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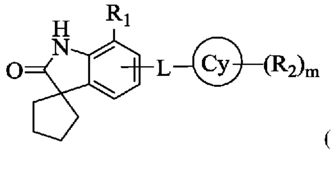

(I)

(57) Abstract: The present invention provides spiro[cyclopentaneane-1,3'-indolin]-2'-one derivatives of formula (I), which are therapeutically useful, more particularly as bromodomain inhibitors. (I) wherein Cy, R_1, R_2, L and 'm' have the meaning given in the specification, and pharmaceutically acceptable salts or pharmaceutically acceptable stereoisomers thereof that are useful in the treatment and prevention of diseases or disorders, in particular their use as bromodomain inhibitors in the treatment and prevention of the associated diseases or disorders. The present invention also provides preparation of the compounds and pharmaceutical formulations comprising at least one of the spiro[cyclopentane-1,3'-indolin]-2'-one derivatives of formula (I), together with a pharmaceutically acceptable carrier, diluent or excipient therefore.

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SPIRO[CYCLOPENTANE-1,3'-INDOLIN]-2'-ONE DERIVATIVES AS BROMODOMAIN INHIBITORS.

RELATED APPLICATION

This application claims the benefit of Indian provisional application number 201641042612, filed on 14th December, 2016; the specifications of which are hereby incorporated by reference in their entirety.

FIELD OF THE INVENTION

The present invention relates to novel spiro[cyclopentane-1,3'-indolin]-2'-one derivatives of formula (I) which are useful as bromodomain inhibitors.

The invention also relates to the process for preparation of the compounds of the present invention thereof, pharmaceutical compositions comprising them, and their use for the treatment and prevention of diseases or disorder, their use in diseases or disorder associated with bromodomain containing proteins.

BACKGROUND OF THE INVENTION

The acetylation of histone lysine is central to providing the dynamic regulation of chromatin-based gene transcription. The bromodomain (BRD), which is the conserved structural module in chromatin-associated proteins and histone acetyltranferases, is the sole protein domain known to recognize acetyl-lysine residues on proteins.

The BET family of bromodomain containing proteins comprises 4 proteins (BRD2, BRD3, BRD4 and BRD-t) which contain tandem bromodomains capable of binding to two acetylated lysine residues in close proximity, increasing the specificity of the interaction. BRD2 and BRD3 are reported to associate with histones along actively transcribed genes and may be involved in facilitating transcriptional elongation (Leroy et al, Mol. Cell. 2008 30(1):51 -60), while BRD4 appears to be involved in the recruitment of the pTEF-[beta] complex to inducible genes, resulting in phosphorylation of RNA polymerase and increased transcriptional output (Hargreaves et al, Cell, 2009 138(1): 129-145). It has also been reported that BRD4 or BRD3 may fuse with NUT (nuclear protein in testis) forming novel fusion oncogenes, BRD4-NUT or BRD3-NUT, in a highly malignant form of epithelial neoplasia (French et al. Cancer Research, 2003, 63, 304-307 and French et al. Journal of Clinical Oncology, 2004, 22 (20), 4135-4139).

Data suggests that BRD-NUT fusion proteins contribute to carcinogenesis (Oncogene, 2008, 27, 2237-2242). BRD-t is uniquely expressed in the testes and ovary. All family members have been reported to have some function in controlling or executing aspects of the cell cycle, and have been shown to remain in complex with chromosomes during cell division suggesting a role in the maintenance of epigenetic memory. In addition, some viruses make use of these proteins to tether their genomes to the host cell chromatin, as part of the process of viral replication (You et al Cell, 2004 117(3):349-60).

Japanese patent application JP2008156311 discloses a benzimidazole derivative which is said to be a BRD2 bromodomain binding agent has utility with respect to virus infection / proliferation.

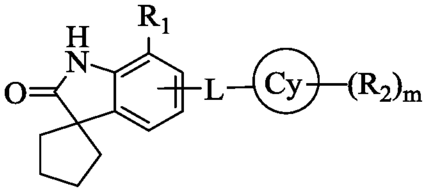
International patent application WO2009084693A1 discloses a series of thieno triazolodiazepiene derivatives that are said to inhibit the binding between an acetylated histone and a bromodomain containing protein which are said to be useful as anti-cancer agents.

International patent application WO2011054846A1 discloses a series of quinoline derivatives that inhibit the binding of BET family bromodomains with acetylated lysine residues.

However, there remains a need for potent bromodomain inhibitors with desirable pharmaceutical properties. Certain spiro[cyclopentane-1,3'-indolin]-2'-onederivatives have been found in the context of this invention to have a class of compounds that inhibit the binding of BET family bromodomains to acetylated lysine residues for controlling the gene expressions in human health and disease. Such compounds will hereafter be referred to as "bromodomain inhibitors".

SUMMARY OF THE INVENTION

The present invention provides a new class of spiro[cyclopentane-1,3'-indolin]-2'-one derivatives of the following formula (I) that inhibit the binding of BET family bromodomains to acetylated lysine residues.



(I)

or a pharmaceutically acceptable salt or a stereoisomer thereof;

wherein;

Cy is a 3-12 membered monocyclic or bicyclic ring containing 0-4 hetero atoms or groups independently selected from N, O, S, NH or C(O);

L represents a linker selected from $-NHS(O)_2-$, $-S(O)_2NH-$, $-NHS(O)_2CH(R_3)-$, $-N=S(O)(R_3)-$ or $-NHC(O)CH(R_3)-$;

R_1 is hydrogen, cyano, nitro, halogen, C_{1-7} alkyl, haloalkyl, $-OR_a$, $-COR_a$, $-COOR_a$, $-O(CO)R_a$, $-CONR_aR_b$, $-NHCOR_a$, $-NR_aR_b$, $-SR_3$, $-S(O_2)R_3$, optionally substituted alkylamino, optionally substituted C_{3-10} cycloalkyl, optionally substituted C_{3-10} cycloalkylalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heterocyclyl or optionally substituted heterocyclylalkyl; wherein the optional substitution at each occurrence is independently 1-3 substituents selected from halogen, C_{1-7} alkyl, C_{1-7} alkoxy, haloalkyl or C_{3-10} cycloalkyl;

R_2 is halogen, C_{1-7} alkyl, $-OR_a$, haloalkyl, amino, alkylamino, cyano, nitro, $-COOR_3$, $-SR_3$, $-S(O_2)R_3$, optionally substituted C_{3-10} cycloalkyl, optionally substituted aryl or optionally substituted heterocyclyl; wherein the optional substitution at each occurrence is independently 1-3 substituents selected from halogen, cyano, nitro, amino, oxo, hydroxy, alkylamino, $-COOR_3$, $-SR_3$, $-S(O_2)R_3$, C_{1-7} alkyl, C_{1-7} alkoxy, C_{3-10} cycloalkyl, aryl or heterocyclyl;

R_3 is hydrogen or C_{1-7} alkyl;

R_a and R_b are independently selected from hydrogen, C_{1-7} alkyl, haloalkyl, optionally substituted alkylamino, optionally substituted C_{3-10} cycloalkyl, optionally substituted C_{3-10} cycloalkylalkyl , optionally substituted heterocyclyl , optionally substituted heterocyclylalkyl, optionally substituted C_{3-12} spiroheterocyclyl, optionally substituted aryl or optionally substituted arylalkyl; wherein the optional substitution at each occurrence is independently 1-3 substituents selected from halogen, cyano, nitro, amino, oxo, hydroxy, alkylamino, $-COOR_3$, $-SR_3$, $-S(O_2)R_3$, C_{1-7} alkyl, C_{1-7} alkoxy, C_{3-10} cycloalkyl, aryl or heterocyclyl; and

'm' is 0, 1, 2 or 3.

In a further aspect of the present invention, it relates to the pharmaceutical composition comprising spiro[cyclopentane-1,3'-indolin]-2'-one derivatives of formula (I) and processes for preparing thereof.

In yet further aspect of the present application, it provides use of spiro[cyclopentane-1,3'-indolin]-2'-one derivatives of formula (I) for the treatment and prevention in diseases or disorder, in particular their use in diseases or disorder for which a bromodomain inhibitor is indicated.

More particularly, the invention relates to the use of substituted spiro[cyclopentane-1,3'-indolin]-2'-one derivatives of formula (I) and pharmaceutically acceptable derivatives, solvates, tautomers, salts and stereoisomers thereof, including mixtures thereof in all ratios as a medicament for which a bromodomain inhibitor is indicated.

DETAILED DESCRIPTION OF THE INVENTION

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as is commonly understood by one of skill in art to which the subject matter herein belongs. As used in the specification and the appended claims, unless specified to the contrary, the following terms have the meaning indicated in order to facilitate the understanding of the present invention.

As used herein, unless otherwise defined the term "alkyl" alone or in combination with other term(s) means saturated aliphatic hydrocarbon chains, including C_1-C_{10} straight or C_1-C_{10} branched alkyl groups. Examples of "alkyl" include but are not limited to methyl, ethyl, propyl, butyl, hexyl, isopropyl, isobutyl, sec-butyl, tert-butyl, isopentyl, neopentyl, and isohexyl and the like.

As used herein the term "alkylamino" refers to either a mono or a dialkylamino group in which the alkyl portion of the group may be straight or branched. Examples of such groups are methylamino, diethylamino, 2-propylamino and the like.

As used herein, the term "alkoxy" refers to the group alkyl-O- or -O-alkyl, where alkyl groups are as defined above. Exemplary C_1-C_{10} alkyl group containing alkoxy- groups include but are not limited to methoxy, ethoxy, n-propoxy, n-butoxy, t-butoxy and the like. An alkoxy group can be unsubstituted or substituted with one or more suitable groups.

As used herein, the term "aryl" alone or in combination with other term(s) means a carbocyclic aromatic system containing one or more rings wherein such rings may be fused. The term "fused" means that the second ring is attached or formed by having two adjacent atoms in common with the first ring. The term "fused" is equivalent to the term "condensed". Unless otherwise specified, an aryl group typically has from 6 to about 14 carbon atoms but the invention is not limited in that respect. Examples of aryl groups include but are not limited to phenyl, naphthyl, indanyl, and the like. Unless otherwise specified, all aryl groups described herein may be optionally substituted.

As used herein, the term “arylalkyl” refers to an aryl moiety attached to the parent structure through C_1-C_5 alkyl group.

As used herein, the term "amino" refers to an $–NH_2$ group.

As used herein, the term "nitro" refers to an $–NO_2$ group.

As used herein, the term “cyano” refers to –CN group.

As used herein, the term "hydroxyl" refers to -OH group.

As used herein, the term "oxo" refers to =O group.

As used herein, the term "halogen" alone or in combination with other term(s) means fluorine, chlorine, bromine or iodine.

As used herein, the term "haloalkyl" refers to an alkyl group, as defined above, wherein one or more of the alkyl group's hydrogen atoms has been replaced with -F, -Cl, -Br or -I. Representative examples of an haloalkyl group include, but are not limited to $-CH_2F$, $-CCl_3$, $-CF_3$, $-CH_2Cl$, $-CH_2CH_2Br$, $-CH_2CH_2I$, $-CH_2CH_2CH_2F$, and $-CH_2CH(Br)CH_3$.

As used herein the term "cycloalkyl" alone or in combination with other term(s) means $-C_3$-C_{10} saturated cyclic hydrocarbon ring. A cycloalkyl may be a single ring, which typically contains from 3 to 7 carbon ring atoms. Examples of single-ring cycloalkyls include but are not limited to cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl and the like.

As used herein, the term "heterocyclyl" alone or in combination with other term(s) includes both "heterocycloalkyl" and "heteroaryl" groups which are as defined herein. Examples of “heterocyclyl” include, but are not limited to azetidinyl, pyrrolidinyl, piperidinyl, pyridyl, indolyl, benzimidazolyl, pyrazinyl, quinuclidine, 1,2,6-trimethylpiperidine, 4-methylmorpholine, tetrahydro-2H-thiopyran 1,1-dioxide, pyrazolyl, imidazolyl, morpholinyl benzothiazolyl and the like.

The term "heterocycloalkyl" refers to a non-aromatic, saturated or partially saturated, monocyclic or polycyclic ring system of 3 to 15 members having at least one heteroatom or hetero group selected from O, N, S, S(O), $S(O)_2$, NH or C(O). Examples of “heterocycloalkyl” include, but are not limited to azetidinyl, oxetanyl, imidazolidinyl, pyrrolidinyl, oxazolidinyl, thiazolidinyl, pyrazolidinyl, tetrahydrofuranyl, piperidinyl, piperazinyl, tetrahydropyranyl, morpholinyl, oxapiperazinyl, oxapiperidinyl, tetrahydrofuryl, tetrahydropyranyl, tetrahydrothiophenyl, dihydropyranyl, indolinyl, indolinylmethyl, 2,3-dihydrobenzo[b][1,4] dioxine,1,2,3,4-tetrahydroisoquinoline, 5,6-dihydropyridin-2(1H)-one, quinoline, 2-oxaspiro[3.3] heptane, 2-azaspiro[3.3]heptane, 2-methyl-2,6-diazaspiro[3.3]heptane, 6-methyl-2,6-diazaspiro [3.4]octane, 2-methyl-1,2,3,4-tetrahydroisoquinoline, 8-methyl-8-azabicyclo[3.2.1]octane, 2-xo bicyclo[2.2.1]heptane, indazole, [1,2,4]triazolo[4,3-a]pyridine, tetrahydro isoquinoline azepanyl and N-oxides thereof. Attachment of a heterocycloalkyl substituent can occur via either a carbon atom or a heteroatom. A heterocycloalkyl group can be optionally substituted with one or more suitable groups by one or more aforesaid groups.

As used herein, the term "heteroaryl" alone or in combination with other term(s) means a completely unsaturated ring system containing a total of 5 to 14 ring atoms. At least one of the ring atoms is a heteroatom (i.e., oxygen, nitrogen, or sulfur), with the remaining ring atoms/groups being independently selected from the group consisting of carbon, oxygen, nitrogen or sulfur. A heteroaryl may be a single-ring (monocyclic) or polycyclic ring system. Examples of "heteroaryl" include but are not limited to pyridyl, indolyl, benzimidazolyl, benzothiazolyl and the like.

The term "heterocyclylalkyl" refers to a heterocyclyl moiety attached to the parent structure through C_1-C_5 alkyl group.

