/z* found 446.89 $[M+H]^{+1}$.

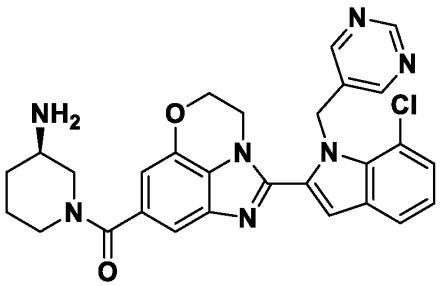
**Step-3: Synthesis of tert-butyl (R)-(1-(2-(7-chloro-1-(pyrimidin-5-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (4)**



**[000292]** To a stirred solution of 2-(7-chloro-1-(pyrimidin-5-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carboxylic acid (**3**, 0.25 g, 0.56 mmol) in dichloromethane (10.0 mL), *tert*-butyl-(*R*)-piperidin-3-ylcarbamate (**3b**, 0.134 g, 0.67 mmol) and triethylamine (0.2 mL, 1.74 mmol) were added, followed by addition of propylphosphonic anhydride (50% solution in ethyl acetate, 0.5 mL, 1.96 mmol). The

reaction mixture was stirred at room temperature for 2 h. After completion of reaction, the reaction mixture was diluted with water and extracted with dichloromethane (10 mL × 2). The combined organic layers were washed with water, brine solution and dried over anhydrous sodium sulfate. The organic layer was filtered and concentrated to get crude product. The crude was purified by CombiFlash using 12.0 g, RediSep column and 70% ethyl acetate in hexane as eluent to afford tert-butyl (R)-(1-(2-(7-chloro-1-(pyrimidin-5-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (**4**) as white solid. Yield: 0.10 g (30%). MS (ESI) 628.13; *m/z* found 629.35 $[M+1]^+$.

**Step-4: Synthesis of (R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(pyrimidin-5-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone (Example-88)**



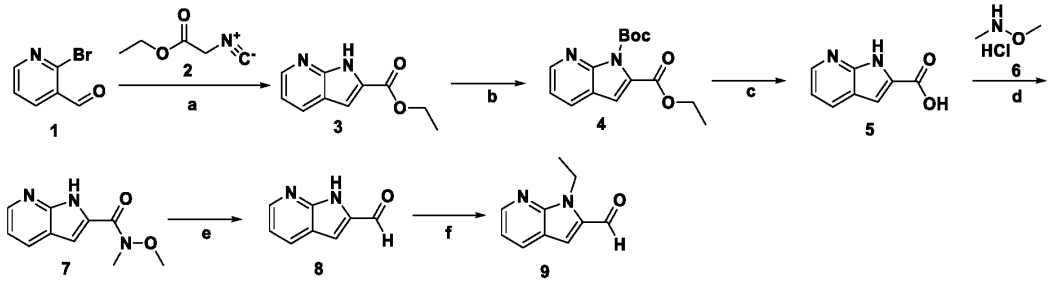

**[000293]** To a stirred solution tert-butyl (R)-(1-(2-(7-chloro-1-(pyrimidin-5-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)carbamate (**4**, 0.1 g, 0.15 mmol) in dichloromethane (5.0 mL), trifluoroacetic acid (1.0 mL) was added at 0 °C and stirred at room temperature for 2 h. After completion of reaction, the reaction mixture was concentrated. The reaction mixture was basified by saturated sodium bicarbonate solution (5.0 mL). The compound was extracted with dichloromethane (10 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under vacuum to afford (R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(pyrimidin-5-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone, as off white solid. Yield: 0.025 g (30%).

**[000294]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ (ppm): 9.03 (s, 1H), 8.40 (s, 2H), 7.76 (d, *J* = 7.84 Hz, 1H), 7.45 (s, 1H), 7.31 (d, *J* = 7.52 Hz, 1H), 7.23 (s, 1H), 7.16 (t, *J* = 7.76 Hz, 1H), 6.76 (s, 1H), 6.44 (s, 2H), 4.70 (d, *J* = 4.28 Hz, 2H), 4.57 (d, *J* = 4.24 Hz, 2H), 4.14 (s, 1H), 3.58 (s, 1H), 2.89 (bs, 1H), 2.69-2.66 (m, 1H), 2.17-1.89 (m, 2H), 1.84

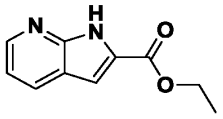
(d, *J* = 11.6 Hz, 1H), 1.63 (bs, 1H), 1.41 (m, 1H), 1.22 (m, 2H). MS (ESI): 528.01; found *m/z* 528.42 $[M+H]^+$.

## SYNTHESIS OF INTERMEDIATES

**Synthesis of 1-ethyl-1H-pyrrolo[2,3-b]pyridine-2-carbaldehyde (Intermediate for Example-5):**



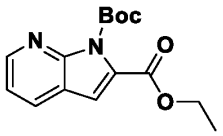

**Step-1: Ethyl 1H-pyrrolo[2,3-b]pyridine-2-carboxylate (3)**



**3**

**[000295]** To the stirred solution of 2-bromonicotinaldehyde (**1**, 10.0 g, 53.7 mmol) in DMSO (100 mL), was added $Cs_2CO_3$ (35.0 g, 107 mmol), CuI (1.05 g, 5.37 mmol) followed by ethyl-2- isocyanoacetate (**2**, 7.9 mL, 69.8 mmol) and stirred at 80°C for 16h (reaction condition **a**). The reaction mixture was cooled to room temperature and filtered through celite. To this added water (100 mL) and compound was extracted with EtOAc (200 mL). Organic layer was dried over anhydrous $Na_2SO_4$ and evaporated under vacuum. Crude was purified by column chromatography using 30-50% EtOAc in Hexane to afford the product as brown gum. (Yield: 45%, 4.5 g). MS (ESI): mass calcd. for $C_{10}H_{10}N_2O_2$, 190.20; *m/z* found 191.0 $(M+H)^+$.

**Step-2: 1-(Tert-butyl) 2-ethyl 1H-pyrrolo[2,3-b]pyridine-1,2-dicarboxylate (4)**

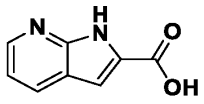


**4**

**[000296]** To the stirred solution of ethyl 1H-pyrrolo[2,3-b]pyridine-2-carboxylate (**3**, 34.5 g, 23.6 mmol) in THF (50 mL), was added triethylamine (6.5 mL, 47.3 mmol)

followed by Boc anhydride (3.6 g, 35.5 mmol) and stirred at room temperature for 16 h (reaction condition **b**). To the reaction mixture was added water (100 mL) and extracted with EtOAc (200 mL). Organic layer was dried over anhydrous $Na_2SO_4$ and evaporated under vacuum. Crude was purified by column chromatography using silica gel and eluent 20-30% EtOAc in hexane to afford the product as brown gum. (Yield: 81%, 5.5 g). MS (ESI): mass calcd. for $C_{15}H_{18}N_2O_4$ , 290.32; *m/z* found, 291.1 $(M+H)^+$.

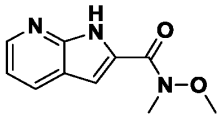
**Step-3: 1H-pyrrolo[2,3-b]pyridine-2-carboxylic acid (5)**



**5**

**[000297]** To a stirred solution 1-(tert-butyl) 2-ethyl 1H-pyrrolo[2,3-b]pyridine-1,2-dicarboxylate (**4**, 5.5 g, 18.9 mmol) in THF (40 mL), LiOH (3.9 g, 94.8 mmol) in water (10 mL) and stirred at room temperature for 4h. The reaction mixture was evaporated and dissolved in minimum amount of water. To this, added saturated citric acid solution till acidic and precipitate formed was collected by filtration, dried to afford the product as white solid. (Yield: 81%, 2.5 g). MS (ESI): mass calcd. for $C_8H_6N_2O_2$, 162.04; *m/z* found, 163.1 $(M+H)^+$.

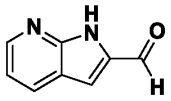
**Step-4: N-methoxy-N-methyl-1H-pyrrolo[2,3-b]pyridine-2-carboxamide (7)**



**7**

**[000298]** To the stirred solution of 1H-pyrrolo[2,3-b]pyridine-2-carboxylic acid (**5**, 2.5 g, 15.4 mmol) and N,O-dimethylhydroxylamine hydrochloride (**6**, 1.8 g, 18.5 mmol in DCM (50 mL), was added triethylamine (10.6 mL, 77.1 mmol), HOBt (3.54 g, 23.14 mmol) followed by EDC.HCl (4.42 g, 23.18 mmol) at 0°C and the reaction mixture was stirred at room temperature for 16h. The reaction mixture was cooled to room temperature, filtered through celite and evaporated the filtrate. To the crude, added water (10 mL) and compound was extracted with DCM (30mL). Organic layer was dried over sodium sulfate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using silica gel and eluent 2-4% MeOH in DCM to afford the product as off white solid. (Yield: 82%, 2.6 g). MS (ESI): mass calcd. for $C_{10}H_{11}N_3O_2$, 205.09; *m/z* found, 206.1 $(M+H)^+$.

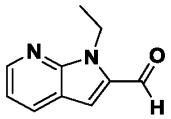
**Step-5: 1H-pyrrolo[2,3-b]pyridine-2-carbaldehyde (8)**



8

**[000299]** To a stirred solution N-methoxy-N-methyl-1H-pyrrolo[2,3-b]pyridine-2-carboxamide (**7**, 0.5 g, 2.43 mmol) in THF (10 mL), was added 1M LAH in THF (3.6 mL, 3.65 mmol) at -78°C and the reaction mixture was stirred at same temperature for 3 h. The reaction mixture was basified using saturated $Na_2CO_3$ solution and extracted with DCM (2 X 25mL). The reaction was quenched with saturated $NH_4Cl$ (10 mL) solution and compound was extracted with EtOAc (50 mL). The organic layer was dried over anhydrous $Na_2SO_4$. Crude was purified by flash column chromatography using 25-30% EtOAc in hexane to get the compound as white solid. (Yield: 85%, 0.3g). MS (ESI): mass calcd. for $C_8H_6N_2O$, 146.15; *m/z* found, 147.1 $(M+H)^+$.

**Step-6: 1-ethyl-1H-pyrrolo[2,3-b]pyridine-2-carbaldehyde (9)**

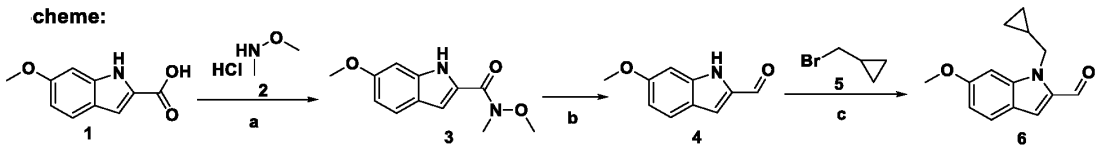


9

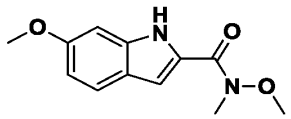
**[000300]** To a stirred solution 1H-pyrrolo[2,3-b]pyridine-2-carbaldehyde (**8**, 0.3 g, 2.19 mmol) in DMF (10 mL), was added $K_2CO_3$ (0.91 g, 6.57 mmol) followed by ethyl iodide (0.5 g, 3.28 mmol) and the reaction mixture was stirred at same temperature for 16 h. To the reaction mixture was added water (15 mL) and extracted with EtOAc (50 mL). The organic layer was dried over anhydrous $Na_2SO_4$. Crude was purified by flash column chromatography using 15-20% EtOAc in hexane to get the compound as colourless oil. (Yield: 95%, 0.34 g). $^1$HNMR (400 MHz, DMSO-$d_6$) δ, ppm: 9.94 (s, 1H), 8.52 (d, $J$ = 4.0 Hz, 1H), 8.23 (d, $J$ = 8.0 Hz, 1H), 7.49 (s, 1H), 7.23 (t, $J$ = 5.2 Hz, 1H), 4.65-4.60 (m, 2H), 1.27 (t, $J$ = 6.4 Hz, 3H). MS (ESI): mass calcd. for $C_{10}H_{10}N_2O$, 174.08; *m/z* found, 175.2 $(M+H)^+$.

**Synthesis of 1-(cyclopropylmethyl)-6-methoxy-1H-indole-2-carbaldehyde (Intermediate for Example-74):**

cheme:



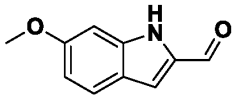
**Step-1: Preparation of N,6-dimethoxy-N-methyl-1H-indole-2-carboxamide (3)**



**3**

**[000301]** To a stirred solution 6-methoxy-1H-indole-2-carboxylic acid (**1**, 3 g, 15.69 mmol) in DCM (20 mL), was added N,O-dimethylhydroxylamine hydrochloride (**2**, 3 g, 31.38 mmol), followed by hydroxybenzotriazole (3.6 g, 23.5 mmol), *N*-(3-dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (4.5 g, 23.5 mmol) and TEA (11.3 mL, 120.7 mmol), and the reaction mixture was stirred at same temperature for 5 h. The reaction mixture was quenched with water, extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate, filtered and evaporated to get crude product. Crude residue was purified by gradient column chromatography using 25-30% ethyl acetate in hexane to get the product as beige colour solid. (Yield: 75%, 0.86 g). MS (ESI): mass calcd. for $C_{12}H_{14}N_2O_3$, 234.10; *m/z* found, 235 $(M+H)^+$.

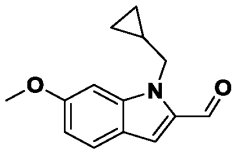
**Step-2: Preparation of 6-methoxy-1H-indole-2-carbaldehyde (4)**



**4**

**[000302]** To a stirred solution of N,6-dimethoxy-N-methyl-1H-indole-2-carboxamide (**3**, 2 g, 8.54 mmol) in THF (20 mL), was added LAH 1M soln. in THF (12.8 mL, 12.75 mmol) slowly under cooling condition, and then the reaction mixture was allowed to stir at room temperature for 1h. The reaction mixture was quenched with ammonium chloride, extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate, filtered and evaporated to get crude product. Crude residue was purified by gradient column chromatography using 5-10% ethyl acetate in hexane to get the product as white solid. (Yield: 60%, 0.9 g). MS (ESI): mass calcd. for $C_{10}H_9NO_2$, 175.06; *m/z* found, 176.1 $(M+H)^+$.

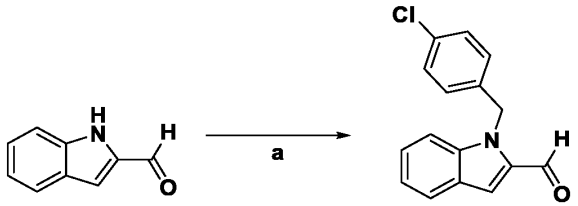
**Step-3:Preparation of 1-(cyclopropylmethyl)-6-methoxy-1H-indole-2-carbaldehyde (6)**



6

**[000303]** To a stirred solution of 6-methoxy-1H-indole-2-carbaldehyde (**4**, 0.28 g, 1.6 mmol) in DMF (5 mL), was added potassium carbonate (1.1 g, 8 mmol) followed by (bromomethyl)cyclopropane (**5**, 0.23 mL, 1.72 mmol) and the reaction mixture was stirred at same temperature for 4h. The reaction mixture was quenched with water, extracted with ethyl acetate (20 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate, filtered and evaporated to get crude product. Crude residue was purified by gradient column chromatography using 5-10% ethyl acetate in hexane to get the product as brown liquid. (Yield: 63%, 0.23 g). $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 9.72 (s, 1H), 7.62 (d, *J* = 8 Hz, 1H), 7.3 (s, 1H), 7.07 (s, 1H), 6.78 (d, *J* = 8 Hz, 1H), 4.43 (d, *J* = 8 Hz, 2H), 3.84 (s, 3H), 1.26-1.21 (m, 1H), 0.40-0.38 (m, 4H). MS (ESI): mass calcd. for $C_{14}H_{15}NO_2$, 229.1; *m/z* found, 230.2 $(M+H)^+$.

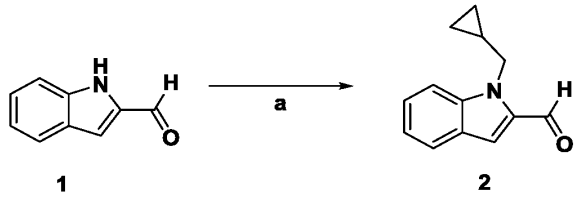
**Synthesis of 1-(4-chlorobenzyl)-1H-indole-2-carbaldehyde (Intermediate for Example-13)**



1 2

**[000304]** To a stirred solution 1H-indole-2-carbaldehyde (**1**, 0.5 g, 3.44 mmol) in DMF (10 mL), was added potassium carbonate (1.42 g, 10.3 mmol) followed by 1-(bromomethyl)-4-chlorobenzene (0.84 g, 4.13 mmol) and the reaction mixture was stirred at same temperature for 4 h. The reaction mixture was quenched with water, extracted with ethyl acetate (30 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate, filtered and evaporated to get crude product. Crude residue was purified by gradient column chromatography using 10-15% ethyl acetate in hexane to get the product as half white solid. (Yield: 93.4%, 0.86 g). $^1$HNMR (400 MHz, DMSO $d_6$) δ(ppm): 9.9 (s, 1H), 7.79 (d, *J* = 8 Hz, 1H), 7.60-7.56 (m, 2H), 7.39-7.36 (m, 1H), 7.31 (d, *J* = 8 Hz, 2H), 7.18-7.14 (m, 1H), 7.06 (d, *J* = 8 Hz, 2H), 5.8 (s, 2H). MS (ESI): mass calcd. for $C_{16}H_{12}ClNO$, 269.73; *m/z* found, 270.1 $(M+H)^+$.

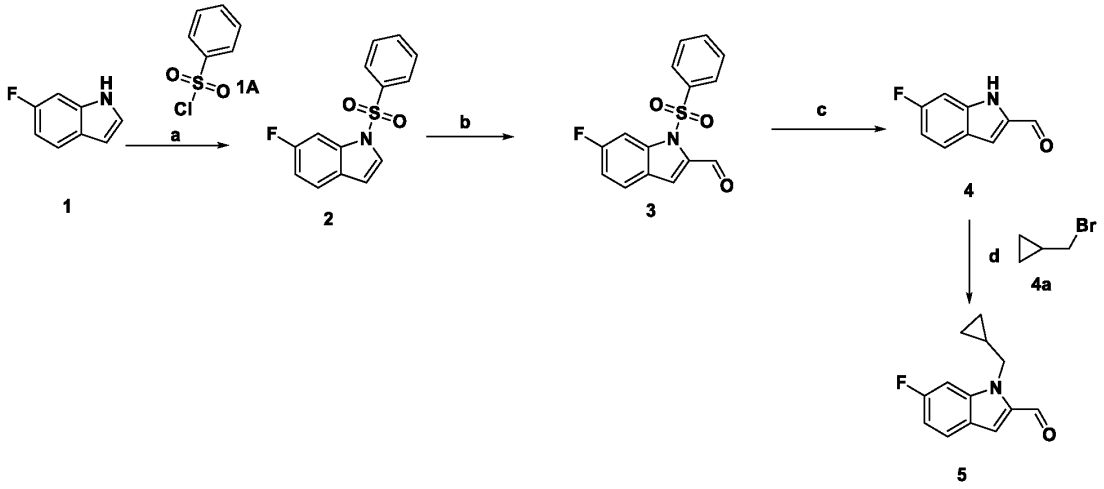
**Synthesis of 1-(cyclopropylmethyl)-1H-indole-2-carbaldehyde (Intermediate for Examples-1, 2, 4, 6, 7, 38, 62, 72, 76, 78, 79, 85 and 86)**




1 2

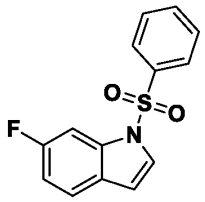
**[000305]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 1 g, 6.89 mmol) in DMF (20 mL), were added potassium carbonate (2.8 g, 20.67 mmol) and (bromomethyl)cyclopropane (0.68 mL, 7.58 mmol) at room temperature. The reaction mixture was stirred at room temperature for 12 h. The reaction mixture was diluted with water and extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using 3-7% ethyl acetate in hexane to afford the 1-(cyclopropylmethyl)-1H-indole-2-carbaldehyde as yellow solid (1 g, 76% Yield). $^1$HNMR (400 MHz, DMSO $d_6$) δ(ppm): 9.88 (s, 1H), 7.75 (d, $J$ = 8 Hz, 1H), 7.64 (d, $J$ = 8 Hz, 1H), 7.46 (s, 1H), 7.41-7.37 (m, 1H), 7.16-7.12 (m, 1H), 4.45 (d, $J$ = 8 Hz, 2H), 1.24-1.14 (m, 1H), 0.39-0.35 (m, 4H). MS (ESI): mass calcd. for $C_{13}H_{13}NO$, 199.1; *m/z* found, 200.1 $(M+H)^+$.

**Synthesisof1-(cyclopropylmethyl)-6-fluoro-1H-indole-2-carbaldehyde (Intermediate for Example-65)**




1 2 3

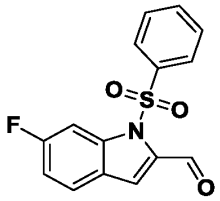
**Step 1: Preparation of 6-fluoro-1-(phenylsulfonyl)-1H-indole (2)**



2

**[000306]** To a solution of sodium hydride (0.88 g, 22.2 mmol) in DMF (50 mL) was added solution of 6-fluoro-1H-indole (**1**, 3.0 g, 22.2 mmol) in DMF at 0°C, dropwise over 15 min. Benzenesulfonyl chloride in DMF (2.86 mL, 22.2 mmol) was added at 0°C and stirred for 2 h at room temperature under $N_2$ atmosphere. To the reaction mixture was added ice cold water (50 mL), then filtered off the precipitate and washed with ice cold water to obtain white solid. (6.0 g, yield 98.19 %).