The term "cycloalkylalkyl" refers to a cycloalkyl moiety attached to the parent structure through C_1-C_5 alkyl group.

The term " monocyclic or bicyclic ring containing 0-4 heteroatoms/groups” refers to monocyclic or bicyclic aromatic or non-aromatic cyclic ring with 3-12 ring atoms in which 0-4 of the ring carbon atoms have been independently replaced with C(O), N, NH, O, S, S(O) or $S(O)_2$ groups. The representative examples of such rings include, but are not limited to phenyl, pyridine, pyrimidine, morpholine, piperidine, piperazine, cyclohexyl, 2,3-dihydrobenzo[b][1,4] dioxine, 1,2,3,4-tetrahydroisoquinoline, 5,6-dihydropyridin-2(1H)-one, quinoline, 2-oxobicyclo [2.2.1]heptane, indazole, [1,2,4] triazolo[4,3-a]pyridine and tetrahydroisoquinoline.

The term "heteroatom/group" as used herein designates a C(O), N, NH, O, S, S(O) and $S(O)_2$.

The term "spiroheterocyclyl" refers to a bicyclic heterocyclic ring as defined above wherein the two rings are joined through a common ring carbon atom.

As used herein, the term "optionally substituted" refers to replacement of one or more hydrogen radicals in a given structure with a radical of a specified substituent including, but not limited to: halo, alkyl, alkenyl, alkynyl, aryl, heterocyclyl, alkylthio, alkylthioalkyl, arylthioalkyl, alkylsulfonyl, alkylsulfonylalkyl, arylsulfonylalkyl, alkoxy, aryloxy, aralkoxy, aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, alkoxycarbonyl, aryloxycarbonyl, haloalkyl, amino, trifluoromethyl, cyano, nitro, alkylamino, arylamino, alkylaminoalkyl, arylaminoalkyl, aminoalkylamino, hydroxy, alkoxyalkyl, carboxyalkyl, alkoxycarbonylalkyl, aminocarbonylalkyl, acyl, aralkoxycarbonyl, carboxylic acid, arylthio, thiol, sulfonic acid, sulfonyl, phosphonic acid, aryl, heteroaryl, heterocyclic, and aliphatic. It is understood that the substituent may be further substituted.

As used herein, the term 'compound(s)' comprises the compounds disclosed in the present invention.

As used herein, the term "comprises" or "comprising" is generally used in the sense of include, that is to say permitting the presence of one or more features or components.

As used herein, the term "or" means "and/or" unless stated otherwise.

As used herein, the term "including" as well as other forms, such as "include", "includes" and "included" is not limiting.

As used herein, the term "composition" is intended to encompass a product comprising the specified ingredients in the specified amounts, as well as any product which results, directly or indirectly, from combination of the specified ingredients in the specified amounts. By "pharmaceutically acceptable" it is meant the carrier, diluent or excipient must be compatible with the other ingredients of the formulation and not deleterious to the recipient thereof.

As used herein, the term "treat", "treating" and "treatment" refer to a method of alleviating or abrogating a disease and/or its attendant symptoms.

As used herein, the term "prevents", "preventing" and "prevention" refer to a method of preventing the onset of a disease and/or its attendant symptoms or barring a subject from acquiring a disease. As used herein, "prevent", "preventing" and "prevention" also include delaying the onset of a disease and/or its attendant symptoms and reducing a subject's risk of acquiring a disease.

As used herein, the term "therapeutically effective amount" refers to that amount of the compound being administered sufficient to prevent development of or alleviate to some extent one or more of the symptoms of the condition or disorder being treated.

"Pharmaceutically acceptable" means that, which is useful in preparing a pharmaceutical composition that is generally safe, non-toxic and neither biologically nor otherwise undesirable and includes that which is acceptable for veterinary as well as human pharmaceutical use.

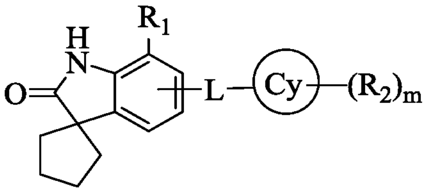
“Pharmaceutically acceptable salt” refers to the salts of the compounds, that is pharmaceutically acceptable and that possesses the desired pharmacological activity of the parent compound. Pharmaceutically acceptable salts of the compounds of this invention include those derived from suitable inorganic and organic acids and bases. Such salts include: acid addition salts, formed with inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid, and the like; or formed with organic acids such as acetic acid, propionic acid, hexanoic acid, cyclopentanepropionic acid, glycolic acid, pyruvic acid, lactic acid, malonic acid, succinic acid, malic acid, maleic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, 3-(4-hydroxybenzoyl)benzoic acid, cinnamic acid, mandelic acid, methane sulfonic acid, ethane sulfonic acid, 1,2-ethane-disulfonic acid, 2-hydroxyethanesulfonic acid, benzene sulfonic acid, 4-chlorobenzenesulfonic acid, 2-naphthalenesulfonic acid, 4-toluenesulfonic acid, camphor sulfonic acid, 4-methylbicyclo[2.2.2]-oct-2-ene-1-carboxylic acid, glucoheptonic acid, 3-phenylpropionic acid, trimethylacetic acid, tertiary butylacetic acid, lauryl sulfuric acid, gluconic acid, glutamic acid, hydroxyl naphthoic acid, salicylic acid, stearic acid, muconic acid, and the like.

The term "stereoisomers" refers to any enantiomers, diastereoisomers, or geometrical isomers of the compounds of formula (I), (IA), (IB), (IC), (ID), (IE) and (IF); wherever they are chiral or when they bear one or more double bonds. When the compounds of the formula (I), (IA), (IB), (IC), (ID), (IE) and (IF), and related formulae are chiral, they can exist in racemic or in optically active form. It should be understood that the invention encompasses all stereochemical isomeric forms, including diastereomeric, enantiomeric and epimeric forms, as well as *d*-isomers and *l*-isomers and mixtures thereof. Individual stereoisomers of compounds can be prepared synthetically from commercially available starting materials which contain chiral centers or by preparation of mixtures of enantiomeric products followed by separation such as conversion to a mixture of diastereomers followed by separation or recrystallization, chromatographic techniques, direct separation of enantiomers on chiral chromatographic columns, or any other appropriate method known in the art. Starting compounds of particular stereochemistry are either commercially available or can be made and resolved by techniques known in the art. Additionally, the compounds of the present invention may exist as geometric isomers. The present invention includes all cis, trans, syn, anti, entgegen (E) and zusammen (Z) isomers as well as the appropriate mixtures thereof.

The present invention provides spiro[cyclopentane-1,3'-indolin]-2'-one derivatives of formula (I) useful as bromodomain inhibitors.

The present invention further provides pharmaceutical compositions comprising the said spiro[cyclopentane-1,3'-indolin]-2'-one derivatives as therapeutic agents.

One of the embodiments of the present invention relates to compounds of formula (I):



(I)

or a pharmaceutically acceptable salt or a stereoisomer thereof;

wherein;

Cy is a 3-12 membered monocyclic or bicyclic ring containing 0-4 hetero atoms or groups independently selected from N, O, S, NH or C(O);

L represents a linker selected from $-NHS(O)_2-$, $-S(O)_2NH-$, $-NHS(O)_2CH(R_3)-$, $-N=S(O)(R_3)-$ or $-NHC(O)CH(R_3)-$;

R_1 is hydrogen, cyano, nitro, halogen, C_{1-7} alkyl, haloalkyl, $-OR_a$, $-COR_a$, $-COOR_a$, $-O(CO)R_a$, $-CONR_aR_b$, $-NHCOR_a$, $-NR_aR_b$, $-SR_3$, $-S(O_2)R_3$, optionally substituted alkylamino, optionally substituted C_{3-10} cycloalkyl, optionally substituted C_{3-10} cycloalkylalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heterocyclyl or optionally substituted heterocyclylalkyl; wherein the optional substitution at each occurrence is independently 1-3 substituents selected from halogen, C_{1-7} alkyl, C_{1-7} alkoxy, haloalkyl or C_{3-10} cycloalkyl;

R_2 is halogen, C_{1-7} alkyl, $-OR_a$, haloalkyl, amino, alkylamino, cyano, nitro, $-COOR_3$, $-SR_3$, $-S(O_2)R_3$, optionally substituted C_{3-10} cycloalkyl, optionally substituted aryl or optionally substituted heterocyclyl; wherein the optional substitution at each occurrence is independently 1-

3 substituents selected from halogen, cyano, nitro, amino, oxo, hydroxy, alkylamino, -COOR$_3$, -SR$_3$, -S(O$_2$)R$_3$, C$_{1-7}$ alkyl, C$_{1-7}$ alkoxy, C$_{3-10}$ cycloalkyl, aryl or heterocyclyl;

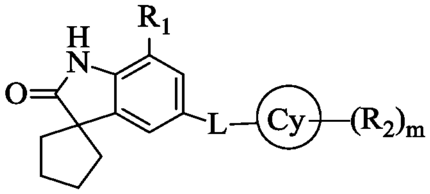
R$_3$ is hydrogen or C$_{1-7}$ alkyl;

R$_a$ and R$_b$ are independently selected from hydrogen, C$_{1-7}$ alkyl, haloalkyl, optionally substituted alkylamino, optionally substituted C$_{3-10}$ cycloalkyl, optionally substituted C$_{3-10}$ cycloalkylalkyl , optionally substituted heterocyclyl , optionally substituted heterocyclylalkyl, optionally substituted C$_{3-12}$ spiroheterocyclyl, optionally substituted aryl or optionally substituted arylalkyl; wherein the optional substitution at each occurrence is independently 1-3 substituents selected from halogen, cyano, nitro, amino, oxo, hydroxy, alkylamino, -COOR$_3$, -SR$_3$, -S(O$_2$)R$_3$, C$_{1-7}$ alkyl, C$_{1-7}$ alkoxy, C$_{3-10}$ cycloalkyl, aryl or heterocyclyl; and

'm' is 0, 1, 2 or 3.

The embodiment below are illustrative of the present invention and are not intended to limit the claims to the specific embodiments exemplified.

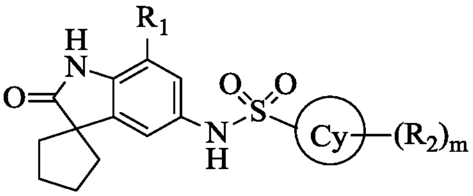
According to yet another embodiment of the present invention, the compound of formula (I) is a compound of formula (IA):



(IA),

or a pharmaceutically acceptable salt or a stereoisomer thereof; wherein, R$_1$, R$_2$, L, Cy and 'm' are same as defined in formula (I).

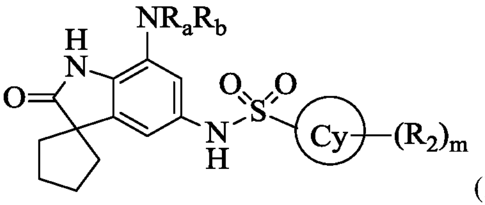
According to yet another embodiment of the present invention, the compound of formula (I) or (IA) is a compound of formula (IB):



(IB),

or a pharmaceutically acceptable salt or a stereoisomer thereof; wherein, R$_1$, R$_2$, Cy and 'm' are same as defined in formula (I).

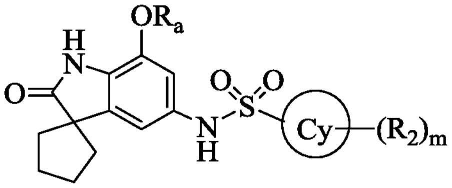
According to yet another embodiment of the present invention, the compound of formula (I) or (IA) is a compound of formula (IC):



(IC),

or a pharmaceutically acceptable salt or a stereoisomer thereof; wherein, R_2, Cy, R_a, R_b and ‘m’ are same as defined in formula (I).

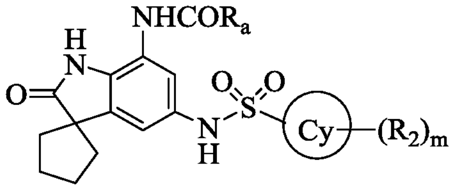
According to yet another embodiment of the present invention, the compound of formula (I) or (IA) is a compound of formula (ID):



(ID),

or a pharmaceutically acceptable salt or a stereoisomer thereof; wherein, R_2, Cy, R_a and ‘m’ are same as defined in formula (I).

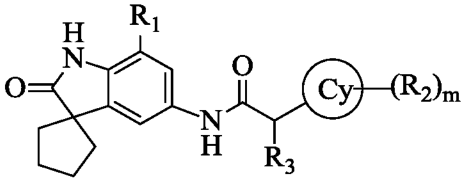
According to yet another embodiment of the present invention, the compound of formula (I) or (IA) is a compound of formula (IE):



(IE),

or a pharmaceutically acceptable salt or a stereoisomer thereof; wherein, R_2, Cy, R_a and ‘m’ are same as defined in formula (I).

According to yet another embodiment of the present invention, the compound of formula (I) or (IA) is a compound of formula (IF):



(IF),

or a pharmaceutically acceptable salt or a stereoisomer thereof; wherein, R_1, R_2, R_3, Cy and ‘m’ are same as defined in formula (I).

According to yet another embodiment, specifically provided are compounds of formula (I), or according to any other embodiment or subclass referred to above,

wherein L is a linker selected from -NHS(O)$_2$-, -S(O)$_2$NH-, -NHS(O)$_2$CH$_2$-, -N=S(O)CH$_3$- or -NHC(O)CHCH$_3$-.

According to yet another embodiment, specifically provided are compounds of formula (I), or according to any other embodiment or subclass referred to above,

wherein Cy is a 3-8 membered monocyclic ring or 8-12 membered bicyclic ring containing 0-3 heteroatoms independently selected from N, NH, O or C(O).

In a subclass of the above embodiment are compounds wherein Cy is cyclohexyl, phenyl, piperidinyl, pyridinyl, 1,4-benzodioxanyl, 2-oxobicyclo [2.2.1] heptane, [1,2,4] triazolo[4,3-a] pyridine, 1,2,3,4-tetrahydroisoquinoline or quinoline. In another subclass Cy is phenyl.

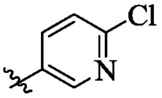
According to yet another embodiment, specifically provided are compounds of formula (I), or according to any other embodiment or subclass referred to above,

wherein R$_2$ is selected from halogen, C$_{1-7}$ alkyl, C$_{1-7}$ alkoxy, -OR$_a$ or 4-10 membered heterocyclic ring containing 1-3 heteroatoms independently selected from O, N, NH or C(O); wherein R$_a$ is selected from haloalkyl, heterocyclyl, C$_{1-7}$ alkyl substituted C$_{3-12}$ spiroheterocyclyl; and 'm' is 0, 1, 2 or 3.

In a subclass of the above embodiment are compounds wherein heterocyclic ring is optionally substituted with 1-2 substituents selected from halogen or C$_{1-7}$ alkyl;

According to yet another embodiment, specifically provided are compounds of formula (I), or according to any other embodiment or subclass referred to above,

wherein Cy-(R$_2$)$_m$ is selected from one of the following groups or tautomers thereof



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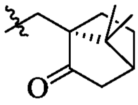

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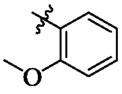

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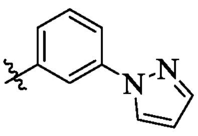

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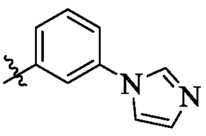

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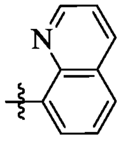

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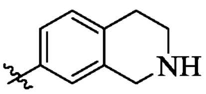

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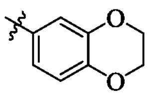

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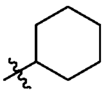
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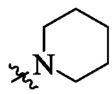

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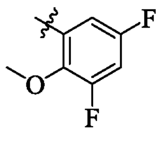

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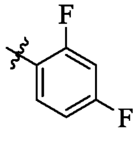

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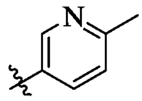

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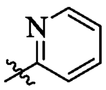
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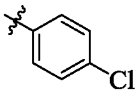
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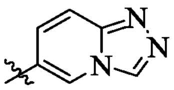
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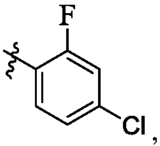
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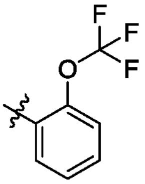
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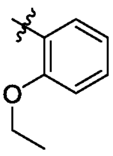
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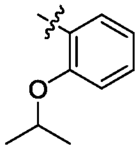
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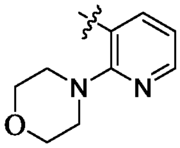
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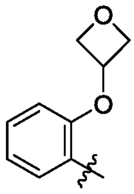
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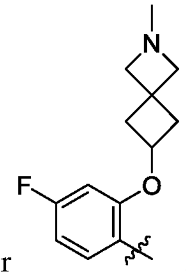
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According to yet another embodiment, specifically provided are compounds of formula (I), or according to any other embodiment or subclass referred to above,

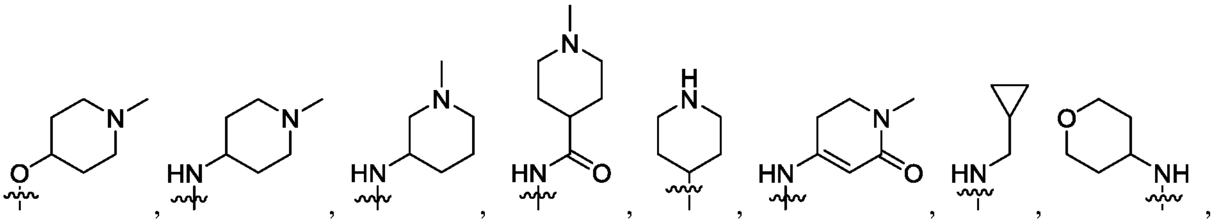
wherein R_1 is hydrogen, cyano, halogen, C_{1-7} alkyl, $-OR_a$, $-COR_a$, $-O(CO)R_a$, $-CONR_aR_b$, $-NHCOR_a$, $-NR_aR_b$, optionally substituted C_{3-10} cycloalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heterocyclyl or optionally substituted heterocyclylalkyl; wherein the optional substitution is selected from halogen or C_{1-7} alkyl;

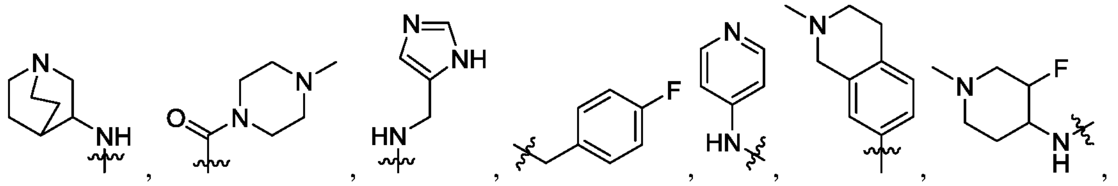
In a subclass of the above embodiment are compounds wherein R_a and R_b are independently selected from hydrogen, optionally substituted alkylamino, optionally substituted C_{3-10} cycloalkylalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl or optionally substituted C_{3-12} spiroheterocyclyl; wherein the optional substitution at each occurrence is independently 1-3 substituents selected from halogen, amino, oxo, $-S(O_2)R_3$, C_{1-7} alkyl or C_{3-10} cycloalkyl;

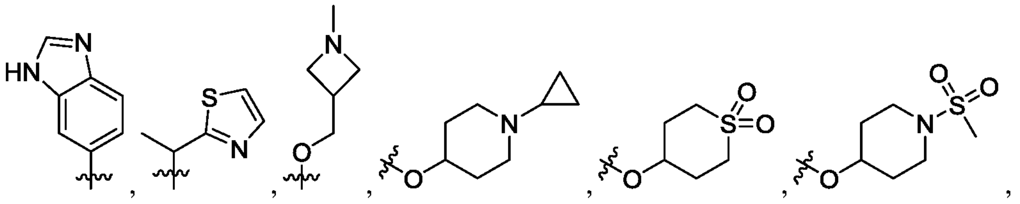
wherein the heterocyclyl group is a 3-10 membered mono or bicyclic ring containing 1-3 heteroatoms independently selected from N, NH, O, S or C(O).

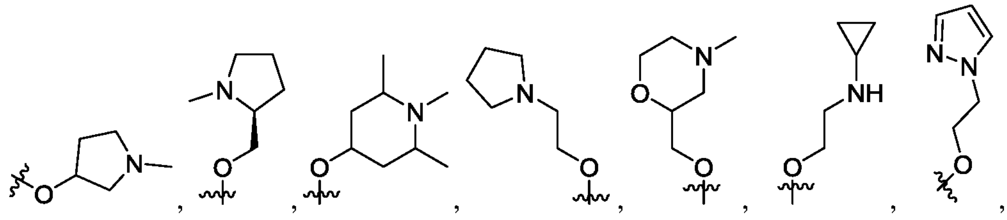
According to yet another embodiment, specifically provided are compounds of formula (I), or according to any other embodiment or subclass referred to above,

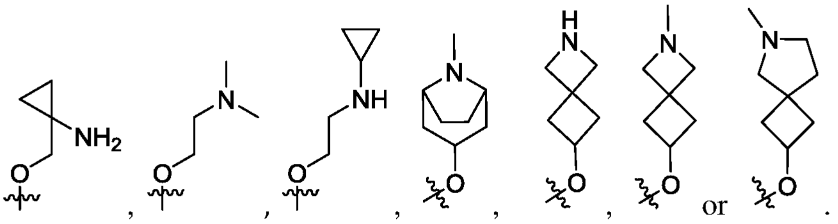
wherein R_1 is selected from one of the following groups or tautomers thereof hydrogen, hydroxyl, amino, bromo, chloro, cyano, methyl, CONH$_2$, cyclopropyl,











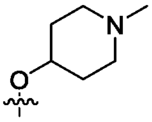
According to yet another embodiment, specifically provided are compounds of formula (I), or according to any other embodiment or subclass referred to above,

wherein Cy is cyclohexyl, phenyl, piperidinyl, pyridinyl, 1,4-benzodioxanyl, 2-oxobicyclo[2.2.1]heptane, [1,2,4]triazolo[4,3-a]pyridine, 1,2,3,4-tetrahydroisoquinoline or quinoline;

L is -NHS(O)$_2$-;

R$_2$ is halogen, C$_{1\text{-}7}$ alkyl or C$_{1\text{-}7}$ alkoxy;

R$_1$ is hydrogen, hydroxyl, amino, bromo, chloro, cyano, methyl, CONH$_2$, cyclopropyl,



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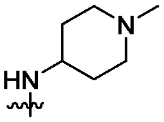

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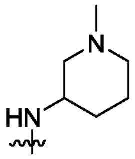

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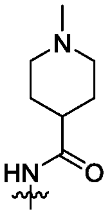

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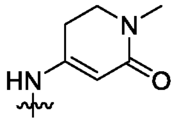

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According to one embodiment, specifically provided are compounds of formula (I), or according to any other embodiment or subclass referred to above,

Wherein R_1 is selected from halogen (such as chloro and bromo), C_{1-7} alkyl (such as methyl, ethyl and isopropyl) and C_{3-10} cycloalkyl (such as cyclopropyl).

In yet another particular embodiment of the present invention, the compound of formula (I) is:

Comp No	IUPAC name
1.	6-chloro-N-(2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)pyridine-3-sulfonamide;
2.	1-((1R)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl)-N-(2'-oxospiro[cyclo pentane-1,3'-indolin]-5'-yl)methanesulfonamide;
3.	2-methoxy-N-(2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)benzene sulfonamide;
4.	N-(2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-3-(1H-pyrazol-1-yl)benzene sulfonamide;
5.	3-(1H-imidazol-1-yl)-N-(2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)benzene sulfonamide;
6.	N-(2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)quinoline-8-sulfonamide;
7.	N-(2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-1,2,3,4-tetrahydroisoquinoline-7-sulfonamide;
8.	N-(7'-bromo-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2,3-dihydrobenzo[b][1,4]dioxine-6-sulfonamide;
9.	N-(2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)cyclohexanesulfonamide;
10.	N-(2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)piperidine-1-sulfonamide;
11.	6-chloro-N-(7'-methyl-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)pyridine-3-sulfonamide;
12.	N-(7'-bromo-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-3,5-difluoro-2-methoxybenzene sulfonamide;

13.	N-(7'-chloro-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-3-(1H-pyrazol-1-yl) benzene sulfonamide;
14.	N-(7'-cyclopropyl-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2,4-difluoro benzene sulfonamide;
15.	N-(7'-cyclopropyl-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-6-methyl pyridine-3 sulfonamide;
16.	N-(7'-cyclopropyl-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-methoxy benzene sulfonamide;
17.	N-(7'-cyclopropyl-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)pyridine-2-sulfonamide;
18.	N-(7'-bromo-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-6-chloropyridine-3-sulfonamide;
19.	2-(4-chlorophenyl)-N-(2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)propanamide;
20.	N-(7'-bromo-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-(2-methoxyphenyl) propanamide;
21.	N-(2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-[1,2,4]triazolo[4,3-a]pyridine-6-sulfonamide;
22.	N-(7'-amino-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2,4-difluorobenzene sulfonamide;
23.	N-(7'-amino-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-methoxybenzene sulfonamide;
24.	2,4-difluoro-N-(7'-((1-methylpiperidin-4-yl)amino)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
25.	2,4-difluoro-N-(7'-((1-methylpiperidin-3-yl)amino)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
26.	2-methoxy-N-(7'-((1-methylpiperidin-4-yl)amino)-2'-oxospiro[cyclopentane-1,3' indolin]-5'-yl)benzenesulfonamide;
27.	2-methoxy-N-(7'-((1-methylpiperidin-3-yl)amino)-2'-oxospiro[cyclopentane-1,3' indolin]-5'-yl)benzenesulfonamide;
28.	2,4-difluoro-N-(7'-((1-methyl-6-oxo-1,2,3,6-tetrahydropyridin-4-yl)amino)-2'-

	oxospiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
29.	N-(7'-cyano-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2,4-difluorobenzene sulfonamide;
30.	5'-(2,4-difluorophenylsulfonamido)-2'-oxospiro[cyclopentane-1,3'-indoline]-7'-carboxamide;
31.	N-(2-methoxyphenyl)-2'-oxospiro[cyclopentane-1,3'-indoline]-5'-sulfonamide;
32.	N-(5'-((2,4-difluorophenyl)sulfonamido)-2'-oxospiro[cyclopentane-1,3'-indolin]-7'-yl)-1-methylpiperidine-4-carboxamide;
33.	N-(7'-hydroxy-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-methoxybenzene sulfonamide;
34.	2-methoxy-N-(7'-((1-methylpiperidin-4-yl)oxy)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
35.	4-chloro-2-fluoro-N-(7'-((1methylpiperidin4yl)oxy)-2'-oxospiro[cyclopentane-1,3'-indolin]5'-yl)benzenesulfonamide;
36	N-(2'-oxo-7'-(piperidin-4-yl)spiro[cyclopentane-1,3'-indolin]-5'-yl)-2-(trifluoro methoxy)benzenesulfonamide;
37	N-(7'-((cyclopropylmethyl)amino)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-methoxybenzenesulfonamide;
38	2,4-difluoro-N-(2'-oxo-7'-(piperidin-4-ylamino)spiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
39	2,4-difluoro-N-(2'-oxo-7'-((tetrahydro-2H-pyran-4-yl)amino)spiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
40	2,4-difluoro-N-(2'-oxo-7'-(quinuclidin-3-ylamino)spiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
41	2,4-difluoro-N-(7'-(4-methylpiperazine-1-carbonyl)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
42	N-(7'-(((1H-imidazol-5-yl)methyl)amino)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2,4-difluorobenzenesulfonamide;
43	2,4-difluoro-N-(7'-(4-fluorobenzyl)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;