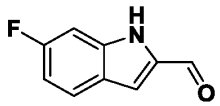
**Step 2: preparation 6-fluoro-1-(phenylsulfonyl)-1H-indole-2-carbaldehyde (3)**



3

**[000307]** To a solution of 6-fluoro-1-(phenylsulfonyl)-1H-indole (**2**, 6.0 g, 22.0 mmol) in dry THF (60 mL) was added lithium diisopropylamide 2M in THF (10.9 mL g, 22.0 mmol) at -78 °C and stirred for 5-8 min, followed by addition of dry DMF (2.5 mL, 33.0 mmol) at -78 °C and stirred for 10 min at -78 °C under $N_2$ atmosphere. To the reaction mixture was added aqueous ammonium chloride (20 mL), then extracted in to EtOAc. Organic layer was washed with saturated $NH_4Cl$ solution and brine, dried over sodium sulphate, filtered and concentrated under reduced pressure to obtain yellow solid (6.0 g, yield 90.90%). MS (ESI): *m/z* 304.2 $(M+H)^+$.

**Step 3: Preparation of 6-fluoro-1-(phenylsulfonyl)-1H-indole-2-carbaldehyde (4)**

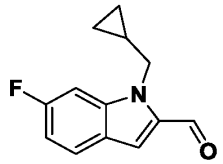


4

**[000308]** To the stirred solution of 6-Difluoro-1-(phenylsulfonyl)-1H-indole-2-carbaldehyde (**3**,1g, 3.3 mmol) in THF (50 mL), was added TBAF (1M in THF) (9.15 mL, 16.5mmol) at room temperature. The reaction mixture was stirred at room

temperature for 12 h. The reaction mixture was diluted with water and extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using 15-25% ethyl acetate in hexane to afford 6-fluoro-1-(phenylsulfonyl)-1H-indole-2-carbaldehyde as sticky solid (0.45 g, 90% Yield) MS (ESI): Mass calcd. for $C_9H_6FNO$, 163 m/z; found, 164 $(M+H)^+$.

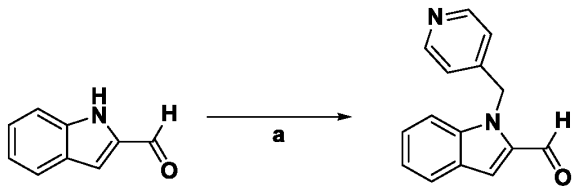
**Step 4: Preparation of1-(cyclopropylmethyl)-6-fluoro-1H-indole-2-carbaldehyde (5)**



**5**

**[000309]** To a stirred solution 6-fluoro-1H-indole-2-carbaldehyde (**4**, 0.5 g, 3.44 mmol) in DMF (10 mL), was added potassium carbonate (1.42 g, 10.3 mmol) followed by (bromomethyl)cyclopropane (0.84 g, 4.13 mmol) and the reaction mixture was stirred at same temperature for 4 h. The reaction mixture was quenched with water, extracted with ethyl acetate (30 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate, filtered and evaporated to get crude product. Crude residue was purified by gradient column chromatography using 10-15% ethyl acetate in hexane to get the product as half white solid. (Yield: 93.4%, 0.86 g). $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 9.81 (s, 1H), 7.69-7.66 (m, 1H), 7.25 (d, $J$ = 6.8 Hz, 1H), 7.07 (d, $J$ = 8 Hz, 1H), 6.97-6.91 (m, 1H), 4.43 (d, $J$ = 8 Hz, 2H), 1.32-1.25 (m, 1H), 0.5-0.45 (m, 2H), 0.42-0.38 (m, 2H). MS (ESI): mass calcd. for $C_{13}H_{12}FNO$, 217.09; *m/z* found, 218.0 $(M+H)^+$.

**Synthesis of 1-(pyridin-4-ylmethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-10)**

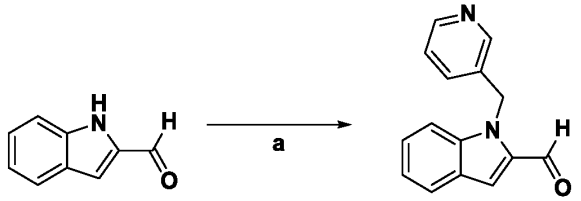



**1** **2**

**[000310]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 1 g, 6.89 mmol) in DMF (20 mL), were added cesium carbonate (6.7g, 20.68 mmol) and (4-(bromomethyl)pyridine (1.1 g, 6.89 mmol) at room temperature. The reaction mixture was refluxed at 80°C for 12 h. The reaction mixture was diluted with water and extracted

with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using 3-7% ethyl acetate in hexane to afford the 1-(pyridin-4-ylmethyl)-1H-indole-2-carbaldehyde as yellow solid (0.5 g, 31% Yield). $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): δ 9.92 (s, 1H), 8.54 (d, *J* = 8 Hz, 2H), 7.79 (d, *J* = 8 Hz, 1H), 7.67-7.64 (m, 1H), 7.56 (d, *J* =12 Hz, 2H), 7.37-7.33 (m, 1H), 7.22-7.19 (m, 1H), 6.88 (d, *J* = 8 Hz, 1H), 5.89 (s, 2H). MS (ESI): mass calcd. for $C_{15}H_{12}N_2O$, 236.09; *m/z* found, 237.0 $(M+H)^+$.

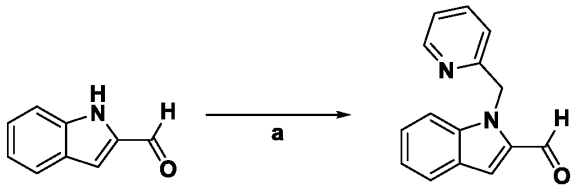
**Synthesis of 1-(pyridin-3-ylmethyl)-1H-indole-2-carbaldehyde (Intermediate for Examples-16, and 66)**




1 2

**[000311]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 1 g, 6.89 mmol) in DMF (20 mL), were added cesium carbonate (6.7g, 20.68 mmol) and 3-(chloromethyl)pyridine hydrochloride (1.1 g, 6.89 mmol) at room temperature. The reaction mixture was refluxed at 80°C for 12 h. The reaction mixture was diluted with water and extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using 3-7% ethyl acetate in hexane to afford the 1-(pyridin-3-ylmethyl)-1H-indole-2-carbaldehyde as yellow solid (0.4 g, 25% Yield). $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 9.92 (s, 1H), 8.41-8.38 (m, 2H), 7.80 (d, *J* = 8 Hz, 1H), 7.68 (d, *J* = 8.4 Hz, 1H ), 7.58 ( bs, 1H)), 7.42-7.38 (m, 2H), 7.28-7.25 (m, 1H), 7.18 (t, *J* = 16 Hz, 1H), 5.85 (s, 2H), MS (ESI): mass calcd. for $C_{15}H_{12}N_2O$, 236.27; *m/z* found, 237.1 $(M+H)^+$.

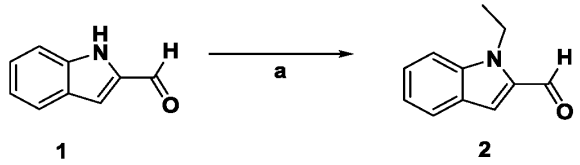
**Synthesis of 1-(pyridin-2-ylmethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-11 & 69)**




1 2

**[000312]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 1 g, 6.89 mmol) in DMF (20 mL), were added cesium carbonate (6.7g, 20.68 mmol) and 2-(bromomethyl)pyridine (1.1g, 6.89 mmol) at room temperature. The reaction mixture was refluxed at 80°C for 12 h. The reaction mixture was diluted with water and extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using 3-7% ethyl acetate in hexane to afford the 1-(pyridin-2-ylmethyl)-1H-indole-2-carbaldehyde as yellow solid (0.8 g, 50% Yield). $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 9.92 (s, 1H), 8.45 (d, $J$ = 4 Hz, 1H), 7.79 (d, $J$ = 8 Hz, 1H), 7.66 (m, 1H), 7.56 (d, $J$ = 12 Hz, 2H), 7.37-7.33 (m, 1H), 7.22-7.19 (m, 1H), 7.17-7.13 (m, 1H), 6.88 (d, $J$ = 8 Hz, 1H), 5.89 (s, 2H). MS (ESI): mass calcd. for $C_{16}H_{12}ClNO$, 269.73; *m/z* found, 270.1 $(M+H)^+$.

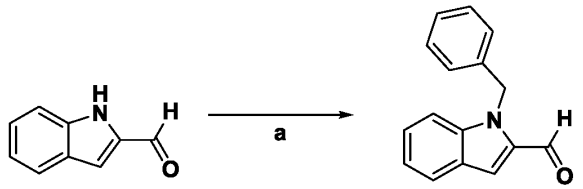
**Synthesis of 1-ethyl-1H-indole-2-carbaldehyde (Intermediate for Example-3)**




1 2

**[000313]** To a stirred solution 1H-indole-2-carbaldehyde (**1**, 1 g, 6.89 mmol) in DMF (15 mL), was added potassium carbonate (2.85 g, 20.6 mmol) followed by iodoethane (0.6 mL, 7.58 mmol) and the reaction mixture was stirred at same temperature for 4 h. Reaction mixture was poured into crushed ice, diluted with water and extracted with ethyl acetate. Organic layer was dried over anhydrous sodium sulfate evaporated under vacuum to give the crude. Crude was purified by flash column chromatography using ethyl acetate and hexane to obtain 1-ethyl-1H-indole-2-carbaldehyde as the viscous liquid. (Yield: 1g, 90%). $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 9.88 (s, 1H), 7.75 (d, $J$ = 8Hz, 1H), 7.61 (d, 1H, $J$ = 8 Hz, 1H), 7.44 (s, 1H), 7.41-7.37 (m, 1H), 7.16-7.12 (m, 1H), 4.58-4.52 (m, 2H), 1.26-1.23 (m, 3H). MS (ESI): mass calcd. for $C_{11}H_{11}NO$, 173.08; *m/z* found, 174.0 $(M+H)^+$.

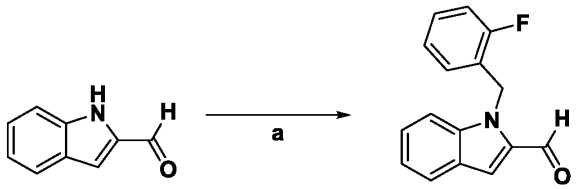
**Synthesis of 1-benzyl-1H-indole-2-carbaldehyde (Intermediate for Example-18)**




1 2

**[000314]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 1 g, 6.89 mmol) in DMF (20 mL), were added potassium carbonate (2.8 g, 20.68 mmol) and (bromomethyl)benzene (1.2 g, 7.58 mmol) at room temperature. The reaction mixture was stirred at room temperature for 12 h. The reaction mixture was diluted with water and extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to give the crude product. The crude residue was purified by gradient column chromatography using 3-7% ethyl acetate in hexane to afford the 1-benzyl-1H-indole-2-carbaldehyde as viscous liquid (0.5 g, 33% Yield). $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 9.92 (s, 1H), 7.78 (d, $J$ = 8 Hz, 1H), 7.58 (d, $J$ = 8 Hz, 1H), 7.54 (s, 1H), 7.38-7.35 (m, 1H), 7.26-7.20 (m, 2H), 7.18-7.13 (m, 2H), 7.05 (d, $J$ = 4 Hz, 2H), 5.82 (s, 2H). MS (ESI): mass calcd. for $C_{16}H_{13}NO$, 235.10; *m/z* found, 236.1 $(M+H)^+$.

**Synthesis of 1-(2-fluorobenzyl)-1H-indole-2-carbaldehyde (Intermediate for Example-14)**

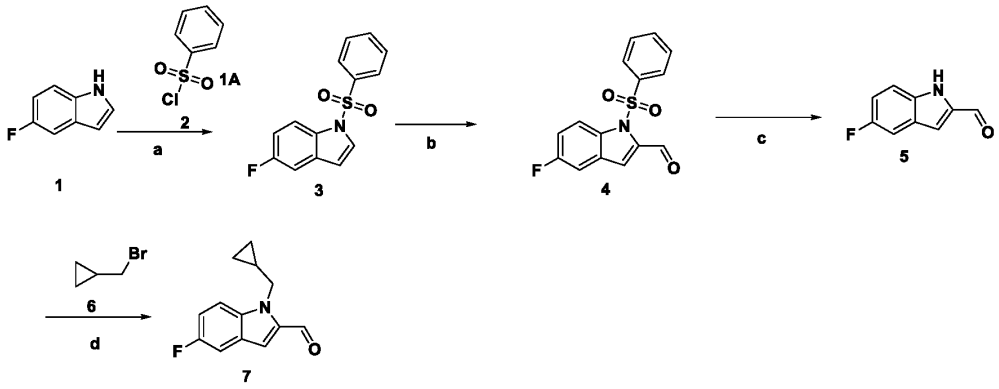



1 2

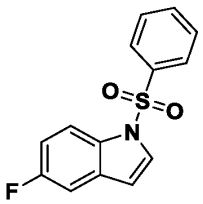
**[000315]** To a stirred solution 1H-indole-2-carbaldehyde (**1**, 1 g, 6.89 mmol) in DMF (15 mL), was added potassium carbonate (2.85 g, 20.6 mmol) followed by 1-(chloromethyl)-2-fluorobenzene (1.19 g, 8.26 mmol) and the reaction mixture was stirred at same temperature for 4 h. Reaction mixture was poured into crushed ice, diluted with water and extracted with ethyl acetate. Organic layer was dried over anhydrous sodium sulfate, evaporated under vacuum to give the crude. Crude was purified by flash column chromatography using ethyl acetate and hexane to afford the 1-(2-fluorobenzyl)-1H-indole-2-carbaldehyde as grey color solid (Yield:1.8g, 96.5%). $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 9.90 (s, 1H), 7.81 (d, $J$ = 8 Hz, 1H), 7.58-7.54 (m, 2H), 7.40-7.36 (m,

1H), 7.28-7.15 (m, 3H), 7.01-6.97 (m, 1H), 6.55-6.51 (m, 1H), 5.88 (s, 2H). MS (ESI): mass calcd. for $C_{16}H_{12}FNO$, 253.09; *m/z* found, 254.0 $(M+H)^+$.

**Synthesis of 1-(cyclopropylmethyl)-5-fluoro-1H-indole-2-carbaldehyde (Intermediate for Examples-9, 64 & 75)**



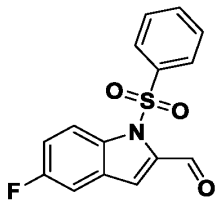

**Step 1: Preparation of 5-fluoro-1-(phenylsulfonyl)-1H-indole (3)**



**3**

**[000316]** To a solution of sodium hydride (0.06 g, 15 mmol) in DMF (10 mL) was added a solution of 5-fluoro-1H-indole (**1**, 0.2 g, 15 mmol) in DMF at 0 °C, drop wise over 15 min. followed by addition of a solution of benzenesulfonyl chloride (**2**, 0.26 g, 15 mmol) in DMF at 0 °C and the reaction mixture was stirred for 2 h at room temperature under $N_2$ atmosphere. To the reaction mixture was added ice cold water (50 mL), then the precipitate was filtered off and washed with ice cold water to obtain brown solid. (0.25 g, 62.50 % Yield). MS (ESI) *m/z* 275.0 $(M+H)^+$.

**Step 2: Preparation of 5-fluoro-1-(phenylsulfonyl)-1H-indole-2-carbaldehyde (4)**

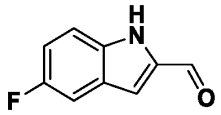


**4**

**[000317]** To a solution of 5-fluoro-1-(phenylsulfonyl)-1H-indole (**3**, 0.250 g, 1.0 mmol) in dry THF (50 mL) was added lithium diisopropylamide 1M in THF (0.5 mL g,

1.0 mmol) at -78 °C, followed by addition of dry DMF (0.11 mL, 1.5 mmol) at -78 °C and stirred for 10 min at -78 °C under $N_2$ atmosphere. To the reaction mixture was added aqueous ammonium chloride (20 mL) and extracted with EtOAc. Organic layer was washed with saturated $NH_4Cl$ solution and brine, dried over sodium sulphate, filtered and concentrated under reduced pressure to obtain brown solid. (0.150 g, 54.54 % Yield). MS (ESI) *m/z* 304.1 $(M+H)^+$.

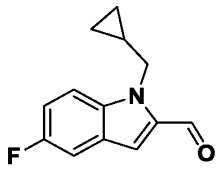
**Step 3: Preparation of 5-fluoro-1H-indole-2-carbaldehyde (5)**



**5**

**[000318]** To the stirred solution of 5-fluoro-1-(phenylsulfonyl)-1H-indole-2-carbaldehyde (**4**, 1.85 g, 6.105 mmol) in THF (50 mL), was added TBAF (1M in THF) (9.15 mL, 9.158 mmol) at room temperature. The reaction mixture was stirred at room temperature for 12 h. The reaction mixture was diluted with water and extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using 15-25% ethyl acetate in hexane to afford the 5-fluoro-1H-indole-2-carbaldehyde as sticky solid (0.65 g, 65% Yield) MS (ESI): Mass calcd. for $C_9H_6FNO$, 163.15; m/z found, 162.0 $[M-H]^-$.

**Step 4: Preparation of 1-(cyclopropylmethyl)-5-fluoro-1H-indole-2-carbaldehyde (7)**

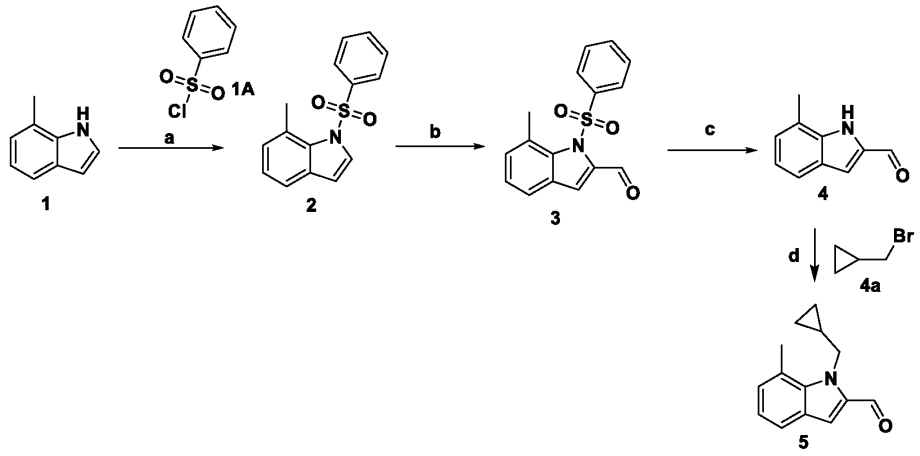


**7**

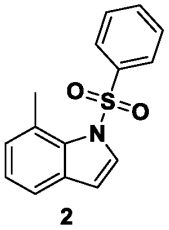
**[000319]** To the stirred solution of 5-fluoro-1H-indole-2-carbaldehyde (**5**, 0.65 g, 3.98 mmol) in DMF (50 mL), were added potassium carbonate (1.64 g, 11.94 mmol) and (bromomethyl)cyclopropane (**6**, 0.58 mL, 5.98 mmol) at room temperature. The reaction mixture was stirred at room temperature for 12 h. The reaction mixture was diluted with water and extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulphate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using 3-7% ethyl acetate

in hexane to afford the 1-(cyclopropylmethyl)-5-fluoro-1H-indole-2-carbaldehyde as sticky solid (0.76 g, 88% Yield). $^1$HNMR (400 MHz, DMSO-d6): δ 9.90 (s, 1H), 7.73-7.69 (m, 1H), 7.55-7.52 (m, 1H), 7.44 (s, 1H), 7.29-7.24 (m, 1H), 4.50 (d, *J* = 7.2 Hz, 2H), 1.23-1.16 (m, 1H), 0.41-0.32 (m, 4H). MS (ESI): Mass calcd. for $C_{13}H_{12}FNO$, 217.24: m/z found, 218.1 $[M+H]^+$.

**Synthesis of 1-(cyclopropylmethyl)-7-methyl-1H-indole-2-carbaldehyde (Intermediate for Example-8 & 84)**

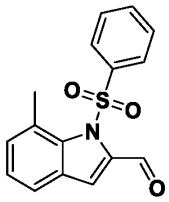



**Step 1: preparation of 7-methyl-1-(phenylsulfonyl)-1H-indole (2)**




**[000320]** To a solution of sodium hydride (0.92 g, 23 mmol) in DMF (10 mL) was added solution of 7-methyl-1H-indole (**1**, 3.0 g, 23 mmol) in DMF at 0 °C, dropwise over 15 min. Benzenesulfonyl chloride in DMF (2.96 mL, 23 mmol) was added at 0°C and stirred for 2 h at room temperature under $N_2$ atmosphere. To the reaction mixture was added ice cold water (50 mL), then filtered off the precipitate and washed with ice cold water to obtain brown solid (5.30 g, 85.50%). MS (ESI) *m/z* 272.1 $(M+H)^+$.