44	5'-((2,4-difluorophenyl)sulfonamido)-2'-oxo-N-(pyridin-4-yl)spiro[cyclopentane-1,3'-indoline]-7'-carboxamide;
45	5'-(cyclohexanesulfonamido)-N-(1-methylpiperidin-4-yl)-2'-oxospiro[cyclopentane-1,3'-indoline]-7'-carboxamide;
46	2,4-difluoro-N-(7'-(2-methyl-1,2,3,4-tetrahydroisoquinolin-7-yl)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
47	5'-((2-ethoxyphenyl)sulfonamido)-N-(1-methylpiperidin-4-yl)-2'-oxospiro[cyclopentane-1,3'-indoline]-7'-carboxamide;
48	N-(1-methylpiperidin-4-yl)-2'-oxo-5'-(piperidine-1-sulfonamido)spiro[cyclopentane-1,3'-indoline]-7'-carboxamide;
49	N-(7'-((3-fluoro-1-methylpiperidin-4-yl)amino)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-methoxybenzenesulfonamide;
50	N-(7'-(1H-benzo[d]imidazol-6-yl)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2,4-difluorobenzenesulfonamide;
51	2-methoxy-N-(2'-oxo-7'-(1-(thiazol-2-yl)ethyl)spiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
52	5'-((2-methoxyphenyl)sulfonamido)-2'-oxospiro[cyclopentane-1,3'-indolin]-7'-yl 4-methylpiperazine-1-carboxylate;
53	2-isopropoxy-N-(7'-((1-methylpiperidin-4-yl)oxy)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
54	2-methoxy-N-(7'-((1-methylazetidin-3-yl)methoxy)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
55	N-(7'-((1-ethylpiperidin-4-yl)oxy)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-methoxybenzenesulfonamide;
56	N-(7'-((1-cyclopropylpiperidin-4-yl)oxy)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-methoxybenzenesulfonamide;
57	5'-(((2-methoxyphenyl)(methyl)(oxo)-l6-sulfaneylidene)amino)-7'-((1-methylpiperidin-4-yl)amino)spiro[cyclopentane-1,3'-indolin]-2'-one;
58	N-(7'-((1,1-dioxidotetrahydro-2H-thiopyran-4-yl)oxy)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-methoxybenzenesulfonamide;

59	N-(7'-(2-(dimethylamino)ethoxy)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-methoxybenzenesulfonamide;
60	4-chloro-2-fluoro-N-(7'-((1-(methylsulfonyl)piperidin-4-yl)oxy)-2'-oxospiro [cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
61	4-chloro-2-fluoro-N-(7'-((1-methylpyrrolidin-3-yl)oxy)-2'-oxospiro[cyclo pentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
62	(S)-2-methoxy-N-(7'-((1-methylpyrrolidin-2-yl)methoxy)-2'-oxospiro[cyclo pentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
63	4-chloro-2-fluoro-N-(2'-oxo-7'-((1,2,6-trimethylpiperidin-4-yl)oxy)spiro[cyclo pentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
64	N-(7'-(2-(cyclopropylamino)ethoxy)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-methoxybenzenesulfonamide;
65	2-methoxy-N-(2'-oxo-7'-(2-(pyrrolidin-1-yl)ethoxy)spiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
66	4-chloro-2-fluoro-N-(7'-((4-methylmorpholin-2-yl)methoxy)-2'-oxospiro[cyclo pentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
67	N-(7'-(2-(1H-pyrazol-1-yl)ethoxy)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-4-chloro-2-fluorobenzenesulfonamide;
68	N-(7'-((1-aminocyclopropyl)methoxy)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-4-chloro-2-fluorobenzenesulfonamide;
69	2-methoxy-N-(7'-((8-methyl-8-azabicyclo[3.2.1]octan-3-yl)oxy)-2'-oxospiro [cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
70	N-(7'-((2-azaspiro[3.3]heptan-6-yl)oxy)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-4-chloro-2-fluorobenzenesulfonamide;
71	N-(7'-((1-methylpiperidin-4-yl)oxy)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-morpholinopyridine-3-sulfonamide;
72	4-chloro-2-fluoro-N-(7'-((2-methyl-2-azaspiro[3.3]heptan-6-yl)oxy)-2'-oxospiro [cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
73	4-chloro-2-fluoro-N-(7'-((6-methyl-6-azaspiro[3.4]octan-2-yl)oxy)-2'-oxospiro [cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;

74	4-fluoro-N-(7'-methoxy-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-((2-methyl-2-azaspiro[3.3]heptan-6-yl)oxy)benzenesulfonamide; and
75	N-(7'-methoxy-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-(oxetan-3-yloxy) Benzenesulfonamide;

or a pharmaceutically acceptable salt or a stereoisomer thereof.

In a further embodiment, the present invention provides processes for preparing spiro[cyclopentane-1,3'-indolin]-2'-one derivatives of formula (I).

In yet another embodiment according to the present patent application, it provides a pharmaceutical composition comprising the compound of formula (I) of the present invention and at least one pharmaceutically acceptable excipient (such as a pharmaceutically acceptable carrier or diluent). Preferably, the pharmaceutical composition comprises a therapeutically effective amount of at least one compound described herein.

In yet another embodiment, compounds of the present invention inhibit one or more of BRD2, BRD3, BRD4, BRDT, and/or another member of the bromodomain-containing proteins, or a mutant thereof.

In yet another embodiment, compounds of the present invention inhibit two or more of BRD2, BRD3, BRD4, BRDT, and/or another member of the bromodomain-containing proteins, or a mutant thereof.

In yet another embodiment, compounds of the present invention are inhibitors of one of more of the bromodomain-containing proteins, such as BRD2, BRD3, BRD4, and/or BRDT and are therefore useful for treating one or more disorders associated with activity of one or more of the bromodomain-containing proteins, such as BRD2, BRD3, BRD4, and/or BRDT. Thus, in yet another embodiment, the present invention provides a method for treating an bromodomain-containing protein-mediated disorder, such as a BET-mediated, a BRD2-mediated, a BRD3-mediated, a BRD4-mediated disorder, and/or a BRDT-mediated disorder comprising the step of inhibiting a bromodomain-containing protein, such as a BET protein, such as BRD2, BRD3, BRD4, and/or BRDT, or a mutant thereof, by administering to a patient in need thereof a provided compound, or a pharmaceutically acceptable composition thereof.

As used herein, the terms “bromodomain-containing protein-mediated”, “BET-mediated”, “BRD2-mediated”, “BRD3-mediated”, “BRD4-mediated”, and/or “BRDT-mediated” disorders or conditions means any disease or other deleterious condition in which one or more of the bromodomain-containing proteins, such as BET proteins, such as BRD2, BRD3, BRD4 and/or BRDT, or a mutant thereof, are known to play a role. Accordingly, another embodiment of the present invention relates to treating or lessening the severity of one or more diseases in which one or more of the bromodomain-containing proteins, such as BET proteins, such as BRD2, BRD3, BRD4, and/or BRDT, or a mutant thereof, are known to play a role.

In yet another embodiment, diseases and conditions treatable according to the methods of this invention include, but are not limited to, cancer and other proliferative disorders, inflammatory diseases, sepsis, autoimmune disease, and viral infection.

In certain embodiments, the disorder or disease is an inflammatory disorder or disease.

In certain embodiments, the disorder or disease is an autoimmune disorder or disease.

In certain embodiments, the disorder or disease is cancer.

In yet another embodiment, a method of treating a subject is having a disease, disorder, or symptom thereof comprising administration of a therapeutically effective amount of a compound or composition of the present invention to the subject.

In yet another embodiment, the present invention provides use of a compound of formula (I) or a pharmaceutically acceptable salt or a stereoisomer thereof; for the manufacture of a medicament for the treatment of a disease or a disorder mediated by bromodomain containing proteins.

In certain embodiments, the subject is a human.

In certain embodiments, the present invention provides compounds for use as a medicament.

In certain embodiments, the invention provides the use of the compounds of the present invention in the manufacture of a medicament.

In certain embodiments, the invention provides the use of the compounds of the present invention in the manufacture of a medicament for the treatment of immune or inflammatory disorder or disease.

In certain embodiments, the present invention provides compounds for use as a medicament for the treatment of immune or inflammatory disorder or disease.

In certain embodiments, the medicament is for treating a disease or disorder mediated by bromodomain containing proteins.

In certain embodiments, the present invention provides a method of modulating the function of a bromodomain in a subject in need thereof by administering to the subject a therapeutically effective amount of a compound of formula (I).

In certain embodiments, the present invention provides compounds of formula (I) for use in the manufacture of a medicament for the treatment or prevention of diseases or disorders mediated by bromodomain containing proteins.

Bromodomain inhibitors are believed to be useful in the treatment of a variety of diseases or conditions related to systemic or tissue inflammation, inflammatory responses to infection or hypoxia, cellular activation and proliferation, lipid metabolism, fibrosis and in the prevention and treatment of viral infections.

Bromodomain inhibitors may be useful in the treatment of a wide variety of chronic autoimmune and inflammatory conditions such as rheumatoid arthritis, osteoarthritis, acute gout, psoriasis, systemic lupus erythematosus, multiple sclerosis, inflammatory bowel disease (Crohn's disease and Ulcerative colitis), asthma, chronic obstructive airways disease, pneumonitis, myocarditis, pericarditis, myositis, eczema, dermatitis, alopecia, vitiligo, bullous skin diseases, nephritis, vasculitis, atherosclerosis, Alzheimer's disease, depression, retinitis, uveitis, scleritis, hepatitis, pancreatitis, primary biliary cirrhosis, sclerosing cholangitis, Addison's disease, hypophysitis, thyroiditis, type I diabetes and acute rejection of transplanted organs.

Bromodomain inhibitors may be useful in the treatment of a wide variety of acute inflammatory conditions such as acute gout, giant cell arteritis, nephritis including lupus nephritis, vasculitis with organ involvement such as glomerulonephritis, vasculitis including giant cell arteritis, Wegener's granulomatosis, Polyarteritisnodosa, Behcet's disease, Kawasaki disease, Takayasu's Arteritis, vasculitis with organ involvement and acute rejection of transplanted organs.

Bromodomain inhibitors may be useful in the prevention or treatment of diseases or conditions which involve inflammatory responses to infections with bacteria, viruses, fungi, parasites or their toxins, such as sepsis, sepsis syndrome, septic shock, endotoxaemia, systemic inflammatory response syndrome (SIRS), multi-organ dysfunction syndrome, toxic shock syndrome, acute lung injury, ARDS (adult respiratory distress syndrome), acute renal failure, fulminant hepatitis, burns, acute pancreatitis, post-surgical syndromes, sarcoidosis, Herxheimer reactions, encephalitis, myelitis, meningitis, malaria and SIRS associated with viral infections such as influenza, herpes zoster, herpes simplex and coronavirus.

Bromodomain inhibitors may be useful in the prevention or treatment of conditions associated with ischaemia-reperfusion injury such as myocardial infarction, cerebro- vascular ischaemia (stroke), acute coronary syndromes, renal reperfusion injury, organ transplantation, coronary artery bypass grafting, cardio-pulmonary bypass procedures, pulmonary, renal, hepatic, gastro-intestinal or peripheral limb embolism.

Bromodomain inhibitors may be useful in the treatment of disorders of lipid metabolism via the regulation of APO-A1 such as hypercholesterolemia, atherosclerosis and Alzheimer's disease.

Bromodomain inhibitors may be useful in the treatment of fibrotic conditions such as idiopathic pulmonary fibrosis, renal fibrosis, post-operative stricture, keloid formation, scleroderma and cardiac fibrosis.

Bromodomain inhibitors may be useful in the prevention and treatment of viral infections such as herpes virus, human papilloma virus, adenovirus and poxvirus and other DNA viruses.

Bromodomain inhibitors may be useful in the treatment of cancer, including hematological, epithelial including lung, breast and colon carcinomas, midline carcinomas, mesenchymal, hepatic, renal and neurological tumors.

In one embodiment the disease or condition for which a bromodomain inhibitor is indicated is selected from diseases associated with systemic inflammatory response syndrome, such as sepsis, burns, pancreatitis, major trauma, haemorrhage and ischaemia. In this embodiment the bromodomain inhibitor would be administered at the point of diagnosis to reduce the incidence of: SIRS, the onset of shock, multi-organ dysfunction syndrome, which includes the onset of acute lung injury, ARDS, acute renal, hepatic, cardiac and gastro-intestinal injury and mortality.

In another embodiment the bromodomain inhibitor would be administered prior to surgical or other procedures associated with a high risk of sepsis, haemorrhage, extensive tissue damage, SIRS or MODS (multiple organ dysfunction syndrome).

In a particular embodiment the disease or condition for which a bromodomain inhibitor is indicated is sepsis, sepsis syndrome, septic shock and endotoxaemia. In another embodiment, the bromodomain inhibitor is indicated for the treatment of acute or chronic pancreatitis. In another embodiment the bromodomain is indicated for the treatment of burns. In one embodiment the disease or condition for which a bromodomain inhibitor is indicated is selected from herpes simplex infections and reactivations, cold sores, herpes zoster infections and reactivations, chickenpox, shingles, human papilloma virus, cervical neoplasia, adenovirus infections, including acute respiratory disease, poxvirus infections such as cowpox and smallpox and African swine fever virus. In one particular embodiment a bromodomain inhibitor is indicated for the treatment of Human papilloma virus infections of skin or cervical epithelia.

The term "diseases or conditions for which a bromodomain inhibitor is indicated", is intended to include each of or all of the above disease states.

While it is possible that for use in therapy, a compound of formula (I) as well as pharmaceutically acceptable salts thereof may be administered as the raw chemical, it is common to present the active ingredient as a pharmaceutical composition.

The compounds and pharmaceutically compositions of the present invention may be used in combination with other drugs that are used in the treatment/prevention/suppression or amelioration of the diseases or conditions for which compounds of the present invention may be useful. Such other drugs may be administered, by a route and in an amount commonly used there for, contemporaneously or sequentially with a compound of the present invention. When a compound of the present invention is used contemporaneously with one or more other drugs, a pharmaceutical composition containing such other drugs in addition to the compound of the present invention may also be preferred. Accordingly, the pharmaceutical compositions of the present invention include those that also contain one or more other active ingredients, in addition to a compound of the present invention.

A pharmaceutical composition of the invention may be formulated as being compatible with its intended route of administration, which may preferably be an oral administration. For example the pharmaceutical compositions of the invention may be formulated for administration by inhalation, such as aerosols or dry powders; for oral administration, such in the form of tablets, capsules, gels, syrups, suspensions, emulsions, elixirs, solutions, powders or granules; for rectal or vaginal administration, such as suppositories; or for parenteral injection (including intravenous, subcutaneous, intramuscular, intravascular, or infusion) such as a sterile solution, suspension or emulsion.

The compounds of the present invention may also be entrapped in microcapsules prepared, for example, by coacervation techniques or by interfacial polymerization, for example, hydroxymethyl cellulose or gelatin-microcapsules and poly-(methylmethacylate) microcapsules, respectively, in colloidal drug delivery systems (for example, liposomes, albumin microspheres, microemulsions, nano-particles and nanocapsules) or in macroemulsions. Such techniques are disclosed in Remington's Pharmaceutical Sciences 16th edition, *Osol, A. Ed.* (1980).

The spiro[cyclopentane-1,3'-indolin]-2'-one derivatives of formula (I) according to the present invention may be prepared from readily available starting materials using the following general methods and procedures. It will be appreciated that where typical or preferred experimental conditions (i.e. reaction temperatures, time, moles of reagents, solvents etc.) are given, other experimental conditions can also be used unless otherwise stated. Optimum reaction conditions may vary with the particular reactants or solvents used, but such conditions can be determined by the person skilled in the art, using routine optimization procedures. The specifics of the processes according to the present invention are detailed in the example section mentioned below.

In a further aspect, the compounds of the present invention can also contain unnatural proportions of atomic isotopes at one or more of the atoms that constitute such compounds. For example, the present invention also embraces isotopically-labeled variants of the present invention which are identical to those recited herein, but for the fact that one or more atoms of the compound are replaced by an atom having the atomic mass or mass number different from the predominant atomic mass or mass number usually found in nature for the atom. All isotopes of any particular atom or element as specified are contemplated within the scope of the compounds of the invention, and their uses. Exemplary isotopes that can be incorporated in to compounds of the invention include isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorous, sulfur, fluorine, chlorine and iodine, such as ^{2}H ("D"), ^{3}H, ^{11}C, ^{13}C, ^{14}C, ^{13}N, ^{15}N, ^{15}O, ^{17}O, ^{18}O, ^{32}P, ^{33}P, ^{35}S, ^{18}F, ^{36}Cl, ^{123}I and ^{125}I. Isotopically labeled compounds of the present inventions can generally be prepared by following procedures analogous to those disclosed in the Schemes and/or in the examples herein below, by substituting an isotopically labeled reagent for a non-isotopically labeled reagent.

The abbreviations used in the entire specification may be summarized herein below with their particular meaning.

MeOH – Methanol; EtOH – Ethanol; Me – methyl; Et – Ethyl; DEA – Diethanolamine; DME – 1, 2-dimethoxyethane; DCM – Dichloromethane; DMF – N, N-Dimethyl formamide; DMSO – Dimethylsulfoxide; $CDCl_3$–Deuterated chloroform; EtOAc – Ethyl acetate; THF – Tetrahydrofuran; $NaHCO_3$ - Sodium bicarbonate; PyBOP - benzotriazol-1-yl-oxytripyrrolidino phosphonium hexafluorophosphate; TEA – Triethylamine; DIEA – Diisopropyl ethylamine; HMPA - Hexamethylphosphoramide; mL – milliliter; EDC.HCl - 1-Ethyl-3-(3-dimethylamino propyl) carbodiimide hydrochloride; CaO – Calcium oxide; CS_2 - carbon disulfide; HOBt – 1-Hydroxybenzotriazole; TLC – Thin layer chromatography; KNO_3 – Potassium nitrate; H_2SO_4 – Sulfuric acid; KOAc – Potassium acetate; DPPF - 1 1'-bis(diphenylphosphino)ferrocene; NBS - N-Bromosuccinimide; NCS – N-Chlorosuccinimide; Na_2CO_3 – Sodium carbonate; $SnCl_2.2H_2O$ – Stannous chloride dihydrate; $POCl_3$ – Phosphorous oxy chloride; NaOH – Sodium hydroxide; HCl – Hydrochloric acid; Pd $(pph_3)_4$ –Tetrakis (triphenylphosphine) palladium (0); Pd/C – Palladium on activated carbon; Pd(amphos)Cl_2 - Bis(di-tert-butyl(4-dimethylaminophenyl) phosphine)dichloropalladium(II); H_2O – Water; Fe – Iron powder; h- Hours; RT – room temperature (20-35°C); N – Normality; M- Molarity; s- Singlet; d- Doublet; dd - Doublet of a doublet; t- Triplet; m- Multiplet; ^{1}HNMR – Proton nuclear magnetic resonance; MS – Mass spectroscopy; LC – Liquid chromatography; HPLC- High performance liquid chromatography; ^{1}H – Proton; MHz – Mega hertz; Hz – Hertz; ppm – Parts per million; bs – Broad singlet; ES – Electro spray; Conc – Concentrated; g- Gram; mmol – millimol; min –minutes; μ – micro; nm – nano molar; δ – Chemical shift expressed in ppm; ee- enantiomeric excess.

Although the invention has been illustrated by certain of the preceding examples, it is not to be construed as being limited thereby; but rather, the invention encompasses the generic area as hereinbefore disclosed. Various modifications and embodiments can be made without departing from the spirit and scope thereof.

The MS data provided in the examples described below were obtained as follows:
Mass spectrum: LC/MS Agilent 6120 Quadrapole LC/MS.

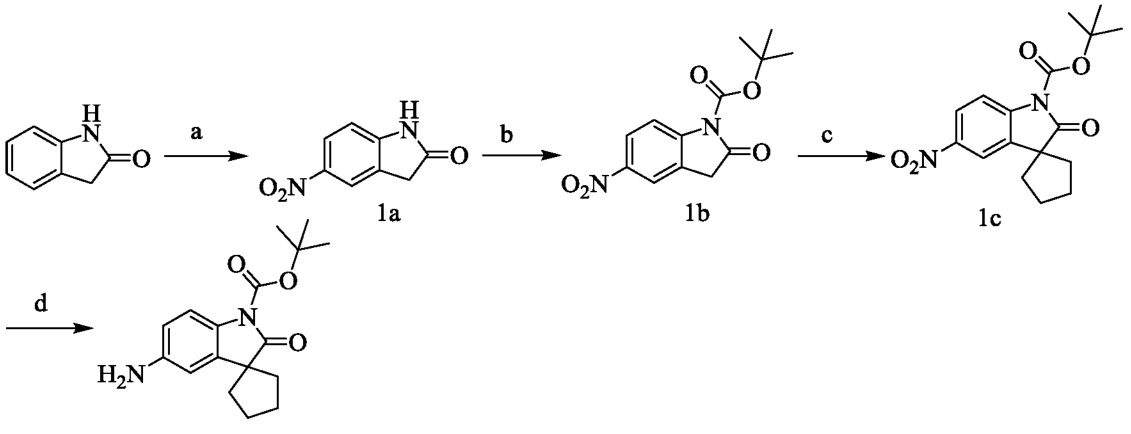
The NMR data provided in the examples described below were obtained as follows:
^{1}H-NMR: Varian 600, 400, 300 MHz.

The microwave chemistry was performed on a CEM Explorer.

The procedure for the compounds of Formula (I) are detailed herein below stepwise including the general synthesis of various intermediates involved in process of manufacture of the compounds according to the present invention.

Examples:

Intermediate-1: Synthesis of *tert*-butyl 5'-amino-2'-oxospiro[cyclopentane-1,3'-indoline]-1'-carboxylate:



Intermediate-1

Step-a: Synthesis of 5-nitroindolin-2-one:

To a stirred solution of oxindole (20 g, 150 mmol) in 100 mL of Conc. H_2SO_4 at -15 °C was added fuming HNO_3 (9.47 g, 150 mmol) drop wise. The reaction mixture was allowed to maintain the temperature at -15 °C for 0.5h. After completion of the reaction, the reaction mixture was poured into crushed ice. The yellow solid precipitate out which was isolated by filtration and dried under vacuum (13 g, 48%). ^{1}H-NMR (300 MHz, DMSO-d_6) δ 11 (s, 1H), 8.20-8.10 (m, 2H), 7.00 (d, *J*=8.4 Hz, 1H), 3.6 (s, 2H).LC-MS: *m/z* 177 $(M-H)^-$.

Step-b: Synthesis of tert-butyl 5-nitro-2-oxoindoline-1-carboxylate:

Di-tert-butyl dicarbonate (5.51 g, 25.27 mmol) and sodium hydrogen carbonate (12.73 g, 151.65 mmol) were added to a stirred solution of 5-nitroindolin-2-one (3.0 g, 16.85 mmol) in tetrahydrofuran (150 mL) and the mixture was heated to 60 °C. After 3h the reaction mixture was cooled and filtered, the filtrate was concentrated in reduced pressure to obtain a crude compound. The obtained crude was purified by silica gel chromatography using a mixture of 10% ethyl acetate/hexane as an eluent to get the desired compound as a white solid (3.68 g, 51%). ^{1}H-NMR (300 MHz, DMSO- d_6) δ 8.3 (m, 1H), 8.2 (s, 1H), 7.9 (m, 1H), 3.8 (s, 2H), 1.5 (s, 9H); LC-MS: *m/* LC-MS: 278.8 $(M+H)^+$.

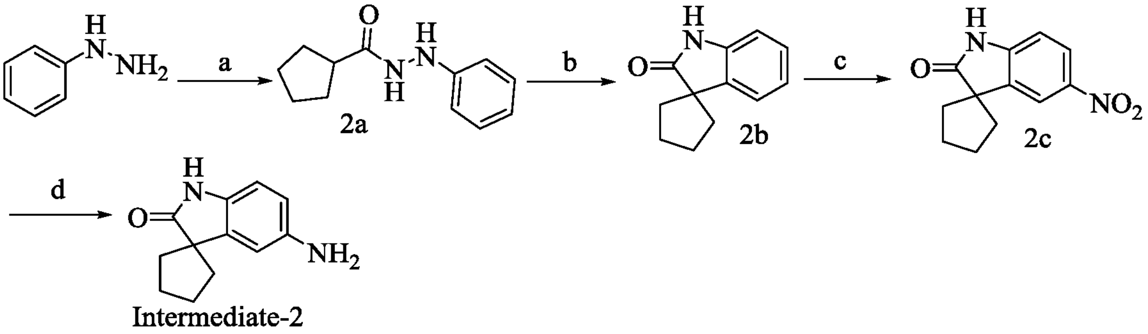
Step-c: Synthesis of tert-butyl 5'-nitro-2'-oxospiro[cyclopentane-1,3'-indoline]-1'-carboxylate:

To a stirred solution of *tert*-butyl 5-nitro-2-oxoindoline-1-carboxylate (2 g, 7 mol), 1, 3-dibromobutane (3.09 g, 14.0 mol) in DMF (20 mL) was added cesium carbonate (6.8 g, 21 mol) in portions. After stirring it for 12 h the mixture was filtered and the filtrate was concentrated under reduced pressure get residue. The residue was purified by column chromatography using 5% ethyl acetate in hexane as eluent to get the title compound as a white solid (1.2 g, 50%). ^{1}H-NMR (300 MHz, DMSO-d_6) δ 8.23-8.20 (m, 1H), 8.07-8.06 (m, 1H), 8.02-7.99 (m, 1H), 2.31-2.24 (m, 2H), 2.15-2.03 (m, 4H), 1.96-1.90 (m, 2H),1.65 (s, 9H).

Step-d: Synthesis of tert-butyl 5'-amino-2'-oxospiro [cyclopentane -1,3'-indoline]-1'-carboxylate:

A stirred solution of tert-butyl 5'-nitro-2'-oxospiro[cyclopentane-1,3'-indoline]-1'-carboxylate (1.2 g, 3.6 mol) in methanol (20 mL) was added Pd-C (300 mg) under nitrogen atmosphere. Then the reaction mixture was stirred under the pressure of hydrogen atmosphere using bladder for 2h. The reaction mixture was filtered through celite® pad and washed with methanol. The filtrate was concentrated to get the title compound as a white solid (1 g, 91%). LC-MS: 303.3 $(M+H)^+$.

Intermediate-2: Synthesis of 5'-aminospiro[cyclopentane-1,3'-indolin]-2'-one:



Step-a: Synthesis of N'-phenylcyclopentanecarbohydrazide:

To a stirred solution of phenyl hydrazine (12.6 mL, 152 mmol) in a mixture of pyridine in 30 mL of DMF, cyclopentanecarbonyl chloride (6.7 g, 50.9 mmol) (5 mL, 50.9 mmol) was added drop wise at room temperature. The reaction mixture was allowed to stir at RT for 1h and poured into 200 mL of a 1M HCl solution. The precipitated solid was filtered, washed with 50 mL water and dried. The obtained solid was washed with 20 mL of diethyl ether and dried under –reduced pressure to afford the title compound as a white solid (3.5 g, 41%). ^{1}H NMR 400 MHz

(DMSO-d_6) δ 9.51 (s, 1H), 7.34 (bs, 1H), 7.91-7.10 (m, 2H), 6.69-6.65 (m, 3H), 2.68-2.60 (m, 1H), 1.84-1.77 (m, 2H), 1.64-1.52 (m, 6H); MS (ES) *m/e* 205.1 $(M+H)^+$.

Step-b: Synthesis of spiro[cyclopentane-1,3'-indolin]-2'-one:

To a stirred suspension of calcium oxide (2.75 g, 49 mmol) in quinoline (10 mL) was added N-phenylcyclopentanecarbohydrazide (1 g, 4.9 mmol). The mixture was heated to 270-310 °C for 75 min. The reaction mixture was cooled to room temperature and 2M aqueous hydrochloric acid was added. The mixture was extracted with ethyl acetate and combined extracts were washed with 2M hydrochloric acid, brine and dried over Na_2SO_4. The obtained crude was purified by chromatography on silica gel (40-60% EtOAc in hexanes) to give the desired product as an orange solid (0.6 g, 65%). ^{1}H NMR 400 MHz (DMSO-d_6) δ 10.25 (bs, 1H), 7.22 (d, J=7.2 Hz, 1H), 7.16-7.14 (m, 1H), 6.95-6.92 (m, 1H), 6.81 (d, J=7.2 Hz, 1H), 1.97-1.90 (m, 6H), 1.76-1.71 (m, 2H); MS (ES) *m/e* 188.1 $(M+H)^+$.