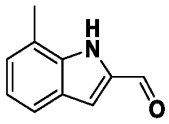
**Step 2: preparation 7-methyl-1-(phenylsulfonyl)-1H-indole-2-carbaldehyde (3)**



3

**[000321]** To a solution of 7-methyl-1-(phenylsulfonyl)-1H-indole (**2**, 5.3 g, 20.0 mmol) in dry THF (50 mL) was added lithium diisopropylamide 1.5M in THF (13.0 mL, 20.0 mmol) at -78 °C and stirred for 5-8 min, followed by addition of dry DMF (2.33 mL, 30.0 mmol) at -78 °C and stirred for 10 min at -78 °C under $N_2$ atmosphere. To the reaction mixture was added aqueous ammonium chloride (20 mL), then extracted in to EtOAc. Organic layer was washed with saturated $NH_4Cl$ solution and brine, dried over sodium sulphate, filtered and concentrated under reduced pressure to obtain red viscous liquid (5.0 g, 85.47 %). MS (ESI) *m/z* 300.2 $(M+H)^+$.

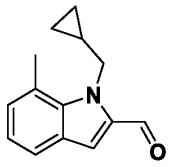
**Step 3: Preparation of 7-methyl-1H-indole-2-carbaldehyde (4)**



4

**[000322]** To the stirred solution of 7-methyl-1-(phenylsulfonyl)-1H-indole-2-carbaldehyde (**3**, 2 g, 6.68 mmol) in THF (20 mL), was added 1M solution of tetrabutyl ammonium fluoride in THF (10 mL, 10.2 mmol) and stirred at 80 °C for 1h. Reaction mixture was cooled to room temperature, added water (20 mL) and extracted with EtOAc (100 mL). Organic layer was dried over anhydrous $Na_2SO_4$ and evaporated under vacuum. Crude was purified by column chromatography using 15-20% EtOAc in Hexane to afford the product as brown solid. (0.8 g, 58% Yield). MS (ESI): Mass calcd. for $C_{10}H_9NO$, 159.07; *m/z* found 160.1 $(M+H)^+$.

**Step 4: 1-(cyclopropylmethyl)-7-methyl-1H-indole-2-carbaldehyde (5)**

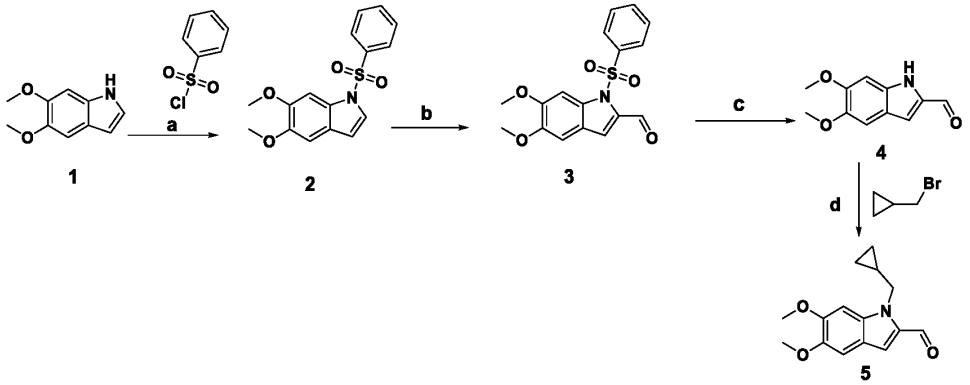


5

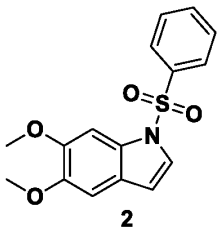
**[000323]** To the stirred solution of 7-methyl-1H-indole-2-carbaldehyde (**4**, 0.85 g, 5.345 mmol) in DMF (20 mL), were added potassium carbonate (2.21 g, 16.035 mmol)

and (bromomethyl)cyclopropane (4a, 0.78 mL, 8.018 mmol) at room temperature. The reaction mixture was stirred at room temperature for 12 h. The reaction mixture was diluted with water and extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using 3-7% ethyl acetate in hexane to afford the 1-(cyclopropylmethyl)-7-methyl-1H-indole-2-carbaldehyde as sticky solid (0.52 g, 45% Yield). $^1$HNMR (400 MHz, $CDCl_3$) δ(ppm): 9.82 (s, 1H), 7.58 (d, *J* = 8.0 Hz, 1H), 7.26 (s, 1H), 7.13 (d , *J* = 6.8 Hz, 1H), 6.26 (m, 1H), 4.83 (d , *J* = 6.8 Hz, 2H), 2.77 (s , 3H), 1.15-1.10 (m, 1H), 0.41-0.33 (m, 4H). MS (ESI): Mass calcd. for $C_{14}H_{15}NO$, 213.28; m/z found, 214.1 $[M+H]^+$.

**Synthesis of 1-(cyclopropylmethyl)-5,6-dimethoxy-1H-indole-2-carbaldehyde (Intermediate for Example-17)**

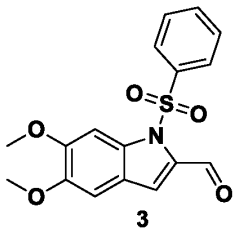



**Step 1: Preparation of 5,6-dimethoxy-1-(phenylsulfonyl)-1H-indole (2)**




**[000324]** To a solution of sodium hydride (0.56 g, 14 mmol) in DMF (50 mL) was added solution of 5,6-dimethoxy-1H-indole (**1**, 2.5 g, 14 mmol) in DMF at 0°C, dropwise over 15 min. Benzenesulfonyl chloride (1.8 mL, 14 mmol) in DMF was added at 0°C and stirred for 2 h at room temperature under $N_2$ atmosphere. To the reaction mixture was added ice cold water (50 mL), then filtered off the precipitate and washed with ice cold water to obtain white solid. (4.20 g, 93.95 % Yield). MS (ESI): mass calcd. for $C_{16}H_{15}NO_4S$, 317.07; m/z found, 318.1 $[M+H]^+$.

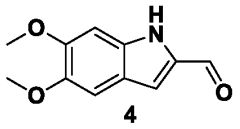
**Step 2: preparation 5,6-dimethoxy-1-(phenylsulfonyl)-1H-indole-2-carbaldehyde (3)**



3

**[000325]** To a solution of 5,6-dimethoxy-1-(phenylsulfonyl)-1H-indole (**2**, 4.2 g, 13.2 mmol) in dry THF (60 mL) was added lithium diisopropylamide 2M in THF (8.8 mL g, 13.2 mmol) at -78 °C and stirred for 5-8 min, followed by addition of dry DMF (1.54 mL, 20.0 mmol) at -78 °C and stirred for 10 min at -78 °C under $N_2$ atmosphere. To the reaction mixture was added aqueous ammonium chloride (20 mL), then extracted in to EtOAc. Organic layer was washed with saturated $NH_4Cl$ solution and brine, dried over sodium sulphate, filtered and concentrated under reduced pressure to obtain yellow solid (3.5 g, 78.26% Yield). MS (ESI): mass calcd. for $C_{17}H_{15}NO_5S$, 345.07; m/z found, 346.1 $[M+H]^+$.

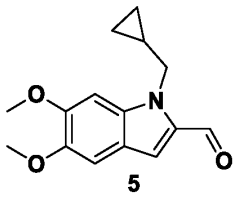
**Step 3: Preparation of 5,6-dimethoxy-1H-indole-2-carbaldehyde (4)**



4

**[000326]** To the stirred solution of 5,6-dimethoxy-1-(phenylsulfonyl)-1H-indole-2-carbaldehyde (**3**, 2 g, 5.5 mmol) in THF (50 mL), was added TBAF (1M in THF) (8.8 mL, 8.2 mmol) at room temperature. The reaction mixture was stirred at room temperature for 12 h. The reaction mixture was diluted with water and extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using 5-10% ethyl acetate in hexane to afford desired compound as gummy solid (1 g, 88.6% Yield). MS (ESI): mass calcd. for $C_{11}H_{11}NO3$, 205.07; m/z found, 206.1 $[M+H]^+$.

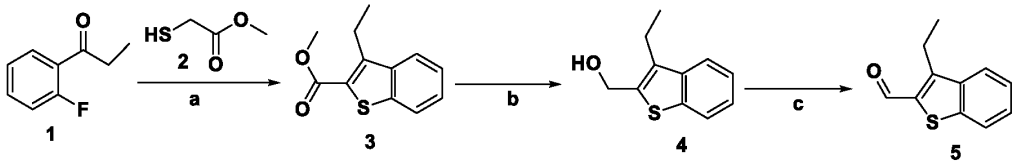
**Step 4: Preparation of 1-(cyclopropylmethyl)-5,6-dimethoxy-1H-indole-2-carbaldehyde (5)**



5

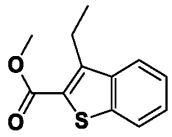
**[000327]** To the stirred solution of 5,6-dimethoxy-1H-indole-2-carbaldehyde (**4**, 1 g, 4.8 mmol) in DMF (20 mL), were added potassium carbonate (1.9 g, 14 mmol) and (bromomethyl)cyclopropane ( 0.7 g, 5.7 mmol) at room temperature. The reaction mixture was stirred at room temperature for 12 h. The reaction mixture was diluted with water and extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using 10% ethyl acetate in hexane to afford title compound as yellow solid (0.7 g, 56.3% Yield). $^1$HNMR (400 MHz, $CDCl_3$) δ(ppm): 9.71 (s, 1H), 7.12 (s, 1H), 7.06 (s, 1H), 6.78 (s, 1H), 4.47 (d, $J$ = 6.4 Hz, 2H), 3.99 (s, 3H), 3.93 (s, 3H), 1.30-1.25 (m, 1H), 0.49-0.41 (m, 4H). MS (ESI): Mass calcd. for $C_{15}H_{17}NO_3$, 259.31; m/z found, 260.2 $[M+H]^+$.

**Synthesis of Ethylbenzo[b]thiophene-2-carbaldehyde (Intermediate for Example-12)**



1 3 4 5

**Step 1: Methyl 3-ethylbenzo[b]thiophene-2-carboxylate (3)**

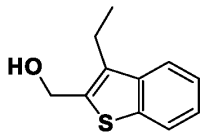


3

**[000328]** To a suspension of NaH (60% in oil, 0.17g, 4.27mmol) in THF (10 mL) was added methyl 2-mercaptoacetate (**2**, 0.41 g, 3.94 mmol) at room temperature and stirred at same temperature for 30 min. To the reaction was added solution of 1-(2-fluorophenyl)propan-1-one (**1**, 0.5 g, 3.28 mmol) in THF and allowed to reflux for 16 h (reaction condition **a**). Completion of the reaction was monitored by LCMS The reaction mixture was cooled to room temperature, diluted with EtOAc and washed with 1N NaOH and water. Organic layer was washed, dried over sodium sulphate, filtered and

concentrated under reduced pressure. The crude mixture was purified by column chromatography to obtain the product as brown oil (Yield: 0.4 g, 57.14 %). MS (ESI): mass calcd. for $C_{12}H_{12}O_2S$, 220.06; m/z found, 221.1 $(M+H)^+$.

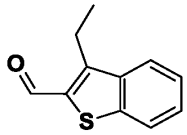
**Step 2: (3-Ethylbenzo[b]thiophen-2-yl) methanol (4)**



**4**

**[000329]** To a solution of methyl 3-ethylbenzo[b]thiophene-2-carboxylate (**3**, 0.5 g, 1.81 mmol) in THF (10 mL) was added 1M solution of LAH in THF (2.7 mL, 2.72 mmol) drop wise at 0°C. The reaction mixture was stirred for 2 h at $25^0$C (Reaction condition **b**). The reaction was monitored by TLC (1:1, EtOAc: hexane). The reaction mixture was quenched with saturated $NH_4Cl$ (10 mL), filtered through celite and extracted with EtOAc. Organic layer was washed with brine, dried over sodium sulphate, filtered and concentrated under reduced pressure. The crude mixture was purified by column chromatography to obtain the product as yellow oil (Yield: 0.24 g, 70.58 %). MS (ESI): mass calcd. for $C_{11}H_{12}OS$, 192.06; m/z found, 192.9 $(M+H)^+$.

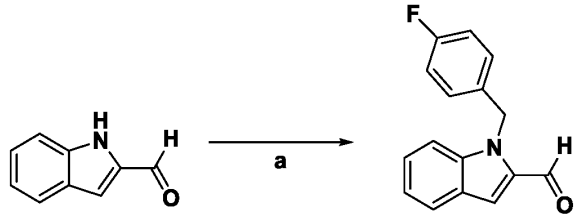
**Step 3: Ethylbenzo[b]thiophene-2-carbaldehyde (5)**



**5**

**[000330]** To a solution of (3-ethylbenzo[b]thiophen-2-yl) methanol (**4**, 0.24 g, 1.25 mmol) in DCM (10 mL) was added Dess martin periodinane (0.79 g, 1.87 mmol) at 0°C (Reaction condition **c**). The reaction mixture was stirred for 2 h at $25^0$C. The reaction was monitored by TLC (1:1, EtOAc: hexane). The reaction mixture was quenched with saturated $NaHCO_3$ (10 mL), filtered through celite and extracted with DCM. Organic layer was washed with brine, dried over sodium sulphate, filtered and concentrated under reduced pressure. The crude mixture was purified by column chromatography to obtain the product as yellow solid. (Yield: 0.18 g, 81.8 %).$^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 10.33 (s, 1H), 8.08-8.02 (m, 2H), 7.56 (t, $J$ = 6.8 Hz, 1H), 7.49 (t, $J$ = 7.6 Hz, 1H), 3.33-3.30 (m, 2H), 1.29 (t, $J$ = 7.2 Hz, 3H). MS (ESI): mass calcd. for $C_{11}H_{10}OS$, 190.05; m/z found, 191.0 $(M+H)^+$.

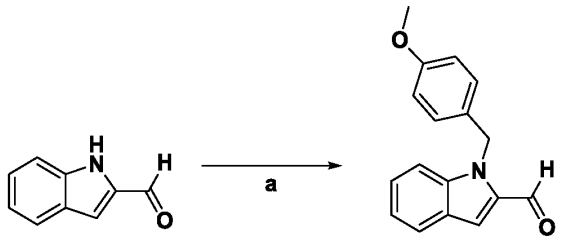
**Synthesis of 1-(4-fluorobenzyl)-1H-indole-2-carbaldehyde (Intermediate for Example-15)**




1 2

**[000331]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 0.5 g, 3.44 mmol) in DMF (20 mL), were added potassium carbonate (1.42 g, 10.34 mmol) and 1-(bromomethyl)-4-fluorobenzene (0.716 g, 3.79 mmol) at room temperature. The reaction mixture was stirred at room temperature for 12 h. The reaction mixture was diluted with water and extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to give the crude product. The crude residue was purified by gradient column chromatography using 3-7% ethyl acetate in hexane to afford the 1-(4-fluorobenzyl)-1H-indole-2-carbaldehyde as solid (0.8 g, 97% Yield). $^1$HNMR (400 MHz, $CDCl_3$) δ(ppm): 9.89 (s, 1H), 7.77 (d, $J$ = 8.4 Hz, 1H), 7.41 (m, 2H), 7.39 (s, 1H), 7.25-7.17 (m, 1H), 7.10-7.00 (m, 2H), 6.95 (t, $J$ = 8 Hz, 2H), 5.79 (s, 2H): MS (ESI): Mass calcd. for $C_{16}H_{12}FNO$, 253.28; m/z found, 254.0 $[M+H]^+$.

**Synthesis of 1-(4-methoxybenzyl)-1H-indole-2-carbaldehyde (Intermediate for Example-19)**

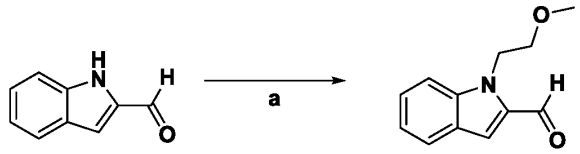



1 2

**[000332]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 0.5 g, 3.44 mmol) in DMF (20 mL), were added potassium carbonate (1.42 g, 10.34 mmol) and 1-(bromomethyl)-4-methoxybenzene (0.76 g, 3.79 mmol) at room temperature. The reaction mixture was stirred at room temperature for 12 h. The reaction mixture was diluted with water and extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude

product. The crude residue was purified by gradient column chromatography using 3-7% ethyl acetate in hexane to afford the 1-(4-methoxybenzyl)-1H-indole-2-carbaldehyde as solid (0.4 g, 43% Yield). $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 9.75 (s, 1H), 7.93 (d, *J* = 8.4 Hz, 1H), 7.82 (m, 2H), 7.36 (s, 1H), 7.25-7.17 (m, 1H), 7.12 (m, 2H), 6.83 (t, *J* = 8 Hz, 2H), 5.81 (s, 2H), 3.81 (s, 3H), MS (ESI): Mass calcd. for C17H15NO2, 265.31; m/z found, 266.1 $[M+H]^+$.

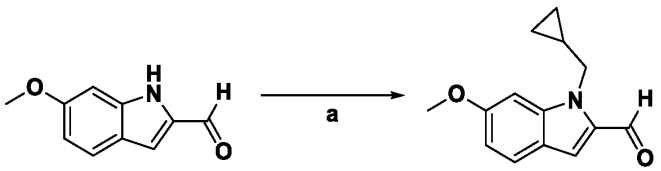
**Synthesis of 1-(2-methoxyethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-20)**




1 2

**[000333]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 0.80 g, 5.5 mmol) in *N, N*-dimethylformamide (20 mL), cesium carbonate (5.36 g, 90.5mmol) and 1-bromo-2-methoxyethane (0.62 mL, 6.7 mmol) were added at room temperature. The reaction mixture was stirred at 60 °C for 1 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (20 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 20% ethyl acetate in hexanes as eluent, to afford the 1-(2-methoxyethyl)-1H-indole-2-carbaldehyde as pale yellow oil. Yield: 3.0 g (42%). $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 9.89 (s, 1H), 7.75 (d, *J* = 7.9 Hz, 1H), 7.63 (d, *J* = 8.5 Hz, 1H), 7.47 (s, 1H), 7.39 (t, *J* = 7.2 Hz, 1H), 7.15 (t, *J* = 7.5 Hz, 1H), 4.70 (t, *J* = 5.44 Hz, 2H), 3.61 (t, *J* = 5.3 Hz, 2H), 3.15 (s, 3H).

**Synthesis of 1-(cyclopropylmethyl)-6-methoxy-1H-indole-2-carbaldehyde (Intermediate for Example-23)**

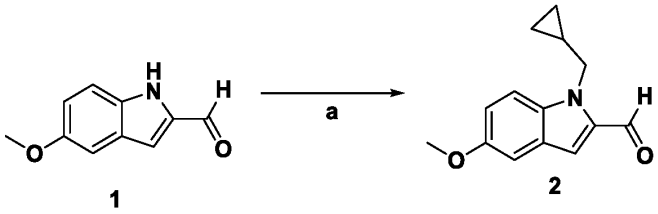



1 2

**[000334]** To the stirred solution of 6-methoxy-1H-indole-2-carbaldehyde (**1**, 2.0 g, 11.4 mmol) in *N, N*-dimethylformamide (20 mL), cesium carbonate (11.14 g, 34.3 mmol) and (bromomethyl)cyclopropane (1.41 mL, 13.7 mmol) were added at room temperature.

The reaction mixture was stirred at room temperature for 2 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (20 mL x 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 20% ethyl acetate in hexanes as eluent, to afford the 1-(cyclopropylmethyl)-6-methoxy-1H-indole-2-carbaldehyde as pale yellow oil. Yield: 0.80 g (31%), MS (ESI) 229.13; *m/z* found 230.1 $[M+H]^{+1}$.

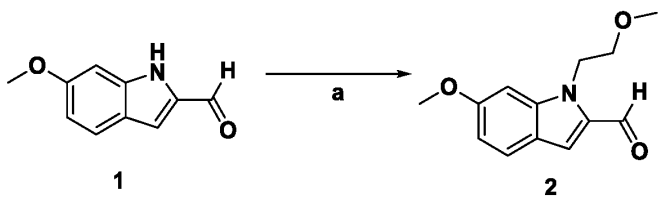
**Synthesis of 1-(cyclopropylmethyl)-5-methoxy-1H-indole-2-carbaldehyde (Intermediate for Example-60)**




1 2

**[000335]** To the stirred solution of 6-methoxy-1H-indole-2-carbaldehyde (**1**, 2.0 g, 11.4 mmol) in *N, N*-dimethylformamide (20 mL), cesium carbonate (11.14 g, 34.3 mmol) and (bromomethyl)cyclopropane (1.41 mL, 13.7 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 2 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (20 mL x 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 20% ethyl acetate in hexanes as eluent, to afford the 1-(cyclopropylmethyl)-5-methoxy-1H-indole-2-carbaldehyde as pale yellow oil. Yield: 0.79 g (30%), MS (ESI) 229.13; *m/z* found 230.1 $[M+H]^{+1}$.

**Synthesis of 6-methoxy-1-(2-methoxyethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-21)**

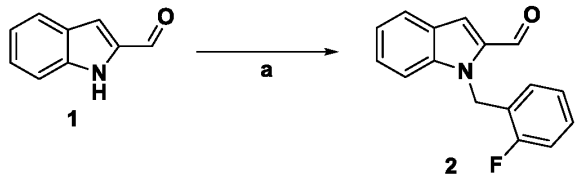



1 2

**[000336]** To the stirred solution of 6-methoxy-1H-indole-2-carbaldehyde (**1**, 0.80 g, 4.57 mmol) in *N, N*-dimethylformamide (3 mL), cesium carbonate (4.4 g, 13.7 mmol)

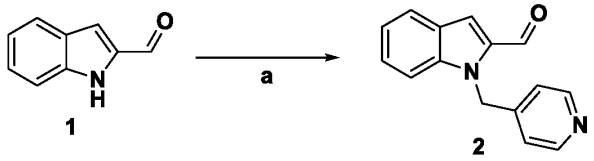
and 1-bromo-2-methoxyethane (0.51 mL, 5.48 mmol) were added at room temperature. The reaction mixture was stirred at 60 °C for 16 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (200 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by combiFlash using 12 g RediSep and 20% ethyl acetate in hexane as eluent to afford the 6-methoxy-1-(2-methoxyethyl)-1H-indole-2-carbaldehyde as off white semi solid. Yield: 0.60 g, 60%, MS (ESI): 235; *m/z* found 234.10 $[M-1]^{-1}$.