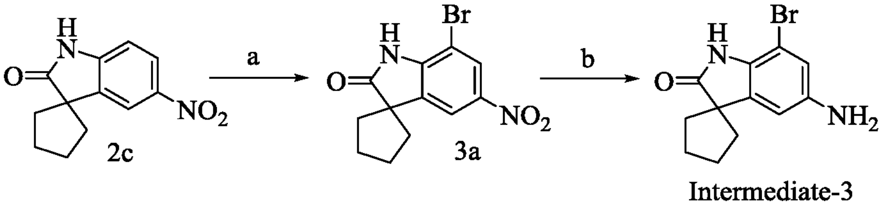
Step-c: Synthesis of 5'-nitrospiro[cyclopentane-1,3'-indolin]-2'-one:

To a stirred solution of Spiro[cyclopentane-1,3'-indolin]-2'-one (0.6 g) in 5.0 mL of concentrated sulfuric acid at -15 °C was added fuming nitric acid (0.2 mL) drop wise. The reaction mixture was allowed stir at RT for 0.5h and then poured into ice water. A yellow precipitate formed was collected by filtration. The desired product obtained as a white solid. (0.5 g, 67%). This was taken as such to next step. ^{1}HNMR (400 MHz, DMSO-d_6) δ 10.98 (bs, 1H), 8.15 (dd, J=2.2 & 8.6 Hz, 1H), 8.09 (d, J=1.6 Hz, 1H), 7.01 (d, J=8.3 Hz, 1H), 1.99-1.91 (m, 6H), 1.89-1.86 (m, 2H); MS (ES) *m/e* 233.2 $(M+H)^+$.

Step-d: Synthesis of 5'-aminospiro[cyclopentane-1,3'-indolin]-2'-one:

The process for this step was depicted in step-d of intermediate-1 by using 5'-nitrospiro[cyclopentane-1,3'-indolin]-2'-one as starting material. The desired product obtained as a white solid (0.1 g, 21%). ^{1}H NMR (400 MHz, DMSO- d_6) δ 9.80 (bs, 1H), 6.52 (d, J=2.0 Hz, 1H), 6.49 (d, J=8.0 Hz, 1H), 6.36-6.34 (m, 1H), 4.60 (bs, 2H), 1.98-1.87 (m, 6H), 1.67-1.65 (m, 2H); MS (ES): *m/e* 203.2 $(M+H)^+$.

Intermediate-3: Synthesis of 5'-amino-7'-bromospiro[cyclopentane-1,3'-indolin]-2'-one:



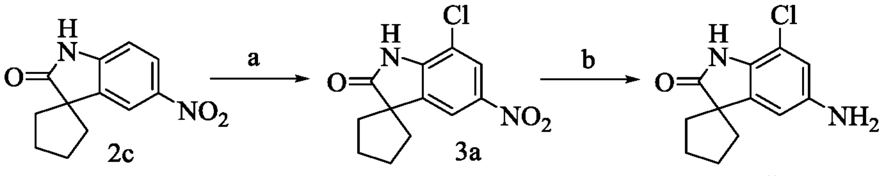
Step-a: Synthesis of 7'-bromo-5'-nitrospiro[cyclopentane-1,3'-indolin]-2'-one:

N-Bromosuccinamide (1.265 g, 7.1 mmol) was added in portions to 5'-nitrospiro [cyclo pentane-1,3'-indolin]-2'-one (1.1 g, 4.7 mmol, step-c product of intermediate-2) in 10 mL of Con.H_2SO_4. The reaction mixture was stirred for 5h at room temperature and poured into 200 mL of cold water. The precipitated solid was filtered, and then the solid was washed with 50 mL water and dried under reduced pressure to afford the title compound as a white solid (1.4 g, 95%). ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.2-10.95 (bs, 1H), δ 8.3 (m, 1H), 8.1 (m, 1H), 2.0-1.9 (m, 4H), 1.65-1.55(m, 4H); LC-MS: *m/z* 311 $(M+H)^+$.

Step-b: Synthesis of 5'-amino-7'-bromospiro[cyclopentane-1,3'-indolin]-2'-one:

The process for this step was depicted in step-d of Intermediate-1 by using 7'-bromo-5'-nitrospiro[cyclopentane-1,3'-indolin]-2'-one as starting material. The desired product obtained as white solid (1.1 g, 87%). LC-MS: *m/z* 281.2 $(M+H)^+$.

Intermediate-4: Synthesis of 5'-amino-7'-chlorospiro[cyclopentane-1,3'-indolin]-2'-one:



Intermediate-4

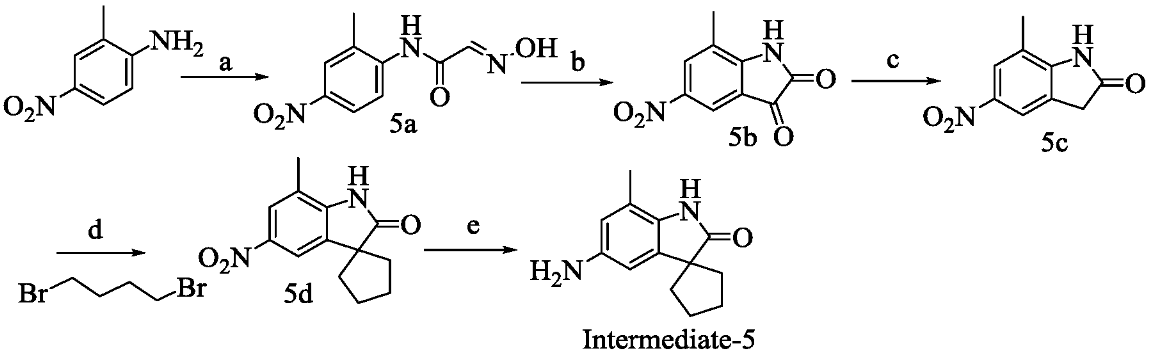
Step-a: Synthesis of 7'-chloro-5'-nitrospiro[cyclopentane-1,3'-indolin]-2'-one:

The process for this step was depicted in step-a of intermediate-3 by using 5'-nitrospiro[cyclopentane-1,3'-indolin]-2'-one (step-c product of intermediate-2) as starting material. The desired product obtained as an off-white solid. The compound used in the next step without analysis.

Step-b: Synthesis of 5'-amino-7'-chlorospiro[cyclopentane-1,3'-indolin]-2'-one:

The process for this step was depicted in step-d of intermediate-1 by using 7'-chloro-5'-nitrospiro[cyclopentane-1,3'-indolin]-2'-one as starting material. The desired product obtained as an off-white (0.33 g, 90%). ^{1}H-NMR (300 MHz, DMSO-d_6) δ 10.1 (s, 1H), 6.48 (m, 1H), 6.39 (m, 1H), 4.94 (s, 2H), 1.99-1.87 (m, 6H), 1.69-1.67 (m, 2H); LC-MS: *m/z* 237 $(M+H)^+$.

Intermediate-5: Synthesis of 5'-amino-7'-methylspiro[cyclopentane-1,3'-indolin]-2'-one:



Step-a: Synthesis of (*E*)-2-(hydroxyimino)-N-(2-methyl-4-nitrophenyl) acetamide:

To a stirred suspension of 2-methyl-4-nitro aniline (5 g, 32.8 mmol) in water (100 mL) were added chloral hydrate (5.42 g, 32.8 mmol), anhydrous sodium sulphate (37.3 g, 36.0 mmol), hydroxylamine hydrochloride (7.54 g, 108 mmol) and 5 mL of Conc. HCl. The resulting mixture was stirred at 120 °C for 40 min. Then the reaction mixture was cooled to room temperature and the precipitated solid was collected and dried to afford the title compound as a pale-yellow solid (7 g, 95%). ^{1}H-NMR (400 MHz, DMSO-d_6): δ 12.41 (s, 1H), 9.67 (s, 1H), 8.09-8.01 (m, 2H), 7.78 (s, 1H), 7.75 (s, 1H), 2.24 (s, 3H); MS (ES): 222.1 *m/z* (M-H)$^-$.

Step-b: Synthesis of 7-methyl-5-nitroindoline-2,3-dione:

To a conc.H_2SO_4 (70 mL) was added (*E*)-2-(hydroxyimino)-N-(2-methyl-4-nitrophenyl) acetamide (7 g, 31.39 mmol) in portions at 60-70 °C. After completion of addition, the reaction mixture was heated to 80 °C for 20 min. The reaction mixture was then allowed to cool to room temperature and poured into ice cooled water. The precipitated solid was filtered and dried to afford the title compound as a brick red solid (3 g, 46%); ^{1}H-NMR (400 MHz, DMSO-d_6) δ 11.71 (s, 1H) 8.32 (s, 1H), 8.06 (s, 1H), 2.38 (s, 3H); MS (ES): 205.1 *m/z* (M-H)$^-$.

Step-c: Synthesis of 7-methyl-5-nitroindolin-2-one:

To a stirred suspension of 7-methyl-5-nitroindoline-2,3-dione (1 g, 4.8 mmol) in 20 ml of ethylene glycol was added hydrazine hydrate (0.233 g, 7.2 mmol). The reaction mixture was heated at 120 °C for 16h. After completion of the reaction, the reaction mixture was cooled and the solid was filtered which was purified by column chromatography (3-10 % MeOH in CH_2Cl_2) over silica gel (60-120 mesh) to afford the title compound as a pale-yellow solid (0.55 g, 59%)^{1}H-NMR (400 MHz, DMSO-d_6): δ 11.09 (bs, 1H), 8.00 (s, 1H), 7.96 (s, 1H), 3.64 (s, 2H), 2.32 (s, 3H). MS (ES): 191.2 m/z (M-H)$^-$.

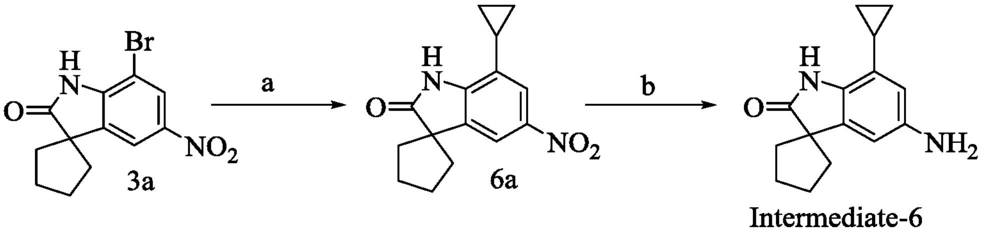
Step-d: Synthesis of 7'-methyl-5'-nitrospiro[cyclopentane-1,3'-indolin]-2'-one:

To a stirred solution of 7-methyl-5-nitroindolin-2-one (0.5g, 2.0 mmol) in dry THF was added potassium *tert*-butoxide (0.683 g, 6.0 mmol) in portions at -15 °C and stirred for 30 min. Subsequently 1,4 dibromobutane (0.521 g, 2.04 mmol) was added and the reaction mixture was stirred at 0 °C for 1h. The reaction mixture was quenched with 1N HCl and extracted with ethyl acetate, dried over sodium sulphate and concentrated under reduced pressure. The crude material was purified by column chromatography using 5% ethyl acetate in hexanes as eluent to afford the title compound as a pale-yellow solid (0.190 g, 29%). ^{1}H-NMR (400 MHz, DMSO-d$_6$): δ 11.03 (bs, 1H), 8.00 (d, J=1.6 Hz, 1H), 7.94 (d, J=2.4 Hz, 1H), 2.33 (s, 3H), 2.08-1.94 (m, 8H); MS (ES): 245.2 m/z (M-H)$^-$.

Step-e: Synthesis of 5'-amino-7'-methyl spiro[cyclopentane-1,3'-indolin]-2'-one:

The process for this step was depicted in step-d of Intermediate-1 by using 7'-methyl-5'-nitrospiro[cyclopentane-1,3'-indolin]-2'-one as starting material. The desired product obtained as brown solid (0.150 g, 90%). ^{1}H-NMR (400 MHz, DMSO-d$_6$): δ 9.87 (bs, 1H), 6.33 (d, J=1.6 Hz, 1H), 6.18 (d, J=2.0 Hz, 1H), 4.56 (bs, 2H), 2.08 (s, 3H), 1.96-1.66 (m, 8H); MS (ES): 217.1 m/z (M+H)$^+$.

Intermediate-6: Synthesis of 5'-amino-7'-cyclopropylspiro[cyclopentane-1,3'-indolin]-2'-one:



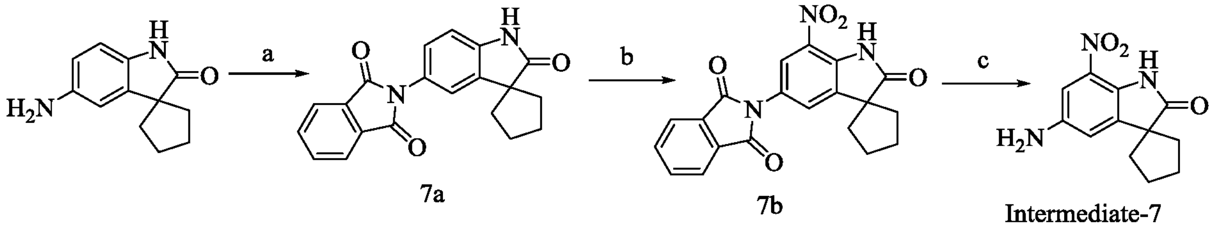
Step-a: Synthesis of 7'-cyclopropyl-5'-nitrospiro[cyclopentane-1,3'-indolin]-2'-one:

To a stirred mixture of 7'-bromo-5'-nitrospiro[cyclopentane-1,3'-indolin]-2'-one (2 g, 6.43 mmol, step-a product of intermediate-3), potassium phosphate (3.40 g, 16.07 mmol) in 1,4-dioxane/water (25 mL/8 mL) was added cyclopropylboronic acid (1.65 g, 19.29 mmol). This mixture was purged with argon for 10 min and added PdCl$_2$(Amphos) (0.45 g, 0.64 mmol and heated to 100 °C for 12h. The reaction mixture was then cooled to RT, diluted with ethyl acetate, washed with water, the organic layer was dried over sodium sulfate and concentrated to give the title compound as white solid (1.5g, 85%). ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 9.87 (bs, 1H), 6.33 (d, J=1.6 Hz, 1H), 6.18 (d, J=2.0 Hz, 1H), 4.56 (bs, 2H), 2.08 (s, 3H), 1.96-1.66 (m, 8H). MS (ES): 271.1 m/z (M-H)$^-$.

Step-b: Synthesis of 5'-amino-7'-cyclopropylspiro[cyclopentane-1,3'-indolin]-2'-one:

The process for this step was depicted in step-d of intermediate-1 by using 7'-cyclopropyl-5'-nitrospiro[cyclopentane-1,3'-indolin]-2'-one as starting material. The desired product obtained as pale-yellow solid (0.8g, 89.9%). ^{1}H NMR (300 MHz, DMSO-d$_6$): δ 10.05 (s, 1H), 6.317(d, J=1.8 Hz, 1H), 5.886(d, J=1.8 Hz, 1H), 4.75 (bs, 2H), 1.96-1.66 (m, 8H), 1.64-1.1 (m, 1H), 0.85-0.8 (m, 2H), 0.53-0.48 (m, 2H). MS (ES): 243.0 m/z (M+H)$^+$.

Intermediate-7: Synthesis of 5'-amino-7'-nitrospiro[cyclopentane-1,3'-indolin]-2'-one:



Step-a: Synthesis of 2-(2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)isoindoline-1,3-dione:

To a stirred solution of 5'-aminospiro[cyclopentane-1,3'-indolin]-2'-one (2.8 g, 13.84 mmol, intermediate-2) in AcOH (30 mL) was added pthalic anhydride (3.1 g, 20.76 mmol) and heated to 100 °C for 2h. Then the reaction mixture was poured into crushed ice, the precipitated solid was filtered off, washed with water and dried under reduced pressure to afford the title product as an off white solid (3.4 g, 73%). ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 10.47 (s, 1H), 7.96-7.89 (m, 4H), 7.33 (d, J=2.0 Hz , 1H), 7.21 (dd, J=2.0 Hz & 7.8 Hz, 1H), 6.94 (d, J=8.4 Hz, 1H), 2.02-1.91 (m, 6H), 1.78-1.75 (m, 2H); LC-MS: m/z 333.1 (M+H)$^+$.

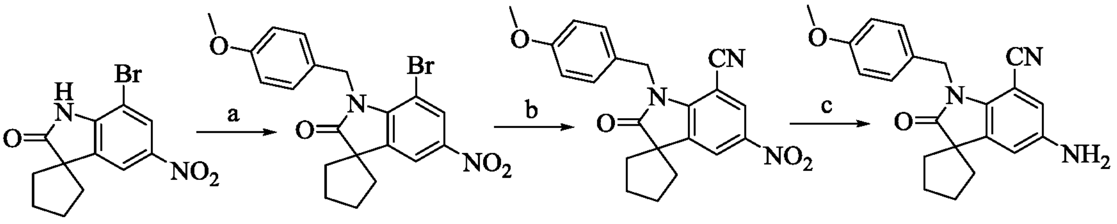
Step-b: Synthesis of 2-(7'-nitro-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)isoindoline-1,3-dione:

To a stirred solution of 2-(2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)isoindoline-1,3-dione (3.0 g, 9.02 mmol) in AcOH (30 mL) at room temperature was added nitric acid (2.4 mL) drop wise and heated to 110 °C for 2h. Then the reaction mixture was poured into crushed ice, the precipitated solid was filtered off, washed with water and dried under reduced pressure to afford the title compound as yellow solid (3.2 g). ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 11.23 (s, 1H), 8.14 (d, J=1.9 Hz, 1H), 7.99-7.91 (m, 4H), 7.81 (d, J=1.4 Hz, 1H), 2.09-2.05 (m, 2H), 1.96-1.83 (m, 6H); LC-MS: m/z 378.1 (M+H)$^+$.

Step-c: Synthesis of 5'-amino-7'-nitrospiro[cyclopentane-1,3'-indolin]-2'-one:

To a stirred solution of 2-(7'-nitro-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)isoindoline-1,3-dione (3.2 g, 8.48 mmol) in EtOH (30 mL) was added hydrazine hydrate (6 mL) and heated to 100 °C for 2h. Then the reaction mixture was poured into crushed ice and the solid formed was filtered off, washed with water and dried under reduced pressure to afford title compound as orange solid (1.9 g). ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.56 (s, 1H), 7.10 (s, 1H), 7.04 (s, 1H), 5.33 (s, 2H), 2.02-1.87 (m, 6H), 1.78-1.74 (m, 2H); LC-MS: *m/z* 248.1 $(M+H)^+$.

Intermediate-8: Synthesis of 5'-amino-1'-(4-methoxybenzyl)-2'-oxospiro[cyclopentane-1,3'-indoline]-7'-carbonitrile:



8a 8b Intermediate-8

Step-a: Synthesis of 7'-bromo-1'-(4-methoxybenzyl)-5'-nitrospiro[cyclopentane-1,3'-indolin]-2'-one:

To a stirred, cooled solution of 7'-bromo-5'-nitrospiro[cyclopentane-1,3'-indolin]-2'-one (5 g, 16.07 mmol, step-a product of intermediate-3) in DMF (25 mL) was added 60% sodium hydride (0.642 g, 16.07 mmol) and stirred for 10 min. Then 1-(chloromethyl)-4-methoxybenzene (2.59 g, 16.09 mmol) was added slowly, warmed to RT and heated to 50 °C for 1h. After completion of the reaction, the reaction mixture was cooled to RT, quenched with saturated ammonium chloride solution, extracted into ethyl acetate, the organic layer was dried over sodium sulfate and concentrated to get the title compound (3.2 g, 46.3%).

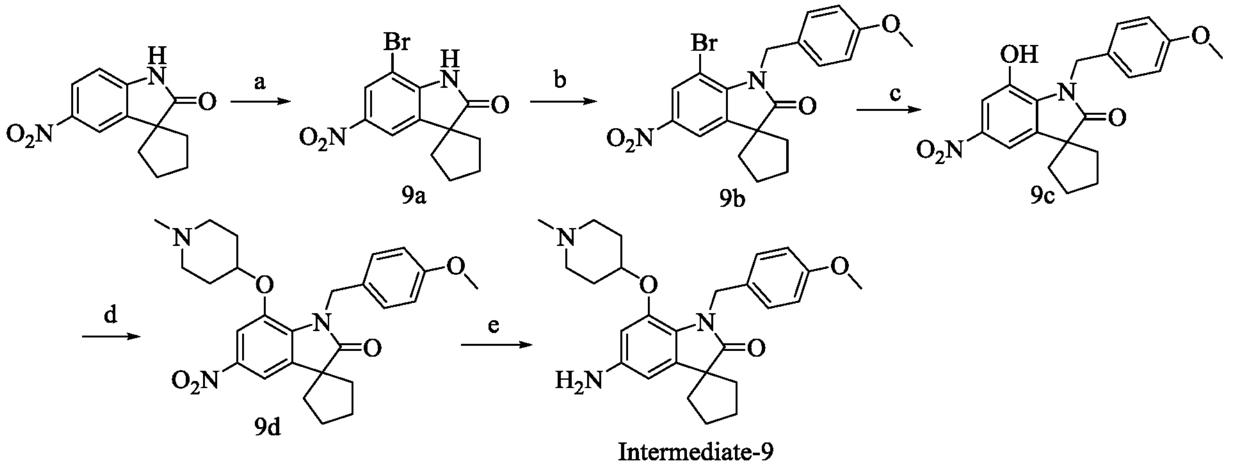
Step-b: Synthesis of 1'-(4-methoxybenzyl)-5'-nitro-2'-oxospiro[cyclopentane-1,3'-indoline]-7'-carbonitrile:

To a degassed mixture of 7'-bromo-1'-(4-methoxybenzyl)-5'-nitrospiro[cyclopentane-1,3'-indolin]-2'-one (2 g, 4.63 mmol), zinc cyanide (0.326 g, 2.78 mmol), zinc (3.6 g, 55mmol) in DMA (20 mL) was added $Pd_2(dba)_3$ (0.084 g, 0.091mmol) and DPPF (0.102 g, 0.18mmol) and heated to 120 °C for 6h in sealed tube. After completion of the reaction, the reaction mixture was cooled to RT, diluted with ethyl acetate, filtered through Celite ® pad, the filtrated was concentrated to get the crude compound. The resultant crude compound was purified by column chromatography using an eluent 30% ethyl acetate in hexanes to afford the title compound (1.6 g, 91.4%). LC-MS: *m/z* 348.3 $(M+H)^+$.

Step-c: Synthesis of 5'-amino-1'-(4-methoxybenzyl)-2'-oxospiro[cyclopentane-1,3'-indoline]-7'-carbonitrile:

To a stirred mixture of 1'-(4-methoxybenzyl)-5'-nitro-2'-oxospiro[cyclopentane-1,3'-indoline]-7'-carbonitrile (1.6 g, 4.23 mmol) in THF/MeOH (1:1mixture, 25 mL) was added ammonium chloride (2.2 g, 42.3 mmol) in 20 mL water. After stirring for 5 min, the zinc (2.7 g, 42.3 mmol) was added in portions by maintaining temperature less than 35 °C. After completion of the addition, the mixture was stirred for 1h at RT. Then solids filtered and the filtrate concentrated under reduced pressure and the residue was extracted with ethyl acetate. Combined organic portion was dried over sodium sulphate and concentrated to get the title compound (1.1 g. 74.8%). LC-MS: *m/z* 348.3 $(M+1)^+$.

Intermediate-9: Synthesis of 5'-amino-1'-(4-methoxybenzyl)-7'-((1-methylpiperidin-4-yl) oxy) spiro[cyclopentane-1,3'-indolin]-2'-one:



Step-a: Synthesis of 7'-bromo-5'-nitrospiro[cyclopentane-1,3'-indolin]-2'-one:

To an ice-cold solution of 5'-nitrospiro[cyclopentane-1,3'-indolin]-2'-one (1.2 g, 5.17 mmol) in sulphuric acid (12 mL) was added N-bromosuccinimide (1.4 g, 7.75 mmol) portion wise and stirred at room temperature for 2h. The reaction mixture was poured into crushed ice and the solid formed was filtered off, washed with water and dried under reduced pressure to afford title compound as pale-yellow solid (1.2 g, tentative). ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.34 (s, 1H), 8.30 (d, *J*=1.9 Hz, 1H), 8.10 (d, *J*=2.0 Hz, 1H), 2.01-1.90 (m, 8H).

Step-b: Synthesis of 7'-bromo-1'-(4-methoxybenzyl)-5'-nitrospiro[cyclopentane-1,3'-indolin]-2'-one:

To an ice-cold solution of 7'-bromo-5'-nitrospiro[cyclopentane-1,3'-indolin]-2'-one (1.2 g, 3.85 mmol) in DMF (15 mL) was added Cs_2CO_3 (2.5 g, 7.70 mmol) followed by 4-methoxybenzyl chloride (0.62 mL, 4.62 mmol) and stirred at room temperature for 3h. The reaction mixture was diluted with ice water, extracted with EtOAc, the organic layer was dried over sodium sulphate and concentrated. The residue was purified by CombiFlash® to afford title compound as pale brown solid (1.4 g, 84 %). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.25 (d, *J*=2.4 Hz, 1H), 8.19 (d, *J*=1.9 Hz, 1H), 7.07 (d, J=8.8 Hz, 2H), 6.89 (d, J=8.8 Hz, 2H), 5.28 (s, 2H), 3.71 (s, 3H), 2.08-2.01 (m, 8H).

Step-c: Synthesis of 7'-hydroxy-1'-(4-methoxybenzyl)-5'-nitrospiro[cyclopentane-1,3'-indolin]-2'-one:

To a solution of 7'-bromo-1'-(4-methoxybenzyl)-5'-nitrospiro[cyclopentane-1,3'-indolin]-2'-one (1.4 g, 3.24 mmol) in 1,4-dioxane (25 mL) and H_2O (5 mL) was added KOH (0.54 g, 9.72 mmol) and degassed with nitrogen purging for 20 min. Then ^{t}BuXPhos (0.14 g, 0.32 mmol) and Pd_2 $(dba)_3$ (0.29 g, 0.32 mmol) were added and again degassed with nitrogen purging for 20 min. Then the reaction mixture was heated at 100 °C for 16h. The reaction mixture was concentrated under reduced pressure and the residue was diluted with EtOAc, washed with water, brine, dried over sodium sulphate and concentrated under reduced pressure and purified by CombiFlash® to afford title compound as pale brown solid (0.8 g, 67 %). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.75 (bs, 1H), 7.69 (d, *J*=2.0 Hz, 1H), 7.61 (d, *J*=1.9 Hz, 1H), 7.18 (d, J=8.8 Hz, 2H), 6.87 (d, J=8.8 Hz, 2H), 5.08 (s, 2H), 3.70 (s, 3H), 2.01-1.87 (m, 8H); LC-MS: m/z 369.0 (M+H).

Step-d: Synthesis of 1'-(4-methoxybenzyl)-7'-((1-methylpiperidin-4-yl)oxy)-5'-nitrospiro [cyclopentane-1,3'-indolin]-2'-one:

To a cold solution of 1-methylpiperidin-4-ol (0.75 g, 6.52 mmol) in THF (10 mL) was added triphenyl phosphine (1.7 g, 6.52 mmol) followed by DIAD (1.3 mL, 6.52 mmol) stirred at 0 °C for 15 minutes, then added 7'-hydroxy-1'-(4-methoxybenzyl)-5'-nitrospiro[cyclopentane-1,3'-indolin]-2'-one (0.6 g, 1.63 mmol) and stirred at room temperature for 16h. The reaction mixture was diluted with EtOAc, washed with water, the organic layer was dried over sodium sulphate and concentrated under reduced pressure. The residue was purified by CombiFlash® to afford title compound as yellow solid (0.75 g). ^{1}H NM R (400 MHz, DMSO-d_6) δ 7.85 (d, *J*=1.9

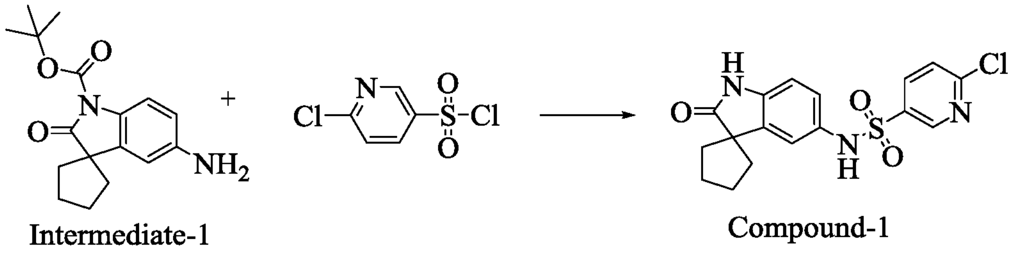
Hz, 1H), 7.76 (d, *J*=1.9 Hz, 1H), 7.05 (d, J=8.3 Hz, 2H), 6.88 (d, J=8.8 Hz, 2H), 5.13 (s, 2H), 4.62-4.58 (m, 1H), 3.70 (s, 3H), 2.51-2.38 (m, 4H), 2.15-1.93 (m, 11H), 1.83-1.80 (m, 2H), 1.51-1.49 (m, 2H); LC-MS: m/z 466.1 (M+H).