**Synthesis of 1-(2-fluorobenzyl)-1H-indole-2-carbaldehyde (Intermediate for Example-70)**




**[000337]** To a solution of 1H-indole-2-carbaldehyde (**1**, 2.0 g, 13.7 mmol) in *N, N*-dimethylformamide (15 mL), potassium carbonate (5.6 g, 41.1 mmol) and 1-(bromomethyl)-2-fluorobenzene (3.1 g, 16.5 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 4 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (20 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 20% ethyl acetate in hexane as eluent to afford 1-(2-fluorobenzyl)-1H-indole-2-carbaldehyde as yellow solid.

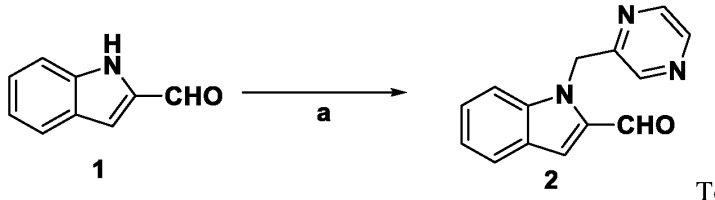
**Synthesis of 1-(pyridin-4-ylmethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-11 and 71)**




**[000338]** To a solution of 1H-indole-2-carbaldehyde (**1**, 1.50 g, 10.3 mmol) in *N, N*-dimethylformamide (40 mL), potassium carbonate (4.2 g, 31.0 mmol) and 4-(bromomethyl)pyridine hydrobromide (3.1 g, 12.4 mmol) were added at room temperature. The reaction mixture was stirred at 60 °C for 4 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (20 mL

× 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 10% ethyl acetate in hexane as eluent to afford 1-(pyridin-4-ylmethyl)-1H-indole-2-carbaldehyde as yellow oil. Yield: 1.0 g (40%). MS (ESI) 236.01; *m/z* found 2.37.12.1 $[M+H]^{+1}$.

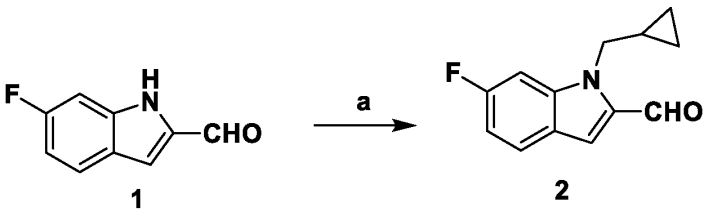
**Synthesis of 1-(pyrazin-2-ylmethyl)-1H-indole-2-carbaldehyde) (Intermediate for Example-25)**




1 2

**[000339]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 1.0 g, 6.81 mmol) in *N, N*-dimethylformamide (20.0 mL), cesium carbonate (11.2 g, 34.4 mmol) and 2-(chloromethyl)pyrazine (1.0 g, 8.27 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (30 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 10% ethyl acetate in hexane as eluent to afford 1-(pyrazin-2-ylmethyl)-1H-indole-2-carbaldehyde as yellow solid (**3a**). Yield: 0.80 g (48%). MS (ESI): 237.26, *m/z* found 238.12 $[M+H]^{+1}$.

**Synthesis of 1-(cyclopropylmethyl)-6-fluoro-1H-indole-2-carbaldehyde (Intermediate for Example-28)**

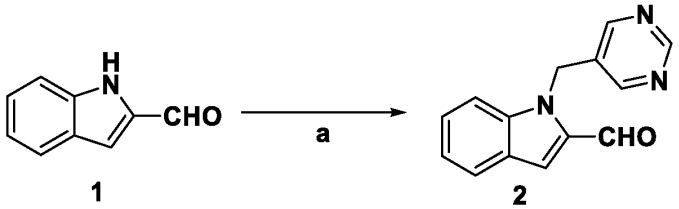



1 2

**[000340]** To the stirred solution of 6-fluoro-1H-indole-2-carbaldehyde (**1**, 1.5 g, 9.2 mmol) in *N, N*-dimethylformamide (30.0 mL), cesium carbonate (8.9 g, 27.6 mmol) and (bromomethyl)cyclopropane (1.47 g, 11.2 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction,

the reaction mixture was diluted with water and extracted with ethyl acetate (30 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 10% ethyl acetate in hexane as eluent to afford 1-(cyclopropylmethyl)-6-fluoro-1H-indole-2-carbaldehyde as yellow solid. Yield: 1.5 g (75%). MS (ESI): 217.24, *m/z* found 218.34 $[M+H]^{+1}$.

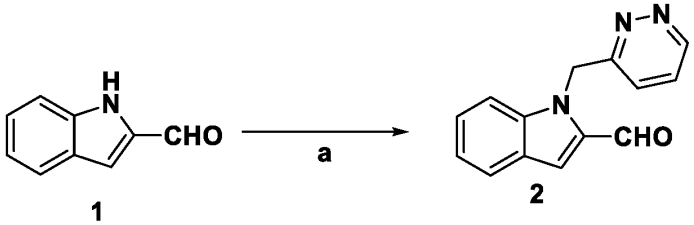
**Synthesis of 1-(pyrimidin-5-ylmethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-29)**




1 2

**[000341]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 1.20 g, 8.27 mmol) in *N, N*-dimethylformamide (20.0 mL), cesium carbonate (8.08 g, 24.01 mmol) and 5-(chloromethyl)pyrimidine (1.0 g, 8.27 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (30 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 10% ethyl acetate in hexane as eluent to afford 1-(pyrimidin-5-ylmethyl)-1H-indole-2-carbaldehyde as brown solid. Yield: 1.60 g (81%). MS (ESI): 237.26, *m/z* found 238.32 $[M+H]^{+1}$.

**Synthesis of 1-(pyridazin-3-ylmethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-30)**

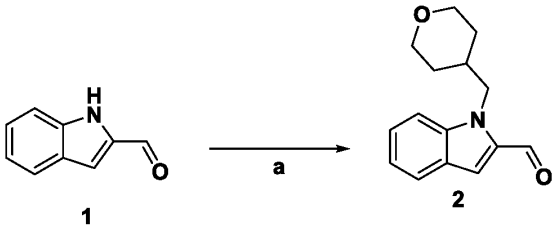



1 2

**[000342]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 1.0 g, 6.81 mmol) in *N, N*-dimethylformamide (10.0 mL), cesium carbonate (6.7 g, 20.01 mmol) and 3-(chloromethyl)pyridazine (1.0 g, 7.10 mmol) were added at room temperature. The

reaction mixture was stirred at room temperature for 3 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (30 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 10% ethyl acetate in hexane as eluent to afford 1-(pyridazin-3-ylmethyl)-1H-indole-2-carbaldehyde as brown solid (**3a**). Yield: 1.40 g (Crude). MS (ESI): 237.26, *m/z* found 238.42 $[M+H]^{+1}$.

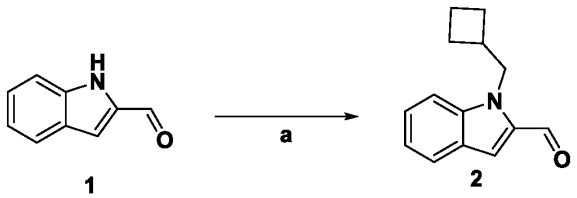
**Synthesis of 1-((tetrahydro-2H-pyran-4-yl)methyl)-1H-indole-2-carbaldehyde) (Intermediate for Example-40)**




1 2

**[000343]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 1.0 g, 6.89 mmol) in *N, N*-dimethylformamide (10 mL), cesium carbonate (6.70 g, 20.68 mmol) and 4-(bromomethyl)tetrahydro-2H-pyran (1.48 g, 8.27 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 1 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (200 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 5% ethyl acetate in hexane as eluent to afford 1-((tetrahydro-2H-pyran-4-yl)methyl)-1H-indole-2-carbaldehyde as white solid). Yield: 0.80 g (48%). MS (ESI);243.13 *m/z* found: 244.17$[M+H]^{+1}$.

**Synthesis of 1-(cyclobutylmethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-41)**



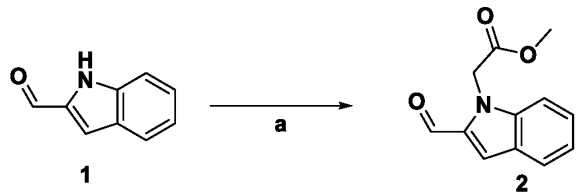

1 2

**[000344]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 0.50 g, 3.44 mmol) in *N, N*-dimethylformamide (10 mL), cesium carbonate (3.3 g, 10.34 mmol) and

cyclobutylmethyl methanesulfonate (**2b**, 0.84 g, 5.17 mmol) were added at room temperature. The reaction mixture was stirred at 100 °C for 1 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (200 mL x 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 5% ethyl acetate in hexane as eluent to afford 1-(cyclobutylmethyl)-1H-indole-2-carbaldehyde as oily liquid (**3a**). Yield: 0.650 g (88%). MS (ESI); 213.12 *m/z* found no ionization.

**[000345]** $^1$HNMR (400 MHz, DMSO-d6): δ 9.89 (s, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.46 (s, 1H), 7.40 (t, *J* = 7.2 Hz, 1H), 7.14 (t, *J* = 7.2 Hz, 1H), 4.60 (d, *J* = 6.8 Hz, 2H), 2.72 (t, *J* = 6.4 Hz, 1H), 1.87-1.71 (m, 6H).

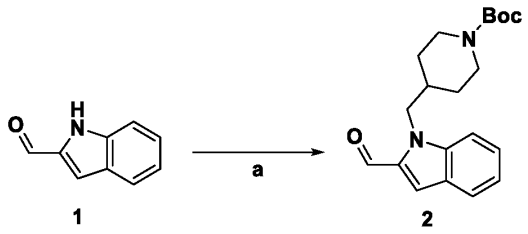
**Synthesis of methyl 2-(2-formyl-1H-indol-1-yl)acetate Intermediate for (Example-42)**




1 2

**[000346]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 1.5 g, 10.3 mmol) in *N, N*-dimethylformamide (40.0 mL), cesium carbonate (10.0 g, 30.9 mmol) and methyl 2-chloroacetate (**2a**, 1.35 g, 12.4 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 1 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (100 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 40 g RediSep and 5% ethyl acetate in hexane as eluent to afford methyl 2-(2-formyl-1H-indol-1-yl)acetate (**3a**) as yellow oil. Yield: 1.2 g (53%). MS (ESI): 217.04, *m/z* found 218.18 $[M+H]^{+1}$.

**Synthesis of tert-butyl 4-((2-formyl-1H-indol-1-yl)methyl)piperidine-1-carboxylate (Intermediate for Example-43)**

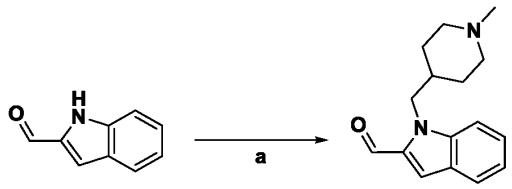



1 2

**[000347]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 1.0 g, 6.81 mmol) in *N, N*-dimethylformamide (10 mL), cesium carbonate (6.72 g, 20.0 mmol) and tert-butyl 4-(bromomethyl)piperidine-1-carboxylate (2.29 g, 8.11 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (50 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 20% ethyl acetate in hexane as eluent to afford the tert-butyl 4-((2-formyl-1H-indol-1-yl)methyl)piperidine-1-carboxylate as yellow solid.Yield: 2.0 g (86%). MS (ESI): found no ionization.

**[000348]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 9.89 (s, 1H), 7.77-7.76 (m, 1H), 7.70-7.68 (m, 1H), 7.49 (s, 1H), 7.40-7.38 (m, 1H), 7.17-7.14 (m, 1H), 4.44 (d, $J$ = 7.41 Hz, 2H), 3.89 (s, 2H), 1.99-1.89 (m, 1H), 1.37 (s, 13H) 1.18-1.13 (m, 2H).

**Synthesis of 1-((1-methylpiperidin-4-yl)methyl)-1H-indole-2-carbaldehyde (Intermediate for Example- 45)**

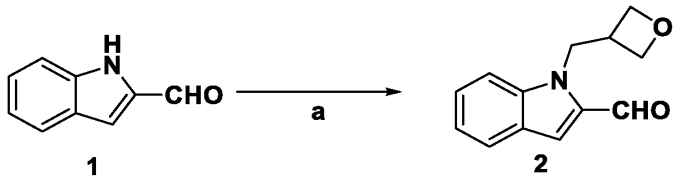



1 2

**[000349]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 1.0 g, 6.81 mmol) in *N, N*-dimethylformamide (10 mL), cesium carbonate (6.72 g, 20.0 mmol) and tert-butyl 4 4-(bromomethyl)-1-methylpiperidine (2.2 g, 8 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (50 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 20% ethyl acetate in hexane as

eluent to afford the 1-((1-methylpiperidin-4-yl)methyl)-1H-indole-2-carbaldehyde as solid. Yield: 2.2 g (85%).

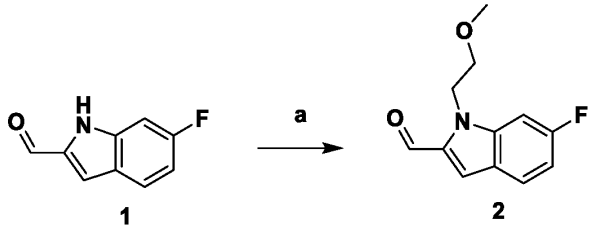
**Synthesis of 1-(oxetan-3-ylmethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-44)**




1 2

**[000350]** To the stirred solution of 1H-indole-2-carbaldehyde (1, 0.700 g, 4.82 mmol) in *N, N*-dimethylformamide (10.0 mL), cesium carbonate (4.7 g, 14.48 mmol) and (3-(chloromethyl)oxetane (0.562 g, 5.31 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 16 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (10 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 30% ethyl acetate in hexane as eluent to afford 1-(oxetan-3-ylmethyl)-1H-indole-2-carbaldehydeas yellow solid. Yield: 0.380 g (63%). MS (ESI): 215.09, *m/z* found 216.18 $[M+H]^{+1}$.

**Synthesis of 6-fluoro-1-(2-methoxyethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-52)**

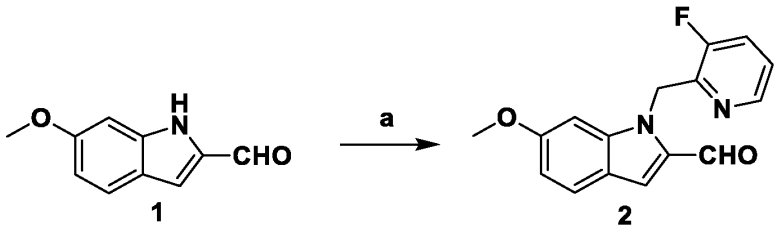



1 2

**[000351]** To the stirred solution of 6-fluoro-1H-indole-2-carbaldehyde (1, 0.90 g, 5.5 mmol) in *N, N*-dimethylformamide (20 mL), potassium carbonate (5.38 g, 16.5 mmol) and 1-bromo-2-methoxyethane (, 0.61 mL, 6.62 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (20 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 20% ethyl acetate in hexanes as eluent, to afford

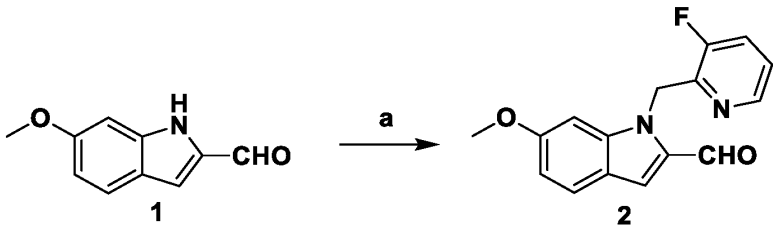
the 6-fluoro-1-(2-methoxyethyl)-1H-indole-2-carbaldehyde as sticky solid. Yield: 0.60 g (60%); MS (ESI) 221.09; *m/z* found 222.10 $[M+H]^{+1}$.

**Synthesis of 1-((3-fluoropyridin-2-yl)methyl)-6-methoxy-1H-indole-2-carbaldehyde (Intermediate for Example-26)**




**[000352]** To the stirred solution of 6-methoxy-1H-indole-2-carbaldehyde (**1**, 0.50 g, 2.85 mmol) in *N, N*-dimethylformamide (10.0 mL), cesium carbonate (2.7 g, 8.57 mmol) and 2-(chloromethyl)-3-fluoropyridine hydrochloride (0.452 g, 3.14 mmol) were added at room temperature. The reaction mixture was stirred at 60°C about 2 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (10 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 30% ethyl acetate in hexane as eluent to afford 1-((3-fluoropyridin-2-yl)methyl)-6-methoxy-1H-indole-2-carbaldehyde as solid Yield: 0.63 g (79%). MS (ESI): 284.10, *m/z* found 285.19 $[M+H]^{+1}$.

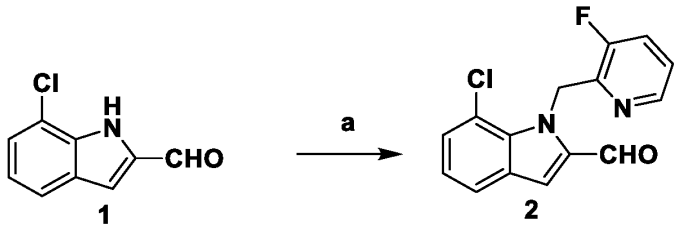
**Synthesis of 1-((3-fluoropyridin-2-yl)methyl)-6-methoxy-1H-indole-2-carbaldehyde (Intermediate for Example-33)**




**[000353]** To the stirred solution of 6-methoxy-1H-indole-2-carbaldehyde (**1**, 0.50 g, 2.85 mmol) in *N, N*-dimethylformamide (10.0 mL), cesium carbonate (2.7 g, 8.57 mmol) and 2-(chloromethyl)-3-fluoropyridine hydrochloride (0.45 g, 3.14 mmol) were added at room temperature. The reaction mixture was stirred at 60°C about 2 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (10 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 30% ethyl acetate in hexane as

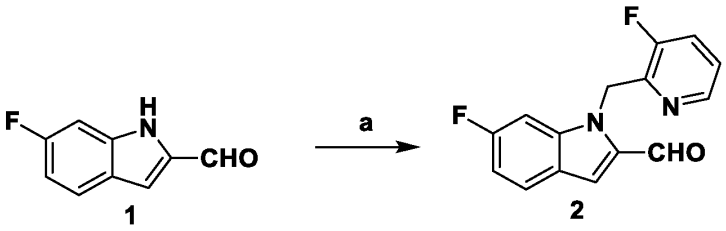
eluent to afford 1-((3-fluoropyridin-2-yl)methyl)-6-methoxy-1H-indole-2-carbaldehyde as yellow solid Yield: 0.66 g (81%). MS (ESI): 284.10, *m/z* found 285.19 $[M+H]^{+1}$.

**Synthesis of 7-chloro-1-((3-fluoropyridin-2-yl)methyl)-1H-indole-2carbaldehyde (Intermediate for Example-34)**




**[000354]** To the stirred solution of 7-chloro-1H-indole-2-carbaldehyde (**1**, 0.4 g, 2.23 mmol) in *N, N*-dimethylformamide (14.0 mL), cesium carbonate (2.1 g, 6.68 mmol) and 2-(chloromethyl)-3-fluoropyridine (0.39 g, 2.67 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (30 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 20% ethyl acetate in hexane as eluent to afford 7-chloro-1-((3-fluoropyridin-2-yl)methyl)-1H-indole-2-carbaldehyde as yellow oil. Yield: 0.30 g (46%). MS (ESI): 288.0, *m/z* found 289.01 $[M+H]^{+1}$.

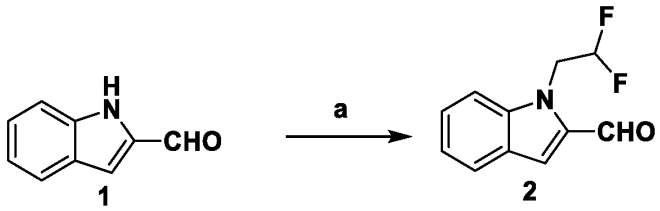
**Synthesis of 6-fluoro-1-((3-fluoropyridin-2-yl)methyl)-1H-indole-2-carbaldehyde (Intermediate for Example-35)**




**[000355]** To the stirred solution of 6-fluoro-1H-indole-2-carbaldehyde (**1**, 0.5 g, 3.06 mmol) in *N, N*-dimethylformamide (6.0 mL), cesium carbonate (2.99 g, 9.2 mmol) and 2-(chloromethyl)-3-fluoropyridine hydrochloride (0.53 g, 3.6 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (20 mL × 2). The combined organic extracts were washed with brine, dried

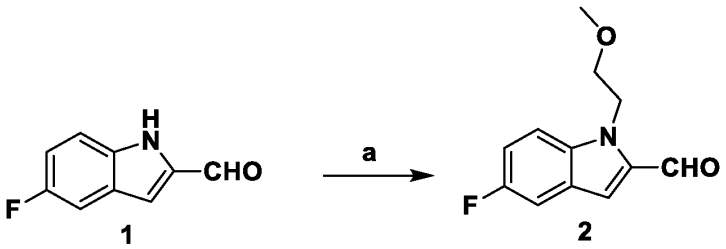
over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 5% ethyl acetate in hexane as eluent to afford 6-fluoro-1-((3-fluoropyridin-2-yl)methyl)-1H-indole-2-carbaldehyde as yellow solid. Yield: 0.72 g (86%). MS (ESI): 272.12, *m/z* found no ionization. $^1$HNMR (400 MHz, DMSO-d6): δ 9.80 (s, 1H), 8.15 (d, *J* = 4.5 Hz, 1H), 7.85-7.82 (m, 1H), 7.73 (t, *J* = 9.1 Hz, 1H), 7.54 (s, 1H), 7.50 (d, *J* = 10.6 Hz, 1H), 7.35-7.28 (m, 1H), 7.05-7.02 (m, 1H), 5.97 (s, 2H).

**Synthesis of 1-(2,2-difluoroethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-47)**



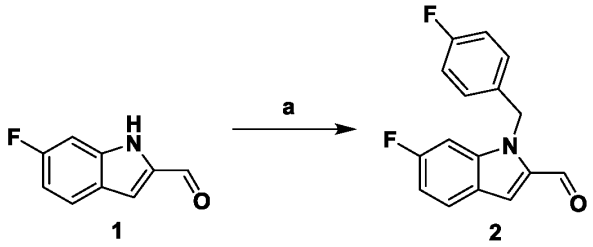

**[000356]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 1.0 g, 6.81 mmol) in *N, N*-dimethylformamide (10.0 mL), cesium carbonate (6.7 g, 20.01 mmol) and 2-bromo-1,1-difluoroethane (1.78 mL, 20.6 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (30 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 10% ethyl acetate in hexane as eluent to afford 1-(2,2-difluoroethyl)-1H-indole-2-carbaldehyde as brown solid. Yield: 0.91 g (63%). MS (ESI): 209.26, *m/z* found no ionization. $^1$HNMR (400 MHz, DMSO-d6): δ 9.98 (s, 1H), 7.82 (d, *J* = 8.1 Hz, 1H), 7.79 (d, *J* = 7.9 Hz, 1H), 7.57 (s, 1H), 7.45 (t, *J* = 8.0 Hz, 1H), 7.20 (t, *J* = 7.6 Hz, 1H), 6.33 (t, *J* = 54.3 Hz, 1H), 5.09-5.01 (m, 2H).

**Synthesis of 5-fluoro-1-(2-methoxyethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-48)**



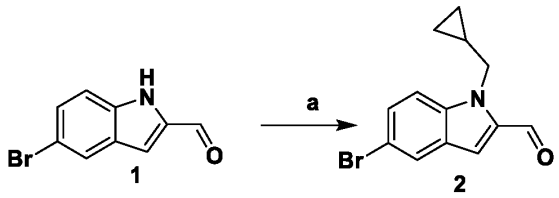
**[000357]** To the stirred solution of 5-fluoro-1H-indole-2-carbaldehyde (**1**, 0.5 g, 3.06 mmol) in *N, N*-dimethylformamide (20.0 mL), cesium carbonate (3.0 g, 9.18 mmol) and 1-bromo-2-methoxyethane (**2a**, 0.34 mL, 3.68 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 2 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (20 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 20% ethyl acetate in hexane as eluent to afford 5-fluoro-1-(2-methoxyethyl)-1H-indole-2-carbaldehyde as brown oil. Yield: 0.58 g (85%), MS (ESI) 221.0; *m/z* found 221.95 $[M+H]^{+1}$.

**Synthesis of 6-fluoro-1-(4-fluorobenzyl)-1H-indole-2-carbaldehyde (Intermediate for Example-49)**



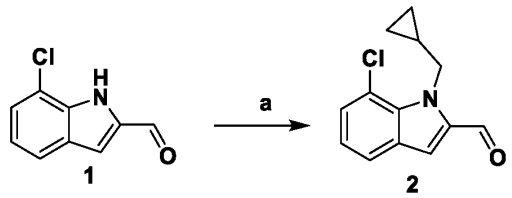

**[000358]** To the stirred solution of 6-fluoro-1H-indole-2-carbaldehyde (1, 1.00 g, 6.13 mmol) in *N, N*-dimethylformamide (10 mL), cesium carbonate (5.98 g, 18.4 mmol) and 1-(bromomethyl)-4-fluorobenzene (1.38 g, 7.36 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 1 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (200 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 5% ethyl acetate in hexane as eluent to afford 6-fluoro-1-(4-fluorobenzyl)-1H-indole-2-carbaldehyde as off white solid. Yield: 1.20 g (75%). MS (ESI); 271.08 *m/z* found: 272.19.

**Synthesis of 5-bromo-1-(cyclopropylmethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-67)**



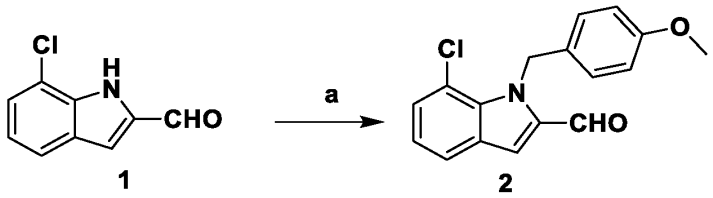

**[000359]** To the stirred solution of 5-bromo-1H-indole-2-carbaldehyde (1, 5 g, 32.9 mmol) in *N, N*-dimethylformamide (60 mL), cesium carbonate (29.5g, 90.5mmol) and (bromomethyl)cyclopropane (4.8 mL, 36.2 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (200 mL x 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by combi flash using 12 g Redisep and 20% ethyl acetate in hexane to afford the 5-bromo-1-(cyclopropylmethyl)-1H-indole-2-carbaldehyde as solid. Yield: 3.5 g (55%). MS (ESI): 278.06; *m/z* found 279.19.

**Synthesis of 1-(cyclopropylmethyl)-7-chloro-1H-indole-2-carbaldehyde (Intermediate for Example-57)**




**[000360]** To the stirred solution of 7-chloro-1H-indole-2-carbaldehyde (1, 5.4 g, 30.9 mmol) in *N, N*-dimethylformamide (60 mL), cesium carbonate (29.5g, 90.5mmol) and (bromomethyl)cyclopropane (4.8 mL, 36.2 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (200 mL x 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by combi flash using 12 g Redisep and 20% ethyl acetate in hexane to afford the 1-(cyclopropylmethyl)-7-chloro-1H-indole-2- carbaldehyde as sticky solid. Yield: 3.0 g (42%). $^1$HNMR (400 MHz, DMSO-d6): δ(ppm): 9.92 (s, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.62 (s, 1H) 7.47 (d, *J* = 8.0 Hz, 1H), 7.16 (t, *J* = 7.6 Hz, 1H), 4.80 (d, *J* = 6.92 Hz, 2H), 1.26 (m, 1H), 0.42-0.34 (m, 4H). MS (ESI): 233.06; *m/z* found 234.19.

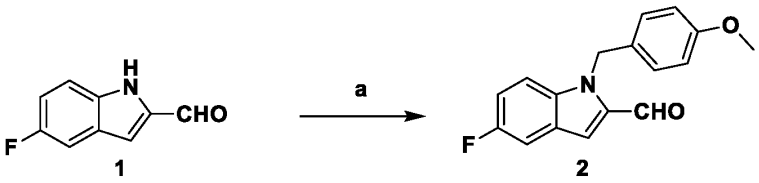
**Synthesis of 7-chloro-1-(4-methoxybenzyl)-1H-indole-2-carbaldehyde (Intermediate for Example-39)**




1 2

**[000361]** To the stirred solution of 7-chloro-1H-indole-2-carbaldehyde, 0.5 g, 2.78 mmol) in *N, N*-dimethylformamide (10.0 mL), cesium carbonate (2.7 g, 8.35 mmol) and 1-(chloromethyl)-4-methoxybenzene (0.52 g, 3.34 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (30 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 10% ethyl acetate in hexane as eluent to afford 7-chloro-1-(4-methoxybenzyl)-1H-indole-2-carbaldehyde as yellow oil. Yield: 0.40 g (47%). MS (ESI): 299.0, *m/z* found 300.19 $[M+H]^{+1}$.

**Synthesis of 5-fluoro-1-(4-methoxybenzyl)-1H-indole-2-carbaldehyde (Intermediate for Example-46)**

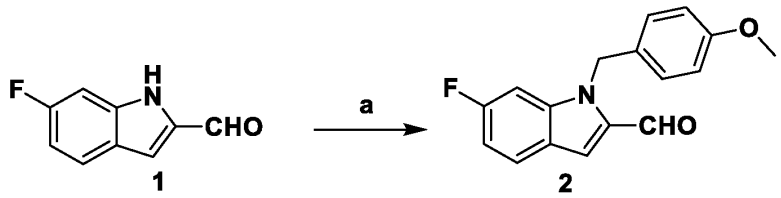



1 2

**[000362]** To the stirred solution of 5-fluoro-1H-indole-2-carbaldehyde (1, 0.5 g, 3.06 mmol) in *N, N*-dimethylformamide (20.0 mL), cesium carbonate (3.0 g, 9.18 mmol) and 1-(chloromethyl)-4-(methoxymethyl)benzene (0.72 mL, 3.68 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 2 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (25 mL x 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 20% ethyl acetate in hexane as eluent to afford 5-fluoro-1-(4-methoxybenzyl)-1H-indole-2-carbaldehyde as yellow oil. Yield: 0.52 g (60%). MS (ESI): 283.06; *m/z* found no ionization. $^1$HNMR (400 MHz,

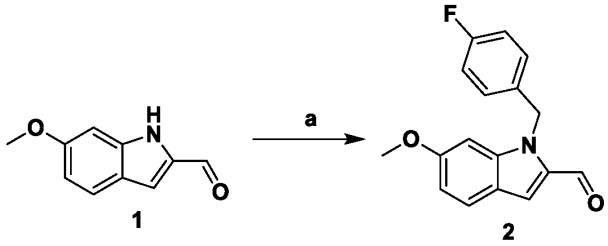
DMSO-d6): δ 9.95 (s, 1H), 7.74 (d, *J* = 6.28 Hz, 1H), 7.70 (d, *J* = 4.28 Hz, 1H), 7.52 (s, 1H), 7.30-7.27 (m, 1H), 7.08 (d, *J* = 13.5 Hz, 2H), 6.82 (d, *J* = 8.7 Hz, 2H), 5.76 (s, 2H), 3.67 (s, 3H).

**Synthesis of 6-fluoro-1-(4-methoxybenzyl)-1H-indole-2-carbaldehyde (Intermediate for Example-50)**




**[000363]** To the stirred solution of 6-fluoro-1H-indole-2-carbaldehyde ( 0.5 g, 3.06 mmol) in *N, N*-dimethylformamide (20.0 mL), cesium carbonate (3.0 g, 9.18 mmol) and 1-bromo-2-methoxyethane ( 0.34 mL, 3.68 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 2 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (20 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 20% ethyl acetate in hexane as eluent to afford 6-fluoro-1-(4-methoxybenzyl)-1H-indole-2-carbaldehyde as brown oil. Yield: 0.51 g (58%), MS (ESI) 283.1; *m/z* found 284.22 $[M+H]^{+1}$.

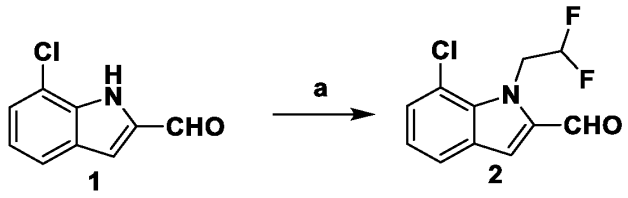
**Synthesis of 1-(4-fluorobenzyl)-6-methoxy-1H-indole-2-carbaldehyde (Intermediate for Example-51)**




**[000364]** To the stirred solution of 6-methoxy-1H-indole-2-carbaldehyde (, 0.70 g, 5.5 mmol) in *N, N*-dimethylformamide (10 mL), cesium carbonate (5.31 g, 16.3 mmol) and 1-(bromomethyl)-4-fluorobenzene (1.22 g, 5.6 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 1 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (200 mL × 2). The combined organic extracts were washed with brine, dried over

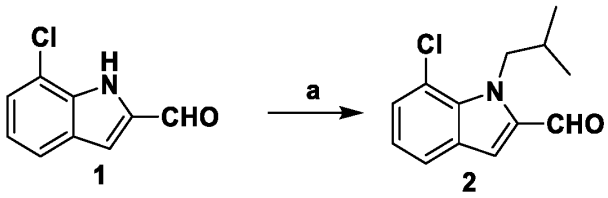
anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 5% ethyl acetate in hexane as eluent to afford 1-(4-fluorobenzyl)-6-methoxy-1H-indole-2-carbaldehyde as yellow solid. Yield: 1.0 g (90%). MS (ESI);283.1 *m/z* found: 284.18.

**Synthesis of 7-chloro-1-(2,2-difluoroethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-56)**




**[000365]** To the stirred solution of 7-chloro-1H-indole-2-carbaldehyde (0.9 g, 5.0 mmol) in *N, N*-dimethylformamide (20.0 mL), cesium carbonate (4.9 g, 15 mmol) and 2-bromo-1,1-difluoroethane (0.868 g, 6.0 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (30 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated to afford **7**-chloro-1-(2,2-difluoroethyl)-1H-indole-2-carbaldehyde. Yield: 1.46 g (Crude). MS (ESI): 243.03, *m/z* found 244.00$[M+H]^{+1}$.

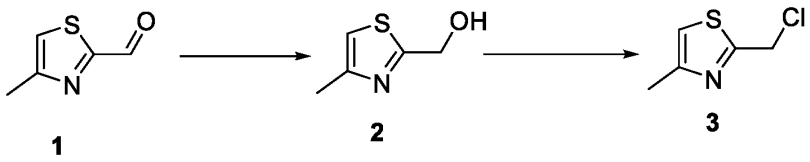
**Synthesis of 7-chloro-1-isobutyl-1H-indole-2-carbaldehyde (Intermediate for Example-55)**



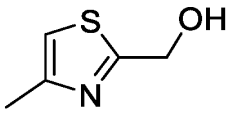

**[000366]** To the stirred solution of 7-chloro-1H-indole-2-carbaldehyde (0.7 g, 3.90 mmol) in *N, N*-dimethylformamide (20.0 mL), cesium carbonate (3.8 g, 11.69 mmol) and 1-bromo-2-methylpropane (0.53 g, 3.90 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (30 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 5% ethyl acetate in hexane as eluent to afford 7-

chloro-1-isobutyl-1H-indole-2-carbaldehyde as yellow oil. Yield: 0.50 g (54%). MS (ESI): 235.71, *m/z* found 236.62 $[M+H]^{+1}$.

**Synthesis of2-(chloromethyl)-4-methylthiazole (Intermediate for Example -59)**

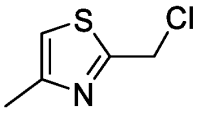



**Step A: (4-methylthiazol-2-yl)methanol**



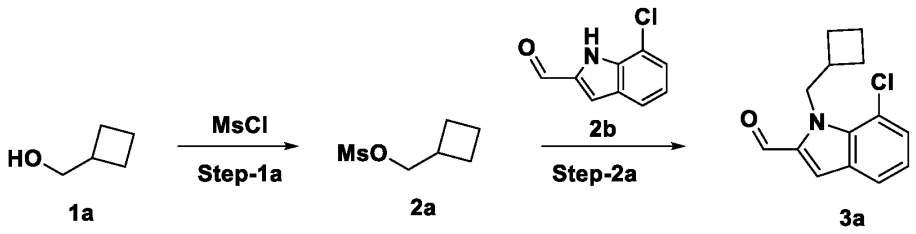

**[000367]** To the stirred solution of 4-methylthiazole-2-carbaldehyde (**1**, 1.0 g, 7 mmol) in MeOH (30 mL) at 0 °C, was added sodium borohydrate (0.52 g, 14 mmol) lot wise. The reaction mixture was stirred at room temperature for 2h. The reaction mixture was diluted with water (15 mL) and extracted with EtOAc (2 X 25 mL). Organic layer was washed with brine (15mL) solution, dried over anhydrous $Na_2SO_4$ and evaporated. The crude residue was purified by gradient column chromatography using 40-60% EtOAc in Hexane to afford the product as pale yellow gummy. (0.9g, 90%, Yield). MS (ESI): mass calcd.for $C_5H_7NOS$, 129.02; *m/z* found 130.1 $(M+H)^+$.

**Step B: 2-(chloromethyl)-4-methylthiazole**



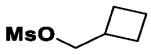

**[000368]** To a stirred solution of (4-methylthiazol-2-yl)methanol (**2**, 0.9 g, 6.97 mmol) in DCM (5 mL), was added $SOCl_2$ (0.83 mL, 11 mmol) drop wise at 0 °C and the reaction mixture was stirred at room temperature for 1 h. The reaction mixture was neutralized using cold $NaHCO_3$ (5 mL) solution and extracted with DCM (2 X 25 mL). Organic layer was washed with brine (5mL) solution, dried over anhydrous $Na_2SO_4$ and evaporated to afford the product as yellow oil. (1 g). MS (ESI): mass calcd.for $C_5H_6ClNS$ , 146.99; *m/z* found 148.1 $(M+H)^+$.

**Synthesis of 7-chloro-1-(cyclobutylmethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-53)**



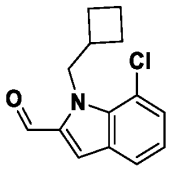

1a 2a 3a

**Step -1a: preparation of cyclobutylmethyl methanesulfonate (2a)**



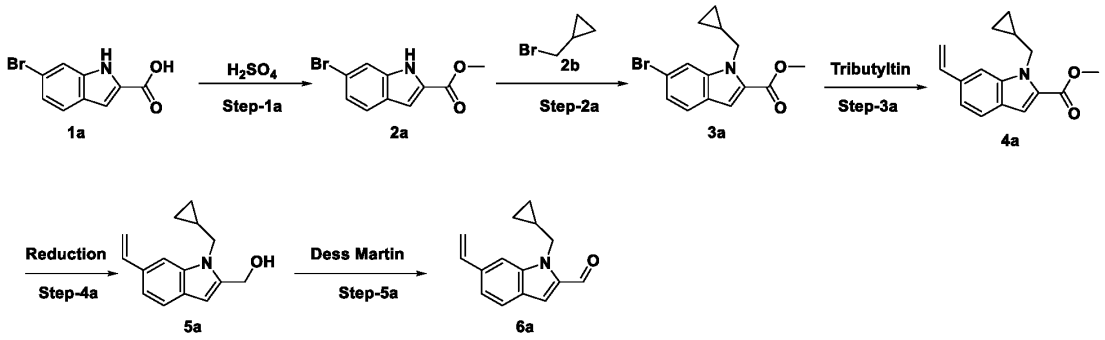

**[000369]** To the stirred solution of cyclobutylmethanol (**1a**, 2.00 g, 23.2 mmol) in dichloromethane (20 mL), triethylamine (6.50 mL, 46.5 mmol) and *N,N*-dimethylaminopyridine (0.28 g, 2.3 mmol) were added at room temperature, mesyl chloride (2.27 mL, 27.9 mmol) was added at 0 °C. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, reaction mixture was diluted with water and extracted with dichloromethane (20 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g Redisep and 10% ethyl acetate in hexanes as eluent, to afford the cyclobutylmethyl methanesulfonate as colorless oil (**2a**). Yield: 2.50 g (66%); MS (ESI) 164.05; *m/z* found no ionization. $^1$HNMR (400 MHz, DMSO-d6): δ(ppm): 4.16 (d, *J* = 6.76 Hz, 2H), 3.16 (s, 3H), 2.67-2.60 (m, 1H), 2.05-1.98 (m, 2H), 1.94-1.76 (m, 4H).

**Step-2a: Synthesis of 7-chloro-1-(cyclobutylmethyl)-1H-indole-2-carbaldehyde (3a)**

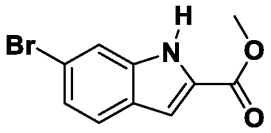



**[000370]** To the stirred solution of 7-chloro-1H-indole-2-carbaldehyde (**2b**, 0.90 g, 5.0 mmol) in *N, N*-dimethylformamide (10 mL), cesium carbonate (4.90 g, 15.1 mmol) and cyclobutylmethyl methanesulfonate (**2a**, 0.98 g, 6.0 mmol) were added at room temperature. The reaction mixture was stirred at 60 °C for 3 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (20 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g Redisep and 20% ethyl acetate in hexanes as eluent, to afford the 7-chloro-1-(cyclobutylmethyl)-1H-indole-2-carbaldehyde as pale yellow sticky solid (**3a**). Yield: 0.32 g (26%); MS (ESI) 247.08; *m/z* found 248.10 $[M+H]^{+1}$.

**Synthesis of 1-(cyclopropylmethyl)-6-vinyl-1H-indole-2-carbaldehyde (Intermediate for Example-61)**

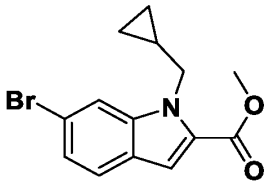



**Step-1a preparation of methyl-6-bromo-1H-indole-2-carboxylate (2a)**




**[000371]** To the stirred solution of 6-bromo-1H-indole-2-carboxylic acid (**1a**, 5.0 g, 20.83 mmol) in methanol (50.0 mL), sulphuric acid (9 mL, 1.8 vol) was added at 0 °C. The reaction mixture was stirred at 80 °C for 12 h. After completion of reaction, the reaction mixture was quenched with ice and precipitated solid was filtered and washed with water (100 mL × 2). The compound obtained was dried under vacuum. The crude was purified by CombiFlash using 40 g RediSep and 10% ethyl acetate in hexane as eluent to afford methyl-6-bromo-1H-indole-2-carboxylate as white solid (**2a**). Yield: 4.5 g (86%). MS (ESI): 252.99 *m/z* found 253.99 $[M+H]^{+1}$.

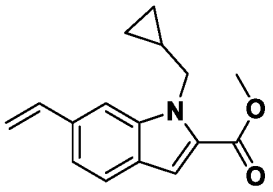
**Step-2a:preparation of methyl 6-bromo-1-(cyclopropylmethyl)-1H-indole-2-carboxylate (3a)**




**[000372]** To the stirred solution of 1H-indole-2-carbaldehyde (**2a**, 4.5 g, 17.85 mmol) in *N, N*-dimethylformamide (40 mL), cesium carbonate (17.4 g, 53.27 mmol) and (bromomethyl)cyclopropane (**2b**, 2.8 g, 21.42 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 2 h. After completion of

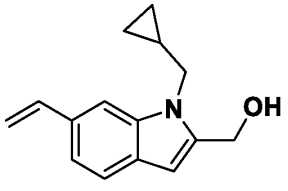
reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (30 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 10% ethyl acetate in hexane as eluent to afford methyl-6-bromo-1-(cyclopropylmethyl)-1H-indole-2-carboxylate as white solid (**3a**). Yield: 4.0 g (74%). MS (ESI): 307.18, *m/z* found 308.04 $[M+H]^{+1}$.

**Step-3a: preparation of methyl-1-(cyclopropylmethyl)-6-vinyl-1H-indole-2-carboxylate (4a)**



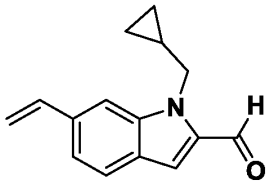

**[000373]** To the stirred solution of methyl-6-bromo-1-(cyclopropylmethyl)-1H-indole-2-carboxylate (**3a**, 4.0 g, 13.02 mmol) in *N, N*-dimethylformamide (40.0 mL), lithium chloride (0.656 g, 15.63 mmol) and tributyl vinyl tin (4.9 g, 15.63 mmol) were added at room temperature. Argon was purged for15 min, tetrakis(triphenylphosphine) palladium (0) (0.75 g, 0.65 mmol) was added at room temperature. The reaction mixture was stirred at 90 °C for 4 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (40 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 40 g RediSep and 5%-10% ethyl acetate in hexane as eluent to afford methyl 1-(cyclopropylmethyl)-6-vinyl-1H-indole-2-carboxylate as brown solid (**4a**). Yield: 3.1 g (92%). MS (ESI): 255.13, *m/z* found 256.11 $[M+H]^{+1}$.

**Step-4a: preparation of (1-(cyclopropylmethyl)-6-vinyl-1H-indol-2-yl) methanol (5a)**



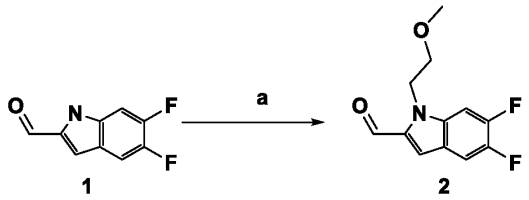
**[000374]** To the stirred solution of methyl-1-(cyclopropylmethyl)-6-vinyl-1H-indole-2-carboxylate (**4a**, 2.7 g, 10.5 mmol) in tetrahydrofuran (30.0 mL), 1.0 M lithium aluminum hydrate in tetrahydrofuran (20 mL, 21.0 mmol) were added at 0 °C . The reaction mixture was stirred at room temperature for 2 h. After completion of reaction, the reaction mixture was diluted with ammonium chloride and extracted with ethyl acetate (30 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12.0 g Redisep and 20% ethyl acetate in hexane as eluent to afford (1-(cyclopropylmethyl)-6-vinyl-1H-indol-2-yl)methanol as white solid (**5a**).Yield: 2.0 g (83%). MS (ESI): 227.13, *m/z* found 228.13 $[M+H]^{+1}$.

**Step-5a: preparation of 1-(cyclopropylmethyl)-6-vinyl-1H-indole-2-carbaldehyde**



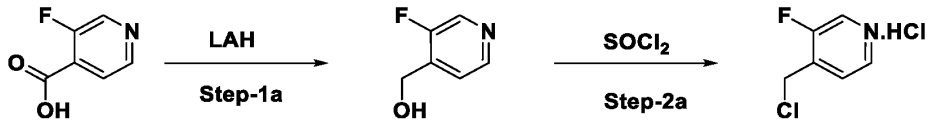

**[000375]** To the stirred solution of (1-(cyclopropylmethyl)-6-vinyl-1H-indol-2-yl)methanol ( 2.0 g, 8.73 mmol) in dichloromethane (20.0 mL), Dess Martin periodinane (4.4g, 10.48 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 4 h. After completion of reaction, the reaction mixture was diluted with water and extracted with dichloromethane (20 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 30% ethyl acetate in hexane as eluent to afford 1-(cyclopropylmethyl)-6-vinyl-1H-indole-2-carbaldehyde as white solid (**6a**). Yield: 1.1 g (55%). MS (ESI): 225.12, *m/z* found 226.12 $[M+H]^{+1}$.

**Synthesis of 5,6-difluoro-1-(2-methoxyethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-54)**



**[000376]** To the stirred solution of 5,6-difluoro-1H-indole-2-carbaldehyde (1, 0.50 g, 2.76 mmol) in *N, N*-dimethylformamide (10 mL), cesium carbonate (2.69 g, 8.28 mmol) and 1-bromo-2-methoxyethane (0.32 mL, 3.31 mmol) were added at room temperature. The reaction mixture was stirred at 60 °C for 3 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (200 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 10% ethyl acetate in hexane as eluent to afford 5,6-difluoro-1-(2-methoxyethyl)-1H-indole-2-carbaldehyde as yellow solid. Yield: 0.66 g (45%). MS (ESI); 239.08 *m/z* found 240.04 $[M+H]^{+1}$.

**Synthesis of 4-(chloromethyl)-3-fluoropyridine hydrochloride (Intermediate for Example-24)**




1a 2a 3a

**Step-1a: preparation of (3-fluoropyridin-4-yl)methanol (2a)**



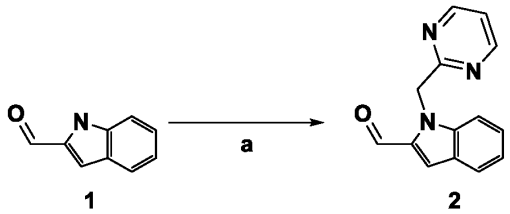

**[000377]** To a solution of 3-fluoroisonicotinic acid (**1a**, 2.0 g, 14.2 mmol) in tetrahydrofuran (20 mL), Lithium aluminium hydride (1M in tetrahydrofuran), (12.0 mL, 21.3 mmol) was added drop wise over 10 min at 0 °C and reaction mixture was stirred for 2 h at 0 °C. After completion of reaction, 40% potassium hydroxide solution was (60 mL) was added to reaction mixture. The solid precipitated was filtered off and washed with diethyl ether. The crude was purified by CombiFlash using 12 g RediSep and 20% ethyl acetate in hexane as eluent to afford (3-fluoropyridin-4-yl) methanol (**2a**) as off white solid. Yield: 0.50 g (28%). MS (ESI): 127.04; *m/z* found, 128.01 $[M+H]^{+1}$.

**Step 2a: *preparation* of 4-(chloromethyl)-3-fluoropyridine hydrochloride (3a)**



**[000378]** To a stirred solution of (3-fluoropyridin-4-yl)methanol (**2a**, 0.70 g, 5.51 mmol) in N,N-dichloromethane (5.0 mL), at 0 °C, was added thionyl chloride (1.00 g, 13.78 mmol), the reaction mixture was then stirred at room temperature for 1 h. After completion of reaction dichloromethane was removed under reduced pressure and crude obtained was washed with diethyl ether and dried to afford 4-(chloromethyl)-3-fluoropyridine hydrochloride **3a** as light brown solid. Yield: 1.0 g (90%). MS (ESI): 180.99; m/z found, 182.02$[M+H]^+$.

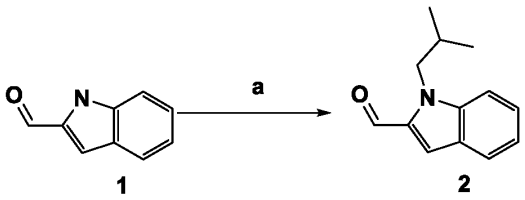
**Synthesis of 1-(pyrimidin-2-ylmethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-27)**




**[000379]** To the stirred solution of 1H-indole-2-carbaldehyde (1, 0.70 g, 4.82 mmol) in *N, N*-dimethylformamide (10 mL), cesium carbonate (7.8 g, 24.1mmol) and 2-(chloromethyl)pyrimidine (0.98 g, 7.24 mmol) were added at room temperature. The reaction mixture was stirred at 60 °C for 3 h. After completion of reaction, reaction mixture was cooled to room temperature, diluted with water and extracted with ethyl acetate (200 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 10% ethyl acetate in hexane as eluent to afford 1-(pyrimidin-2-ylmethyl)-1H-indole-2-carbaldehyde as brown crystalline solid. Yield: 1.30 g (81%). MS (ESI): 237.09; *m/z* found 238.14 $[M+H]^{+1}$.

**[000380]** $^1$HNMR (400 MHz, DMSO-d6): δ 9.87 (s, 1H), 8.68 (d, *J* = 4.8 Hz, 2H), 7.80 (d, *J* = 8.0 Hz, 1H) 7.55 (d, *J* = 5.84 Hz, 2H), 7.36 (d, *J* = 4.72 Hz, 2H), 7.16(t, *J* = 7.36 Hz, 1H), 6.0 (s, 2H).

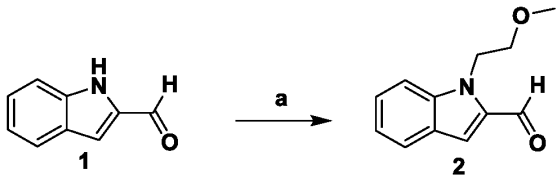
**Synthesis of 1-isobutyl-1H-indole-2-carbaldehyde (Intermediate for Example-31)**



**[000381]** To the stirred solution of 1H-indole-2-carbaldehyde (**1**, 0.70 g, 4.82 mmol) in *N, N*-dimethylformamide (10 mL), cesium carbonate (7.8 g, 24.1mmol) and (1-bromo-2-methylpropane (0.98 g, 7.24 mmol) were added at room temperature. The reaction mixture was stirred at 60 °C for 3 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (200 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 10% ethyl acetate in hexane as eluent to afford 1-isobutyl-1H-indole-2-carbaldehyde as oily liquid. Yield: 0.80 g (82%). MS (ESI); 201.12 *m/z* found 202.30 $(M+H)^+$.

**[000382]** $^1$HNMR (400 MHz, DMSO-d6): δ 9.89 (s, 1H), 7.77 (d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 8.44 Hz, 1H), 7.48 (s, 1H), 7.39 (t, *J* = 7.5 Hz, 1H), 7.15 (t, *J* = 7.4 Hz, 1H), 4.37 (d, *J* = 7.4 Hz, 2H), 2.11-2.04 (m, 1H), 0.81 ((d, *J* = 6.64 Hz, 6H).

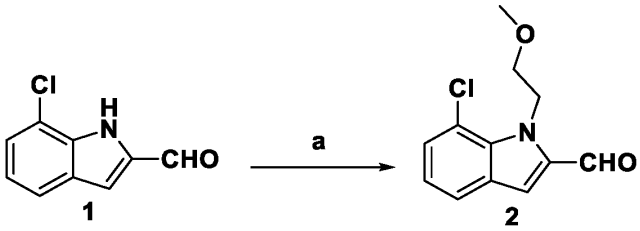
**Synthesis of 1-(2-methoxyethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-22)**




**[000383]** To the stirred solution of 1H-indole-2-carbaldehyde (1, 1.0 g, 6.0 mmol) in *N, N*-dimethylformamide (6.0 mL), cesium carbonate (6.6 g, 20.6 mmol) and 1-bromo-2-methoxyethane (0.76 mL, 8.0 mmol) were added at room temperature. The reaction mixture was stirred at 60 °C for 1.5 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (200 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 20% ethyl acetate in hexane as eluent to afford the 1-(2-methoxyethyl)-1H-indole-2-carbaldehyde as light yellow solid. Yield: 0.9 g (64%). MS (ESI): 203; *m/z* found no ionization.

**[000384]** $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 9.89 (s, 1H), 7.75 (d, *J* = 8.4 Hz, 1H), 7.63 (d, *J* = 8.8 Hz, 1H) 7.47 (s, 1H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.15 (t, *J* = 7.6 Hz, 1H), 4.70 (t, *J* = 5.6 Hz, 2H), 3.61 (t, *J* = 5.2 Hz, 2H), 3.17 (s, 3H).

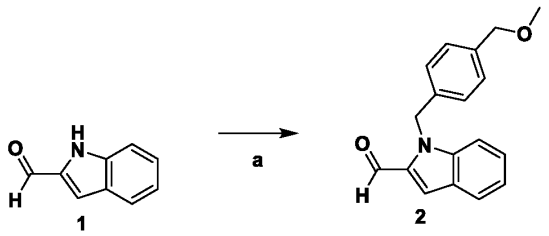
**Synthesis of 7-chloro-1-(2-methoxyethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-36)**




**[000385]** To the stirred solution of 7-chloro-1H-indole-2-carbaldehyde (**1**, 0.5 g, 2.79 mmol) in *N, N*-dimethylformamide (15 mL), cesium carbonate (2.7 g, 8.37 mmol) and 1-bromo-2-methoxyethane (0.31 mL, 3.35 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (50 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12 g RediSep and 20% ethyl acetate in hexane as eluent to afford 7-chloro-1-(2-methoxyethyl)-1H-indole-2-carbaldehyde as yellow oil. Yield: 0.34 g (52%). MS (ESI): 237.06; *m/z* found no ionization.

**[000386]** $^1$HNMR (400 MHz, DMSO-d6): δ(ppm): 9.93 (s, 1H), 7.77 (d, *J* = 8.0 Hz, 1H), 7.56 (s, 1H) 7.45 (d, *J* = 7.5 Hz, 1H), 7.15 (t, *J* = 7.8 Hz, 1H), 5.13 (t, *J* = 5.9 Hz, 2H), 3.62 (t, *J* = 5.9 Hz, 2H), 3.16 (s, 3H).

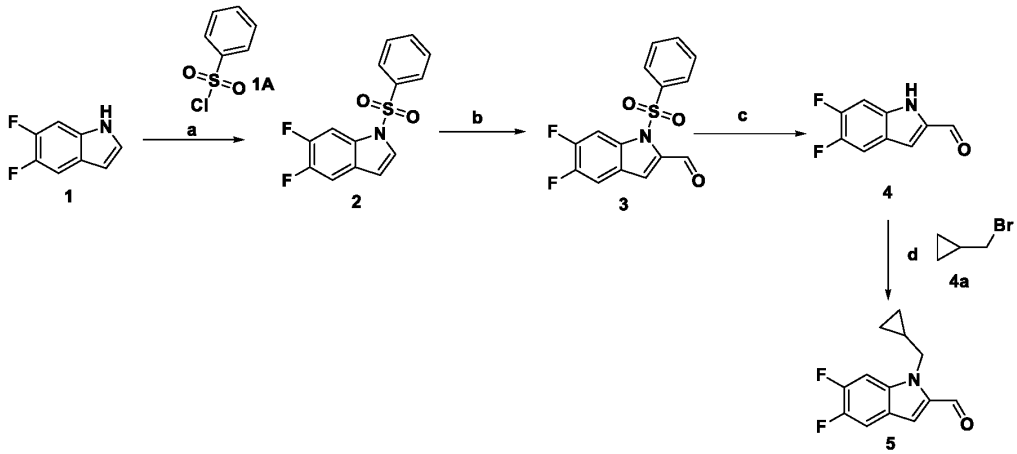
**Synthesis of 1-(4-(methoxymethyl)benzyl)-1H-indole-2-carbaldehyde (Intermediate for Example-37)**



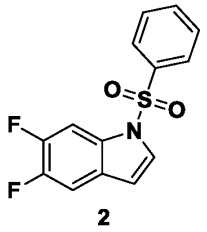

**[000387]** To the stirred solution of 1H-indole-2-carbaldehyde (1, 1.0 g, 6.0 mmol) in *N, N*-dimethylformamide (5.0 mL), cesium carbonate (0.58 g, 1.79 mmol) and (41-(bromomethyl)-4-(methoxymethyl)benzene (0.14 g, 0.72 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 3 h. After completion of reaction, reaction mixture was diluted with water and extracted with ethyl acetate (20 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude

was purified by CombiFlash using 12 g RediSep and 5% methanol in dichloromethane as eluent to afford the 1-(4-(methoxymethyl)benzyl)-1H-indole-2-carbaldehyde.

**Synthesis of 1-(cyclopropylmethyl)-5,6-difluoro-1H-indole-2-carbaldehyde (Intermediate for Example-32 & 77)**

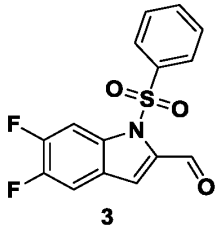



**Step 1a: Preparation of 5,6-Difluoro-1-(phenylsulfonyl)-1H-indole (2)**



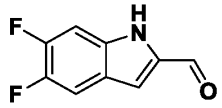

**[000388]** To a solution of sodium hydride (0.26 g, 13 mmol) in DMF (10 mL) was added solution of 5,6-difluoro-1H-indole (**1**, 0.52 g, 13 mmol) in DMF at 0 °C, drop wise over 15 min. Followed by addition of solution of benzenesulfonyl chloride in DMF (1.4 g, 13 mmol) at 0 °C and stirred for 2 h at room temperature under $N_2$ atmosphere. To the reaction mixture was added ice cold water (50 mL), then filtered off the precipitate and washed with ice cold water to obtain brown solid. (1 g, 26 % Yield). MS (ESI) *m/z* 293.0 $(M+H)^+$.

**Step 2b: Preparation of 5,6-Difluoro-1-(phenylsulfonyl)-1H-indole-2-carbaldehyde (3)**



**[000389]** To a solution of 5,6-difluoro-1-(phenylsulfonyl)-1H-indole (**2**, 1 g, 3.42 mmol) in dry THF (50 mL) was added lithium diisopropylamide 1M in THF (3.4 mL g, 6.84mmol) at -78 °C and stirred for 5-8 min, followed by addition of dry DMF (0.5mL, at -78°C and stirred for 10 min at -78°C under $N_2$ atmosphere. To the reaction mixture was added aqueous ammonium chloride (20 mL), then extracted in to EtOAc. Organic layer was washed with saturated $NH_4Cl$ solution and brine, dried over sodium sulphate, filtered and concentrated under reduced pressure to obtain brown solid (0.7 g, 70 %). MS (ESI) *m/z* 322.0 $(M+H)^+$.

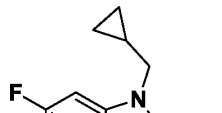
**Step 3c: Preparation of 5,6-Difluoro-1H-indole-2-carbaldehyde (4)**



**4**

**[000390]** To the stirred solution of 5,6-Difluoro-1-(phenylsulfonyl)-1H-indole-2-carbaldehyde (**3**, 0.8 g, 2.49 mmol) in THF (50 mL), was added TBAF (1M in THF) (9.15 mL, 12.45 mmol) at room temperature. The reaction mixture was stirred at room temperature for 12 h. The reaction mixture was diluted with water and extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude product. The crude residue was purified by gradient column chromatography using 15-25% ethyl acetate in hexane to afford the 5-fluoro-1H-indole-2-carbaldehyde as sticky solid (0.4 g, 88% Yield) MS (ESI): Mass calcd. for $C_9H_5F_2NO$, 181.145; m/z found, 182 $(M+H)^+$.

**Step 4d: Preparation of 1-(cyclopropylmethyl)-5,6-difluoro-1H-indole-2-carbaldehyde (5)**

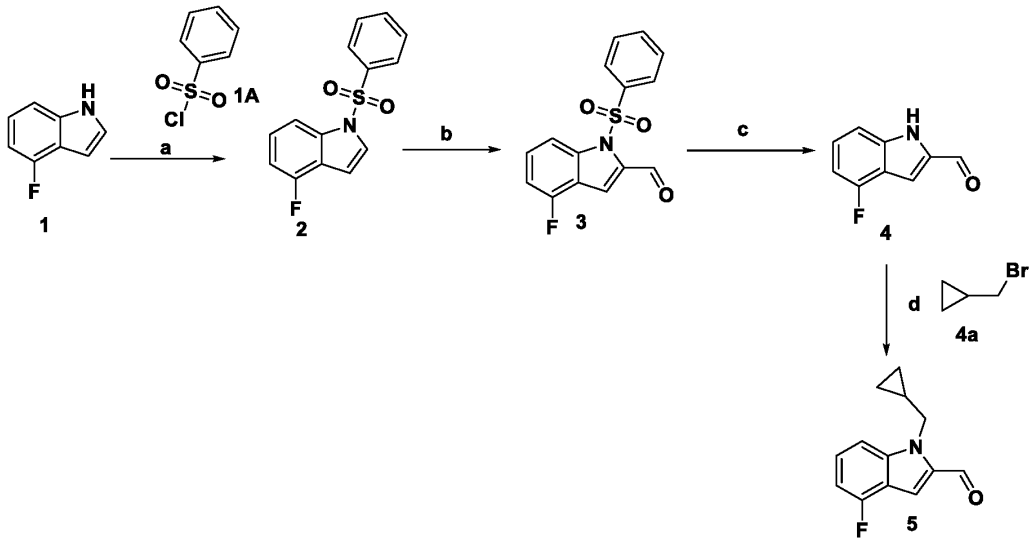


**5**

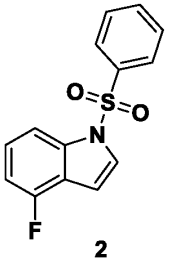
**[000391]** To the stirred solution of 5,6-difluoro-1H-indole-2-carbaldehyde (**4**, 0.3 g, 1.65 mmol) in DMF (20 mL), were added potassium carbonate (0.68g, 4.97 mmol) and (bromomethyl)cyclopropane (4a, 0.16 mL, 1.82 mmol) at room temperature. The reaction mixture was stirred at room temperature for 12 h. The reaction mixture was diluted with water and extracted with ethyl acetate (50 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate and evaporated to get crude product. The

crude residue was purified by gradient column chromatography using 3-7% ethyl acetate in hexane to afford the 1-(cyclopropylmethyl)-5,6-difluoro-1H-indole-2-carbaldehyde as off white solid (0.2 g, 48% Yield). $^1$HNMR (400 MHz, DMSO-$d_6$) δ(ppm): 9.86 (s, 1H), 7.90-7.78 (m, 2H), 7.48 (s, 1H), 4.42 (d, $J$ = 6.8 Hz, 2H), 1.20 ( bs, 1H), 0.39-0.35 (m, 4H), MS (ESI): Mass calcd. for $C_{13}H_{11}F_2NO$, 235.23; m/z found, 236.1 $[M+H]^+$.

**Synthesis of 1-(cyclopropylmethyl)-4-fluoro-1H-indole-2-carbaldehyde (Intermediate for Example-80)**

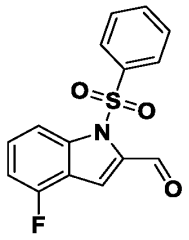



**Step 1: Preparation of 4-fluoro-1-(phenylsulfonyl)-1H-indole (2)**




**[000392]** To a solution of sodium hydride (0.88 g, 22.2 mmol) in DMF (50 mL) was added solution of 4-fluoro-1H-indole (**1**, 3.0 g, 22.2 mmol) in DMF at 0 °C, dropwise over 15 min. Benzenesulfonyl chloride in DMF (2.86 mL, 22.2 mmol) was added at 0$^0$C and stirred for 2 h at room temperature under $N_2$ atmosphere. To the reaction mixture was added ice cold water (50 mL), then filtered off the precipitate and washed with ice cold water to obtain white solid. (7.0 g - crude).

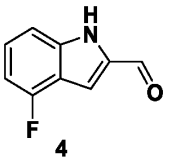
**Step 2: Preparation of 4-fluoro-1-(phenylsulfonyl)-1H-indole-2-carbaldehyde (3)**



3

**[000393]** To a solution of 4-fluoro-1-(phenylsulfonyl)-1H-indole (**2**, 7.0 g, 22.0 mmol) in dry THF (60 mL) was added lithium diisopropylamide 2M in THF (10.9 mL, 22.0 mmol) at -78 °C and stirred for 5-8 min, followed by addition of dry DMF (2.5 mL, 33.0 mmol) at -78 °C and stirred for 10 min at -78 °C under $N_2$ atmosphere. To the reaction mixture was added aqueous ammonium chloride (20 mL), then extracted in to EtOAc. Organic layer was washed with saturated $NH_4Cl$ solution and brine, dried over sodium sulphate, filtered and concentrated under reduced pressure to obtain red liquid (6.80 g, 88.31 %).

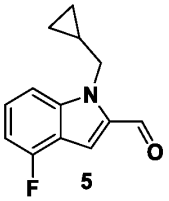
**Step 3: Preparation of 4-fluoro-1H-indole-2-carbaldehyde (4)**



4

**[000394]** To a solution of 4-fluoro-1-(phenylsulfonyl)-1H-indole-2-carbaldehyde (**4,** 3.0 g, 9.9 mmol) in dry THF (20 mL) was added tetrabutyl ammonium fluoride 1M in THF (14.8 mL) and the reaction mixture was stirred for about 12 h under room temperature. The reaction mixture was quenched with water and, then extracted with ethyl acetate (50 mL x 3). Combined organic extracts were washed with brine, dried over sodium sulfate, filtered and evaporated to get crude product. Crude residue was purified by gradient column chromatography using 5-10% ethyl acetate in hexane to get the product as yellow solid. (Yield: 99%, 1.6 g). MS (ESI): Mass calcd. for $C_9H_6FNO$, 163.04; *m/z* found 164 $(M+H)^+$.

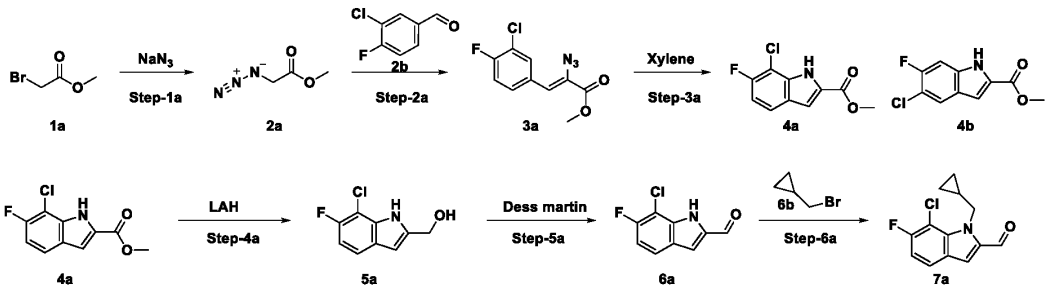
**Step- 4: Preparation of 1-(cyclopropylmethyl)-4-fluoro-1H-indole-2-carbaldehyde (5)**



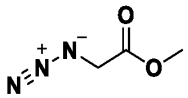
5

**[000395]** To a stirred solution of 4-fluoro-1H-indole-2-carbaldehyde (**4**, 1.6 g, 9.877 mmol) in DMF (10 mL), was added potassium carbonate (6.8g, 49.38mmol) followed by (bromomethyl)cyclopropane (6, 1.4 mL, 10.65 mmol) and the reaction mixture was stirred at room temperature for 12h. The reaction mixture was quenched with water, extracted with ethyl acetate (30 mL x 2). Combined organic extracts were washed with brine, dried over sodium sulfate, filtered and evaporated to get crude product. Crude residue was purified by gradient column chromatography using 5-10% ethyl acetate in hexane to get the product as brown liquid. (Yield: 47.6%, 1 g). $^1$HNMR (400 MHz, DMSO-$d_6$): δ 9.90 (s, 1H), 7.55-7.50 (m, 2H), 7.40-7.35 (m, 1H), 6.95-6.90 (m, 1H), 4.46 (d, *J* = 8 Hz, 2H), 1.22-1.21 (m, 1H), 0.42-0.36 (m, 4H). MS (ESI): Mass calcd. for $C_{13}H_{12}FNO$, 217.24; m/z found, 218 $[M+H]^+$.

**Synthesis of 7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indole-2-carbaldehyde (Intermediate for Example-87)**

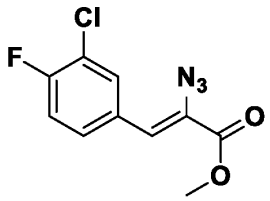



**Step-1a: Synthesis of methyl-2-azidoacetate (2a)**



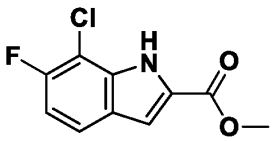
**[000396]** To a stirred solution of methyl-2-bromoacetate (**1a**, 20.0 g, 131.5 mmol) in *N, N*-dimethylformamide (40.0 mL), sodium azide (10.2 g, 157.8 mmol) was added at 0 °C. The reaction mixture was stirred at room temperature for 16 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (100 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure to afford methyl 2-azidoacetate as oily liquid (**2a**). Yield: 11.2 g (74%). ELSD MS (ESI): 115.04, *m/z* found 116.10 $[M+H]^{+1}$.

**Step-2a: Synthesis of methyl (Z)-2-azido-3-(3-chloro-4-fluorophenyl)acrylate (3a)**

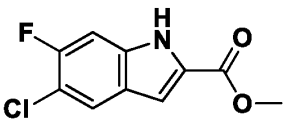



**[000397]** To a stirred solution of methanol (25 mL), sodium metal (1.09 g, 47.46 mmol) was added at room temperature and allowed to stir at room temperature for 10 min. Methyl-2-azidoacetate (**2a**, 2.50 g, 15.80 mmol) and 3-chloro-4-fluorobenzaldehyde (**2b**, 6.10 g, 53.70 mmol) solution in methanol (5.0 mL) were added at -15 °C. The reaction mixture was stirred at -15 °C for 4 h. After completion of reaction, the reaction mixture was neutralized with 1 N Hydrogen chloride at 0 °C up to pH ~7. The precipitated solid was filtered, washed with water (10 mL × 2). The compound obtained was dried under vacuum to afford methyl (Z)-2-azido-3-(3-chloro-4-fluorophenyl)acrylate (**3a**) as light yellow solid. Yield: 1.8 g (45%). MS (ESI): 255.02, *m/z* found 256.25 $[M+H]^{+1}$.

**Step-3a: Synthesis of methyl-7-chloro-6-fluoro-1H-indole-2-carboxylate (4a)**



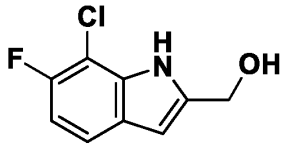

**4a**




**4b**

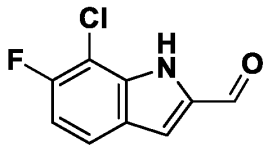
**[000398]** The stirred solution of methyl (Z)-2-azido-3-(3-chloro-4-fluorophenyl)acrylate (**3a**, 1.80 g, 7.05 mmol) in *p*-xylene (80.0 mL) was refluxed at 140 °C for 2 h. After completion of reaction, the reaction mixture was concentrated under reduced pressure. The resulting crude was purified by CombiFlash using 40.0 g RediSep column. Desired methyl-7-chloro-6-fluoro-1H-indole-2-carboxylate (**4a**) was obtained at 2% ethyl acetate in hexanes and methyl 5-chloro-6-fluoro-1H-indole-2-carboxylate (**4b**) was obtained at 5% ethyl acetate in hexanes. Desired fraction was concentrated to afford methyl-7-chloro-6-fluoro-1H-indole-2-carboxylate (**4a**) as light brown solid. Yield: 1.1 g (Crude). MS (ESI): 227.01, *m/z* found 228.01 $[M+H]^{+1}$.

**Step-4a: Synthesis of (7-chloro-6-fluoro-1H-indol-2-yl)methanol (5a)**



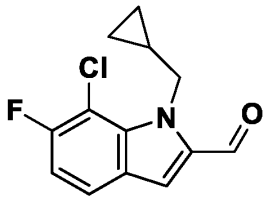

**[000399]** To a stirred solution of methyl-7-chloro-6-fluoro-1H-indole-2-carboxylate (**4a**, 1.0 g, 4.4 mmol) in tetrahydrofuran (20.0 mL), 1.0 M lithium aluminum hydrate in tetrahydrofuran (8.8 ml, 8.80 mmol) was added at 0 °C . The reaction mixture was stirred at room temperature for 2 h. After completion of reaction, the reaction mixture was diluted with ammonium chloride and extracted with ethyl acetate (30 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 40 g RediSep column and 20% ethyl acetate in hexane as eluent to afford (7-chloro-6-fluoro-1H-indol-2-yl)methanol as sticky solid (**5a**). Yield: 8.24 g (91%). MS (ESI): 199.02, *m/z* found 200.05 $[M+H]^{+1}$.

**Step-5a: Synthesis of 7-chloro-6-fluoro-1H-indole-2-carbaldehyde (6a)**



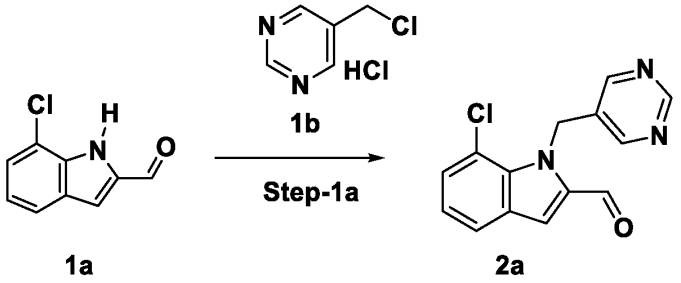

**[000400]** To a stirred solution of (7-chloro-6-fluoro-1H-indol-2-yl)methanol (**5a**, 0.80 g, 4.00 mmol) in dichloromethane (30.0 mL), Dess Martin periodinane (3.4 g, 8.00 mmol) were added at room temperature. The reaction mixture was stirred at room temperature for 4 h. After completion of reaction, the reaction mixture was diluted with water and extracted with dichloromethane (20 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12.0 g RediSep column and 2-5% ethyl acetate in hexane as eluent to afford 7-chloro-6-fluoro-1H-indole-2-carbaldehyde as white solid (**6a**). Yield: 0.63 g (75%). MS (ESI): 197.0, *m/z* found 198.12 $[M+H]^{+1}$.

**Step-6a: Synthesis of 7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indole-2-carbaldehyde (7a)**




**[000401]** To a stirred solution of 7-chloro-6-fluoro-1H-indole-2-carbaldehyde (**6a**, 0.30 g, 1.52 mmol) in *N, N*-dimethylformamide (15.0 mL), cesium carbonate (1.40 g, 4.56 mmol) and (bromomethyl)cyclopropane (**6b**, 0.29 mL, 3.04 mmol) were added at room temperature. The reaction mixture was stirred at 60 °C for 30 min. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (30 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12.0 g RediSep column and 10% ethyl acetate in hexane as eluent to afford 7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indole-2-carbaldehyde as sticky solid (**7a**). Yield: 0.33 g (88%). MS (ESI): 251.05, *m/z* found 252.25 $[M+H]^{+1}$.

**Synthesis of 7-chloro-1-(pyrimidin-5-ylmethyl)-1H-indole-2-carbaldehyde (Intermediate for Example-88)**




**[000402]** To a stirred solution of 7-chloro-1H-indole-2-carbaldehyde (**1a**, 0.500 g, 2.79 mmol) in *N, N*-dimethylformamide (10.0 mL), cesium carbonate (2.7 g, 8.37 mmol) and 5-(chloromethyl) pyrimidine hydrochloride (**1b**, 0.429 g, 3.34 mmol) were added at room temperature. The reaction mixture was stirred at room temperature about 16 h. After completion of reaction, the reaction mixture was diluted with water and extracted with ethyl acetate (10 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude was purified by CombiFlash using 12.0 g RediSep and 30% ethyl acetate in hexane as eluent to afford 7-chloro-1-(pyrimidin-5-ylmethyl)-1H-indole-2-carbaldehyde as yellow solid (**2a**). Yield: 0.260 g (34%). MS (ESI): 271.10, *m/z* found 272.19 $[M+H]^{+1}$.

## BIOLOGICAL ASSAYS:

### FP Binding assay

**[000403]** Binding of compounds with PAD4 enzyme was detected by FP assay. PAD4 enzyme was diluted to 1 uM in assay buffer (100 mM HEPES, 50 mM NaCl, 1 mM DTT, 5% Glycerol and 1 mM CHAPS) and added to wells containing various concentration of compounds or DMSO vehicle (1%) in a 384 well black plate. 10 nM of fluorescein labelled probe (JPAD -00085) was added to the plate. Assay plate was incubated for 60 minutes at room temperature before measuring FP reading at FP module (λex 485/λem 535 nm) on Pherastar. $IC_{50}$ was calculated using XL-fit software model 205. (Ref: Nat Chem Biol. 2015 Mar;11(3):189-91).

### Ammonia Release Biochemical assay

Citrullination assay was detected via ammonia release. PAD4 enzyme was diluted to 120 nM in assay buffer (100 mM HEPES, 50 mM NaCl, 2 mM DDT, 0.6 mg/mL BSA, pH 7.4) added to wells containing various concentration of compound or DMSO vehicle (1 % final) in black 384 well plate. Following a 60-min preincubation at room temperature, the reaction was initiated by the addition of substrate (1.5 mM BAEE in 200 mM HEPES, 50 mM NaCl, 350 uM CaCl2, 2 mM, pH 7.4). The reaction was stopped after 60 min by addition of stop/detection buffer containing 50 mM EDTA, 2.6 mM of o-phthaladehyde and 2.6 mM DTT. Assay was incubated at room temperature for 90 min before measuring fluorescence's (λex 405/λem 460 nm) on Tecan reader. $IC_{50}$ was calculated using XL-fit software model 205. (Ref: Nat Chem Biol. 2015 Mar;11(3):189-91).

### Anti-PAD4 activity:

**[000404]** **Table 1**, below, shows the activity of selected compounds of this disclosure in the PAD4 assays described above. Compounds having an activity designated as "**A**" provided $IC_{50} \leq$ 1uM; compounds having an activity designated as "**B**" provided $IC_{50}$ 1 – 10 uM; and compounds having an activity designated as "C" provided $IC_{50} \geq$10 uM.

**Table 1:** PAD4 enzymatic activity

| Example No. | NH3 release; PAD4 $IC_{50}$ (uM) | FP PAD4 $IC_{50}$ (uM) |
|---|---|---|
| 1 | A | B |

| | | |
|---|---|---|
| 2 | B | nd |
| 3 | B | nd |
| 4 | C | C |
| 5 | B | B |
| 6 | B | nd |
| 7 | B | nd |
| 8 | A | A |
| 9 | A | A |
| 10 | A | A |
| 11 | A | A |
| 12 | A | A |
| 13 | A | B |
| 14 | B | A |
| 15 | A | B |
| 16 | A | B |
| 17 | A | B |
| 18 | A | B |
| 19 | A | A |
| 20 | A | nd |
| 21 | A | nd |
| 22 | A | nd |
| 23 | A | nd |
| 24 | A | nd |
| 25 | A | nd |
| 26 | A | nd |
| 27 | A | nd |
| 28 | A | nd |
| 29 | B | nd |

| | | |
|---|---|---|
| 30 | B | nd |
| 31 | A | nd |
| 32 | A | nd |
| 33 | A | nd |
| 34 | A | nd |
| 35 | A | nd |
| 36 | A | nd |
| 37 | A | nd |
| 38 | C | nd |
| 39 | A | nd |
| 40 | B | nd |
| 41 | A | nd |
| 42 | C | nd |
| 43 | C | nd |
| 44 | B | nd |
| 45 | C | nd |
| 46 | A | nd |
| 47 | A | nd |
| 48 | A | nd |
| 49 | A | nd |
| 50 | A | nd |
| 51 | A | nd |
| 52 | B | nd |
| 53 | A | nd |
| 54 | B | nd |
| 55 | A | nd |
| 56 | A | nd |
| 57 | A | nd |
| 58 | B | nd |

| | | |
|---|---|---|
| **59** | **A** | **nd** |
| **60** | **A** | **nd** |
| **61** | **A** | **nd** |
| **62** | **C** | **nd** |
| **63** | **A** | **A** |
| **64** | **A** | **A** |
| **65** | **A** | **A** |
| **66** | **A** | **B** |
| **67** | **A** | **nd** |
| **68** | **B** | **nd** |
| **69** | **A** | **nd** |
| **70** | **A** | **nd** |
| **71** | **A** | **nd** |
| **72** | **A** | **A** |
| **73** | **A** | **A** |
| **74** | **A** | **nd** |
| **75** | **A** | **nd** |
| **76** | **A** | **B** |
| **77** | **A** | **A** |
| **78** | **A** | **nd** |
| **79** | **B** | **nd** |
| **80** | **B** | **nd** |
| **81** | **C** | **nd** |
| **82** | **B** | **nd** |
| **83** | **B** | **nd** |
| **84** | **A** | **nd** |
| **85** | **A** | **nd** |
| **86** | **A** | **nd** |
| **87** | **A** | **nd** |

| | | |
|---|---|---|
| **88** | **B** | **nd** |

nd= not determined

**[000405]** Table 1 illustrates that most of the compounds (from Examples 1-88) were found to be active against the PAD4 enzyme when evaluated through both Ammonia Release Biochemical and FP Binding assays. The $IC_{50}$ values display the efficacy of the compounds in inhibiting the PAD4 enzyme activity. $IC_{50}$ value indicates how much of a particular drug or a compound is needed to inhibit a given biological process or component of a process such as an enzyme. A low value of $IC_{50}$ denotes high inhibition efficacy of the test compound (Examples 1-88 as described herein). However, in the above Table 1, high efficacy is denoted by "A" , "B", and "C", wherein "A" having least value of $IC_{50}$ and thus most effective.

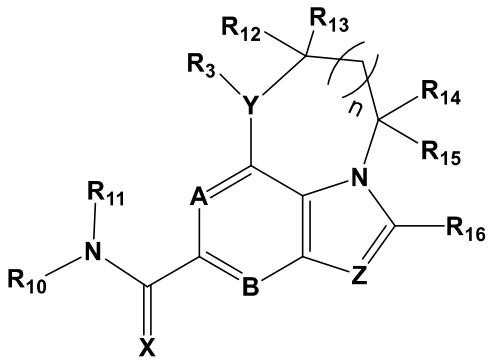
**[000406]** The Ammonia Release Biochemical assay showed that 62 out of 88 compounds showed an $IC_{50}$ value of $\leq$ 1µM denoted by "A". These 62 compounds were Examples- 1, 8-13, 15-28, 31-37, 39, 41, 46-51, 53, 55-57, 59-61, 63-67, 69-78, and 84-88.

**[000407]** On the other hand, the FP Binding assay showed 13 out of 23 tested compounds to be actively inhibiting PAD4 enzyme activity. The individual examples being Examples- 8-12, 14, 19, 63-65, 72, 73, and 77 respectively.

**[000408]** Therefore, it may be inferred that Examples- 1, 8-13, 15-28, 31-37, 39, 41, 46-51, 53, 55-57, 59-61, 63-67, 69-78, and 84-87 are identified, and could be developed, as potential drugs for alleviating PAD4 enzyme activity and thus treating PAD4 mediated disorders.

**I/We claim**:

**1.** A compound of Formula (I)




Formula (I)

their stereoisomers and pharmaceutically acceptable salts thereof, wherein

X is O or S;

Y is O or N;

Z is N;

A is $CR_1$;

B is $CR_2$;

n is 0-1;

$R_1$ and $R_2$ are independently selected from hydrogen;

$R_3$ is absent or is selected from hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, $SO_2C_6$ aryl, and $SO_2C_{1-6}$ alkyl, wherein $SO_2C_{1-6}$ alkyl, and $SO_2C_6$ aryl is optionally substituted with $C_{1-6}$ alkoxy, halogen, and $C_6$ aryl;

$R_{10}$ and $R_{11}$ are taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein,

the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from amino, $-NHC(O)CH=CHCH_2N(CH_3)_2$, or $C_{1-6}$ alkylamino;

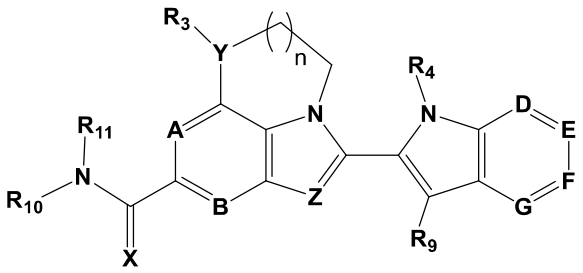
$R_{12}$, $R_{13}$, $R_{14}$ and $R_{15}$ are independently selected from hydrogen or $C_{1-6}$ alkyl; and

$R_{16}$ is 5-10 membered bicyclic heteroaryl with 1-2 heteroatoms selected from N or S, wherein,

5-10 membered bicyclic heteroaryl is optionally substituted with 1-3 substituents selected from the group consisting of halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl- $C_6$ aryl, $C_{2-6}$ alkenyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-}$

$_6$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and -COOH.

**2.** A compound of Formula (II)




Formula (II)

their stereoisomers and pharmaceutically acceptable salts thereof,

wherein,

X is O or S;

Y is O or N;

Z is N;

A is $CR_1$;

B is $CR_2$;

D is selected from N or $CR_5$;

E is $CR_6$;

F is $CR_7$;

G is $CR_8$;

n is 1-2;

$R_1$, $R_2$ and $R_9$ are independently selected from hydrogen;

$R_5$, $R_6$, $R_7$ and $R_8$ are independently selected from the group consisting of hydrogen, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{2-6}$ alkenyl- $C_6$ aryl, and $C_{1-6}$ heteroaryl;

$R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $SO_2C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, and $SO_2C_6$ aryl, wherein, $SO_2C_6$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, and $C_6$ aryl;

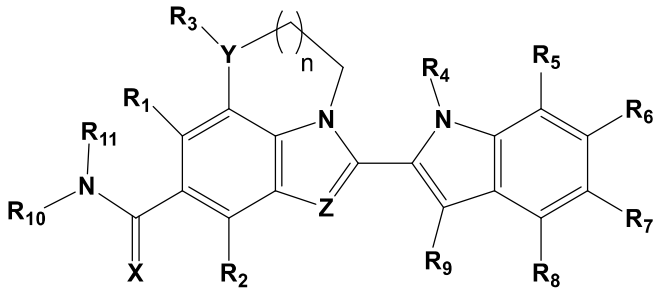
$R_4$ is selected from the group consisting of $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, is

optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and -COOH; and

$R_{10}$ and $R_{11}$ are taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein,

the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, and -$NHC(O)CH=CHCH_2N(CH_3)_2$.

**3.** A compound of Formula (III)




Formula (III)

their stereoisomers and pharmaceutically acceptable salts thereof,

wherein,

X is O or S;

Y is O or N;

Z is N;

n is 1-2;

$R_1$, $R_2$ and $R_9$ are independently selected from hydrogen;

$R_5$, $R_6$, $R_7$ and $R_8$ are independently selected from the group consisting of hydrogen, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{2-6}$ alkenyl- $C_6$ aryl, and $C_{1-6}$ heteroaryl;

$R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $SO_2C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, and $SO_2C_6$ aryl, wherein, $SO_2C_6$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, and $C_6$ aryl;

$R_4$ is selected from the group consisting of $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and -COOH; and

$R_{10}$ and $R_{11}$ are taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein,

the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, and -$NHC(O)CH=CHCH_2N(CH_3)_2$.

**4.** The compound of Formula (I) as claimed in claim 1 or its stereoisomers and pharmaceutically acceptable salts thereof, which is selected from a group consisting of:

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(1)**,

(R)-(3-aminopyrrolidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(2)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-ethyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(3)**,

(2-(aminomethyl)piperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(4)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-ethyl-1H-pyrrolo[2,3-b]pyridin-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(5)**,

(R)-(3-aminopiperidin-1-yl)(1-(1-(cyclopropylmethyl)-1H-indol-2-yl)-8,9-dihydro-7H-6-oxa-2,9a-diazabenzo[cd]azulen-4-yl)methanone **(6)**,

(R)-(3-aminopyrrolidin-1-yl)(1-(1-(cyclopropylmethyl)-1H-indol-2-yl)-8,9-dihydro-7H-6-oxa-2,9a-diazabenzo[cd]azulen-4-yl)methanone **(7)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-methyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(8)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(9)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-4-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(10)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-2-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(11)**,

(R)-(3-aminopiperidin-1-yl)(2-(3-ethylbenzo[b]thiophen-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(12)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(4-chlorobenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(13)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(2-fluorobenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(14)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(4-fluorobenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(15)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-3-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(16)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5,6-dimethoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(17)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-benzyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(18)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(4-methoxybenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(19)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(20)**,
(R)-(3-aminopiperidin-1-yl)(2-(6-methoxy-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(21)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(2-hydroxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(22)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-methoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(23)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-((3-fluoropyridin-4-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(24)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(pyrazin-2-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(25)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-((3-fluoropyridin-2-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(26)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(pyrimidin-2-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(27)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(28)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(pyrimidin-5-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(29)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridazin-3-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(30)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-isobutyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(31)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5,6-difluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(32)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-((3-fluoropyridin-2-yl)methyl)-6-methoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(33)**,
(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-((3-fluoropyridin-2-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(34)**,
(R)-(3-aminopiperidin-1-yl)(2-(6-fluoro-1-((3-fluoropyridin-2-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(35)**,
(*R*)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(36)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(4-(hydroxymethyl)benzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone trifluoroacetic acid salt **(37)**,
(R,E)-N-(1-(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)-4-(dimethylamino)but-2-enamide trifluoroacetic acid salt **(38)**,
(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(4-methoxybenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(39)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-((tetrahydro-2H-pyran-4-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(40)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclobutylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(41)**,
(R)-2-(2-(7-(3-aminopiperidine-1-carbonyl)-3,4-dihydro-5-ox1,2adiazaacenaphthylen-2-yl)-1H-indol-1-yl)acetic acid **(42)**,
(R)- (3-aminopiperidin-1-yl)(2-(1-(piperidin-4-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(43)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(oxetan-3-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(44)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-((1-methylpiperidin-4-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(45)**,
(*R*)-(3-aminopiperidin-1-yl)(2-(5-fluoro-1-(4-methoxybenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(46)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(2,2-difluoroethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(47)**,
(*R*)-(3-aminopiperidin-1-yl)(2-(5-fluoro-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(48)**,
(R)-(3-aminopiperidin-1-yl)(2-(6-fluoro-1-(4-fluorobenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(49)**,
(*R*)-(3-aminopiperidin-1-yl)(2-(6-fluoro-1-(4-methoxybenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(50)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(4-fluorobenzyl)-6-methoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(51)**,
3-aminopiperidin-1-yl)(2-(6-fluoro-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(52)**,
(*R*)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(cyclobutylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(53)**,
(R)-(3-aminopiperidin-1-yl)(2-(5,6-difluoro-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(54)**,
(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-isobutyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(55)**,
(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(2,2-difluoroethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(56)**,
(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(57)**,
(R,E)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-styryl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(58)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-((4-methylthiazol-2-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(59)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-methoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(60)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-(hydroxymethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl) methanone **(61)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,3-dimethyl-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(62)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(63)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(64)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(65)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-3-ylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(66)**,
(R)-(3-aminopiperidin-1-yl)(2-(5-bromo-1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(67)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-(pyridin-3-yl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(68)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-2-ylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(69)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(2-fluorobenzyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(70)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-4-ylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(71)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-methyl-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(72)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-methoxy-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(73)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-methoxy-1H-indol-2-yl)-6-methyl-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(74)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-6-methyl-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(75)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(methylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(76)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5,6-difluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(77)**,
(R)-(3-aminopiperidin-1-yl)(6-cyclopropyl-2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(78)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(phenethylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(79)**,
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-4-fluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(80)**,

(R)-(3-aminopiperidin-1-yl)(6-((4-chlorophenyl)sulfonyl)-2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(81)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(cyclopropylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(82)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-((2-ethoxyethyl)sulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(83)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-methyl-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(84)**,

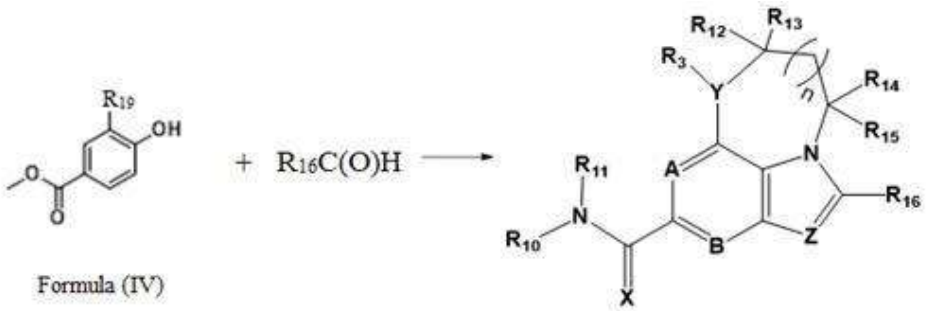
(R)-1-(8-(3-aminopiperidine-1-carbonyl)-2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-4,5-dihydro-6H-imidazo[1,5,4-de]quinoxalin-6-yl)ethan-1-one **(85)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanethione **(86)**,

(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(87)**, and

(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(pyrimidin-5-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(88)**.

**5.** A process of preparation of compounds of Formula (I) as claimed in any of claims 1 and 4 or its stereoisomers and pharmaceutically acceptable salts thereof, the process comprising reacting Formula (IV) and $R_{16}C(O)H$



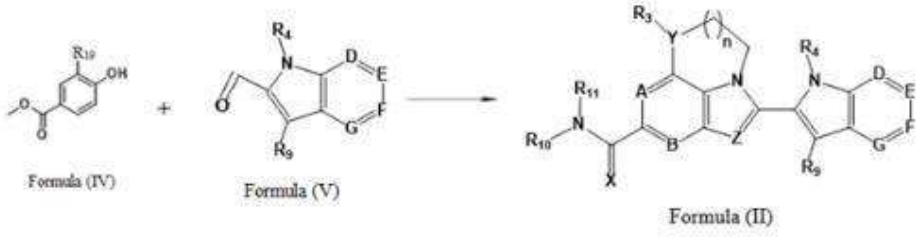

Formula (IV)

Formula (I)

wherein $R_{19}$ of Formula (IV) is selected from nitro and $C_{1-6}$ alkoxy; $R_{16}$ of $R_{16}C(O)H$ is 5-10 membered bicyclic heteroaryl with 1-2 heteroatoms selected from N or S, wherein, 5-10 membered bicyclic heteroaryl is optionally substituted with 1-3 substituents selected from the group consisting of halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{2-6}$ alkenyl- $C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$

heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and -COOH; X of Formula (I) is selected from O or S; Y is selected from O or N; Z is N; A is $CR_1$; B is $CR_2$; n is 0-1; $R_1$ and $R_2$ are independently selected from hydrogen; $R_3$ is absent or is selected from hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $SO_2C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, and $SO_2C_6$ aryl, wherein, $SO_2C_6$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, and $C_6$ aryl; $R_{10}$ and $R_{11}$ are taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein, the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from amino, $C_{1-6}$ alkylamino, and -$NHC(O)CH=CHCH_2N(CH_3)_2$; $R_{12}$, $R_{13}$, $R_{14}$, and $R_{15}$ are independently selected from hydrogen and $C_{1-6}$ alkyl; $R_{16}$ is 5-10 membered bicyclic heteroaryl with 1-2 heteroatoms selected from N or S, wherein, 5-10 membered bicyclic heteroaryl is optionally substituted with 1-3 substituents selected from the group consisting of halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{2-6}$ alkenyl- $C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, $C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl- $C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ heteroaryl, $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, and $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and -COOH.

**6.** A process of preparation of compounds of Formula (II) as claimed in any of claims 2 and 4 or its stereoisomers and pharmaceutically acceptable salts thereof, the process comprising reacting Formula (IV) and Formula (V)

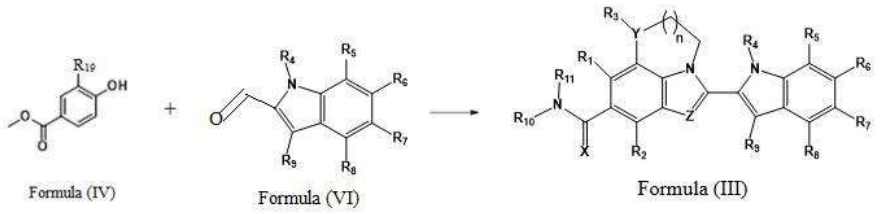



Formula (IV) Formula (V) Formula (II)

wherein $R_{19}$ of Formula (IV) is selected from nitro and $C_{1-6}$ alkoxy; X of Formula (II) is selected from O or S; Y is selected from O or N; Z is N; A is $CR_1$; B is $CR_2$; D is selected from N or $CR_5$; E is $CR_6$; F is $CR_7$; G is $CR_8$; n is 1-2; $R_1$, $R_2$ and $R_9$ are independently selected from hydrogen; $R_5$, $R_6$, $R_7$ and $R_8$ are independently selected

from the group consisting of hydrogen, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{2-6}$ alkenyl- $C_6$ aryl, and $C_{1-6}$ heteroaryl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $SO_2C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, and $SO_2C_6$ aryl, wherein, $SO_2C_6$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy, halogen, and $C_6$ aryl; $R_4$ is selected from the group consisting of $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, $-CH_2OH$, and -COOH; $R_{10}$ and $R_{11}$ are taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, and $-NHC(O)CH=CHCH_2N(CH_3)_2$; D of Formula (V) is selected from N or $CR_5$; E is $CR_6$; F is $CR_7$; G is $CR_8$, $R_9$ is H; and $R_4$ is selected from the group consisting of $C_{1-6}$ alkyl, $C_{1-6}$ haloalkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, $-CH_2OH$, and -COOH.

**7.** A process of preparation of compounds of Formula (III) as claimed in any of claims 3-4 or its stereoisomers and pharmaceutically acceptable salts thereof, the process comprising reacting Formula (IV) and Formula (VI)




wherein $R_{19}$ of Formula (IV) is selected from nitro and $C_{1-6}$ alkoxy; X of Formula (III) is selected from O or S; Y is O or N; Z is N; n is 1-2; $R_1$, $R_2$ and $R_9$ are independently selected from hydrogen; $R_5$, $R_6$, $R_7$ and $R_8$ are independently selected from the group consisting of hydrogen, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{2-6}$ alkenyl- $C_6$ aryl, and $C_{1-6}$ heteroaryl; $R_3$ is absent or is selected from the group consisting of hydrogen, $C_{1-6}$ alkyl, $C_{3-6}$ cycloalkyl, $C(O)C_{1-6}$ alkyl, $SO_2C_{1-6}$ alkyl, $SO_2C_{3-6}$ cycloalkyl, and $SO_2C_6$ aryl, wherein, $SO_2C_6$ aryl, and $SO_2C_{1-6}$ alkyl, is optionally substituted with $C_{1-6}$ alkoxy,

halogen, and $C_6$ aryl; $R_4$ is selected from the group consisting of $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and COOH; $R_{10}$ and $R_{11}$ are taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein, the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, $C_{1-6}$ alkylamino, and -$NHC(O)CH=CHCH_2N(CH_3)_2$; and $R_9$ of formula (VI) is hydrogen; $R_5$, $R_6$, $R_7$ and $R_8$ are independently selected from the group consisting of hydrogen, halogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{2-6}$ alkenyl- $C_6$ aryl, and $C_{1-6}$ heteroaryl; $R_4$ is selected from the group consisting of $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl, wherein, $C_{1-6}$ alkyl, $C_{1-6}$ alkyl-$C_6$ aryl, $C_{1-6}$ alkyl-$C_{1-6}$ heterocyclyl, and $C_{1-6}$ alkyl-$C_{1-6}$ heteroaryl is optionally substituted with one or more groups selected from hydrogen, $C_{1-6}$ alkyl, $C_{1-6}$ alkoxy, $C_{3-8}$ cycloalkyl, halogen, hydroxyl, -$CH_2OH$, and COOH.

**8.** A pharmaceutical composition comprising a compound of Formula (I), Formula (II), and Formula (III) or a pharmaceutically acceptable salt thereof as claimed in any of claims 1-4 together with a pharmaceutically acceptable carrier, optionally in combination with one or more other pharmaceutical compositions.

**9.** The pharmaceutical composition as claimed in claim 8, wherein the composition is in the form selected from the group consisting of a tablet, capsule, powder, syrup, solution, aerosol, and suspension.

**10.** Compounds as claimed in any of the claims 1-4 or a pharmaceutically acceptable salt thereof for use as a medicament.

**11.** An *in vitro* method for inhibiting one or more PAD family in a cell with an effective amount of the compound as claimed in any of the claims 1-4.

**12.** Use of a pharmaceutical composition as claimed in any one of the claim 8 or 9 in the manufacture of a medicament for treating a condition selected from vasculitis, systemic lupus erythematosus, cancer, asthma, rheumatoid arthritis, ulcerative colitis, psoriasis, cystic fibrosis and cutaneous lupus erythematosus.

**13.** Use of the compound of Formula (I), Formula (II), and Formula (III) as claimed in any one of claims 1-4 in the manufacture of a medicament for the treatment of

rheumatoid arthritis, vasculitis, systemic lupus erythematosus, ulcerative colitis, cancer, cystic fibrosis, asthma, cutaneous lupus erythematosus and psoriasis.

**14.** Use of the compound as claimed in any one of claims 1-4 or the pharmaceutical composition as claimed in claim 8, or 9 together with other clinically relevant agents or biological agents in the manufacture of a medicament for the treatment and/or prevention of treatment of rheumatoid arthritis, vasculitis, systemic lupus erythematosus, ulcerative colitis, cancer, cystic fibrosis, asthma, cutaneous lupus erythematosus and psoriasis.

**15.** Use of the compound as claimed in any one of claims 1-4 or the pharmaceutical composition as claimed in claim 8, or 9 together with other clinically relevant agents or biological agents in the manufacture of a medicament for the treatment and/or prevention of acid-induced lung injury, respiratory distress syndrome, allergen induced asthma, allergic bronchopulmonary, chronic lung disease of prematurity, chronic obstructive pulmonary disease, colitis, cystic fibrosis, gouty arthritis, inflammatory bowel disease, inflammatory lung disease, inflammatory pain, juvenile rheumatoid arthritis, kidney disease, kidney injury caused by parasitic infections, kidney transplant rejection prophylaxis, lung injury, lupus, lupus nephritis, multiple sclerosis, muscular dystrophy, non-allergen induced asthma, osteoarthritis, periodontitis, peritoneal endometriosis, psoriasis, pulmonary disease, pulmonary fibrosis, pyogenic sterile arthritis, renal disease, rheumatic disease, rheumatoid arthritis, sepsis, severe pain and ulcerative colitis.

**16.** Use of a therapeutically effective amount of the compound as claimed in any one of the claims 1-4, or the pharmaceutical composition as claimed in claim 8 or 9 in the manufacture of a medicament for the treatment and/or prevention of a condition selected from acid-induced lung injury, respiratory distress syndrome, allergen induced asthma, allergic bronchopulmonary, chronic lung disease of prematurity, chronic obstructive pulmonary disease, colitis, cystic fibrosis, gouty arthritis, inflammatory bowel disease, inflammatory lung disease, inflammatory pain, juvenile rheumatoid arthritis, kidney disease, kidney injury caused by parasitic infections, kidney transplant rejection prophylaxis, lung injury, lupus, lupus nephritis, multiple sclerosis, muscular dystrophy, non-allergen induced asthma, osteoarthritis, periodontitis, peritoneal endometriosis, psoriasis, pulmonary disease, pulmonary fibrosis, pyogenic sterile arthritis, renal disease, rheumatic disease, rheumatoid arthritis, sepsis, severe pain and ulcerative colitis.

**17.** Use of a combination of the compounds as claimed in any of claims 1-4 or the pharmaceutical composition as claimed in claim 8 or 9, with other clinically relevant agents or biological agents in the manufacture of a medicament for the treatment of rheumatoid arthritis.

**18.** Use of a combination of the compounds as claimed in any of claims 1-4 or the pharmaceutical composition as claimed in claim 8 or 9, with other clinically relevant immune modulators agents in the manufacture of a medicament for the treatment of cancer.