Step-e: Synthesis of 5'-amino-1'-(4-methoxybenzyl)-7'-((1-methylpiperidin-4-yl)oxy)spiro [cyclopentane-1,3'-indolin]-2'-one:

To a solution of 1'-(4-methoxybenzyl)-7'-((1-methylpiperidin-4-yl)oxy)-5'-nitrospiro [cyclopentane-1,3'-indolin]-2'-one (0.6 g, 1.29 mmol) in EtOH (10 mL) and H_2O (2 mL) were added iron powder (0.36 g, 6.45 mmol) and NH_4Cl (0.35 g, 6.45 mmol) and heated to 100 °C for 2h. The reaction mixture was cooled to room temperature, filtered through Celite ®, washed with EtOAc, combined filtrate was concentrated, and the residue was diluted with water and extracted with EtOAc, washed with brine, dried over sodium sulphate and concentrated under reduced pressure and purified by CombiFlash® to afford the title compound as pale yellow solid (0.2 g, 35 %). ^1H NMR (400 MHz, DMSO-d_6) δ 7.05 (d, *J*=8.8 Hz, 2H), 6.87 (d, *J*=8.8 Hz, 2H), 6.19 (d, J=1.5 Hz, 1H), 6.15 (d, J=1.5 Hz, 1H), 5.76 (s, 2H), 4.98-4.96 (bs, 2H), 4.30-4.25 (m, 1H), 3.70 (s, 3H), 2.52-2.32 (m, 6H), 1.99-1.88 (m, 9H), 1.74-1.71 (m, 2H), 1.65-1.58 (m, 2H); LC-MS: m/z 436.1 (M+H).

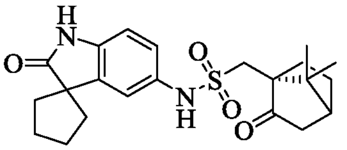
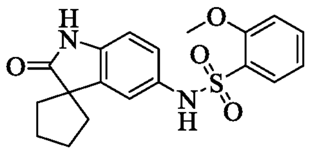
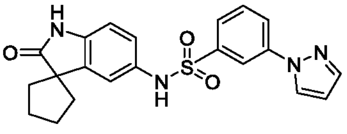
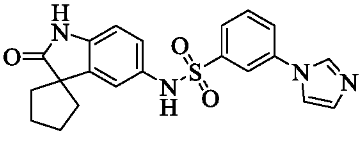
The present invention is further exemplified, but not limited, by the following examples that illustrate the preparation of compounds according to the invention.

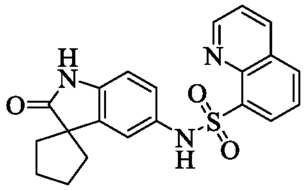
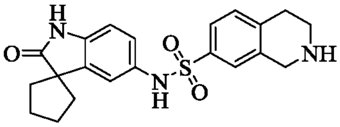
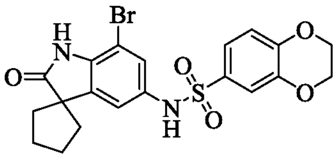
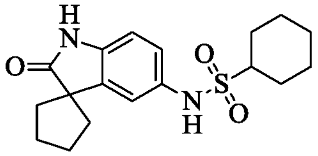
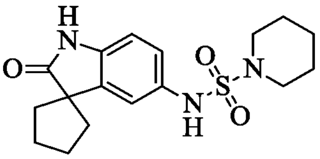
Example-I: Synthesis of 6-chloro-N-(2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)pyridine-3-sulfonamide: (Compound-1)

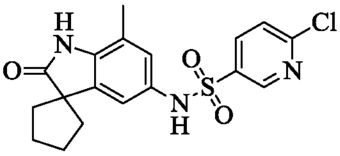
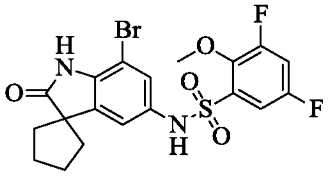
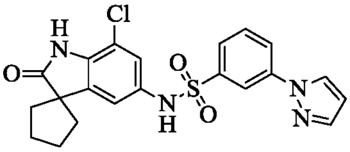
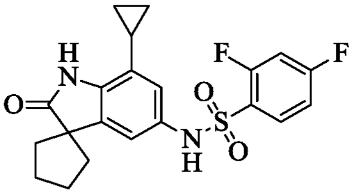
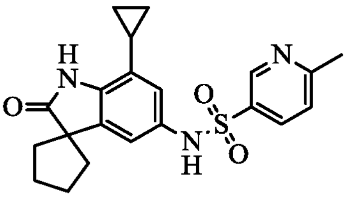


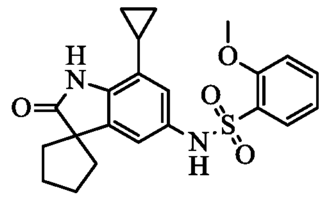
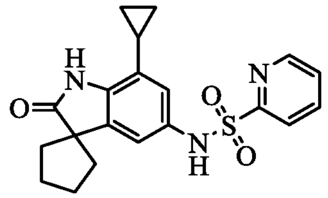
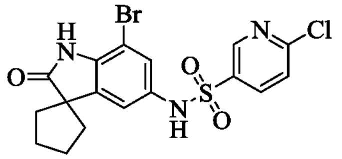
To a stirred solution of tert-butyl 5'-amino-2'-oxospiro[cyclopentane-1,3'-indoline]-1'-carboxylate (0.12 g, 0.37 mmol, Intermediate-1) in DCM (5 mL) and pyridine (0.5 mL) was added 6-chloropyridine-3-sulfonyl chloride (0.1 g, 0.48 mmol) drop wise at -15 °C. Then the resulting mixture was allowed to stir at RT for 1h, the reaction mixture was concentrated to obtain the residue. The obtained residue was treated with *TFA (0.3 mL). After 2h, the solvent was concentrated, and the obtained residue was treated with aq.sodium bicarbonate solution then purified by chromatography using mixture of 40% ethylacetate/hexane as an eluent to get the desired compound as white solid (0.03 g, 20%). ^{1}H-NMR (400 MHz, DMSO-d_6) δ 10.2 (s, 1H), 10.1 (s, 1H), 8.578 (d, J=2.4 Hz, 1H), 8.016 (dd, J=8.4 Hz, J=2.4 Hz, 1H), 7.76-7.74 (d, J=8 Hz, 1H), 6.87-6.85 (d, J=12 Hz, 1H), 6.78-6.74 (m, 2H), 2.08 (m, 4H), 1.78 (m, 2H), 1.59 (m, 2H); LC-MS: 378 $(M+H)^+$. *In this reaction TFA was used for deprotection of Boc.

The below compounds were prepared by procedure like the one described in Example-I with appropriate variations in reactants, quantities of reagents, solvents and reaction conditions. The physiochemical characteristics of the compounds are summarized herein below table.

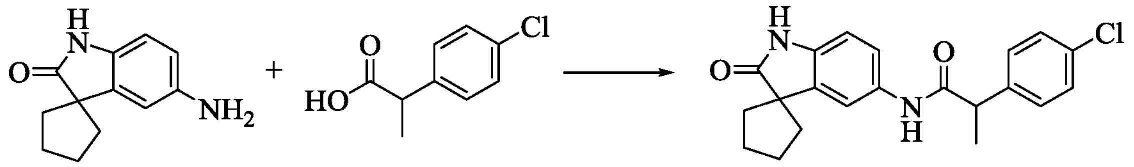
Comp No.	Structure	Analytical Data
2		^{1}H-NMR (400 MHz,CD_3OD) δ 7.25 (s, 1H), 7.1 (m, 1H), 6.85 (m, 1H), 3.0 (m, 1H), 2.4 (m, 2H), 2.2 (m, 3H), 2.1 (m, 5H), 1.95 (m, 1H), 1.9-1.8 (m, 2H), 1.7 (m, 1H), 1.5-1.4 (m, 1H), 1.2 (m, 1H), 1.1 (s, 3H), 0.8 (s, 3H). LC-MS: 417 $(M+H)^+$.
3		^{1}H-NMR (600 MHz, DMSO-D_2O) δ 7.61(d, J=6 Hz, 1H), 7.55-7.52 (m, 1H), 7.16(d, J=8.4 Hz, 1H), 6.99 (t, J=7.8 Hz, 1H), 6.86-6.85 (m, 2H), 6.66 (d, J=9 Hz, 1H), 3.8 (s, 3H), 1.87-1.57 (m, 4H), 1.48-1.46 (m, 4H); LC-MS: 373 $(M+H)^+$.
4		^{1}H-NMR (400 MHz, DMSO-d_6) δ 10.2 (s, 1H), 9.8 (s, 1H), 8.59 (d, J=2.4 Hz, 1H), 8.0 (d, J=2.4 Hz, 2H), 7.82 (d, J=1.5 Hz, 1H), 7.7 (m, 2H), 6.86-6.82 (m, 1H), 6.78-6.77 (m, 1H), 6.7-6.67 (m, 1H), 6.60-6.59 (m, 1H), 1.6-1.7 (m, 6H), 1.5 (m, 2H); LC-MS: 409 $(M+H)^+$.
5		^{1}H-NMR (400 MHz, DMSO-d_6) δ 10.2 (s, 1H), 10.0 (s, 1H), 8.9 (s, 1H), 8.0 (m, 3H), 7.7 (m, 2H), 7.5 (s, 1H), 6.9 (m, 1H), 6.8 (s, 1H), 6.71-6.69 (d, J=8 Hz, 1H), 1.6-1.7 (m, 6H), 1.5 (m, 2H); LC-MS: 409 $(M+H)^+$.

6		^{1}H-NMR (400 MHz, DMSO-d$_6$) δ 10.1 (s, 1H), 9.6 (s, 1H), 9.2 (s, 1H), 8.55 (d, J=8.4 Hz, 1H), 8.2 (m, 2H), 7.7 (m, 1H), 7.68 (t, J=7.6 Hz, 1H), 6.78 (d, J=7.6 Hz, 1H), 6.7 (s, 1H), 6.54 (d, J=8.4 Hz, 1H), 1.7 (m, 4H), 1.6 (m, 2H), 1.3 (m, 2H); LC-MS: 394.1 (M+H)$^+$.
7		^{1}H-NMR (400 MHz, DMSO-d$_6$) δ 10.24 (s, 1H),9.95 (s, 1H), 8.98 (bs, 2H), 7.59 (s, 1H), 7.57-7.55 (m,1H), 7.42-7.40 (m, , 1H), 6.92 (d, J=2.2 Hz, 1H), 6.83-6.80 (m, 1H), 6.77-6.65 (m, 1H), 4.30 (bs, 2H), 3.46-3.27(m, 2H), 3.02 (t, J=6.2Hz, 2H), 1.93-1.81 (m, 6H), 1.61-1.58 (m, 2H),; LC-MS: 398.25 (M+H)$^+$.
8		^{1}H-NMR (400 MHz, DMSO-d$_6$) δ 10.59 (s, 1H), 9.92 (bs, 1H), 7.15-7.02 (m, 2H), 7.00-6.98 (m, 2H), 6.82-6.80 (m, 1H), 4.28-4.27 (m, 4H), 1.92-1.80 (m, 4H), 1.79-1.75 (m, 2H), 1.63-1.59 (m, 2H); LC-MS: 481.00 (M+H)$^+$.
9		^{1}H-NMR (400 MHz, DMSO-d$_6$) δ 10.25 (s, 1H), 9.39 (s, 1H), 7.08 (d, J=2.0 Hz, 1H), 7.01 (dd, J=4.0 & J=8.4 Hz, 1H), 6.76 (d, J=8.0 Hz, 1H), 2.84 (t, J=3.4 Hz, 1H), 2.02-1.85 (m, 6H), 1.76-1.68 (m, 5H), 1.59-1.55 (m, 2H), 1.38-1.08 (m, 5H); MS (ES) m/e 349.4 (M+H)$^+$.
10		^{1}H-NMR (400 MHz, DMSO-d$_6$) δ 10.24 (s, 1H), 9.48 (bs, 1H), 7.09 (s, 1H), 7.08-6.96 (m, 1H), 6.75 (d, J=8.0 Hz, 1H), 3.31-3.04 (m, 4H), 1.95-1.88 (m, 6H), 1.68-1.60 (m, 2H), 1.39-1.30 (m, 6H); MS (ES) m/e 348 (M-H)$^-$.

11		^{1}H-NMR (400 MHz, DMSO-d_6) δ 10.36 (bs, 1H), 10.03 (bs, 1H), 8.57 (d, J=2.4 Hz, 1H), 7.99 (dd, J=8.3 Hz , J=2.5Hz, 1H), 7.74-7.72 (m, 1H), 6.70 (d, J=1.6 Hz, 1H), 6.58 (s, 1H), 2.12 (s, 3H), 1.90-1.55 (m, 8H); MS (ES): 390.4 m/z (M-H)$^-$.
12		^{1}H-NMR (400 MHz, DMSO-d_6) δ 10.6 (s, 1H), 10.5 (s, 1H), 7.65 (t, J=10 Hz, 1H), 7.40-7.36 (t, J=7.2 Hz, 1H), 7.04 (s, 1H), 6.91 (s, 1H), 3.83 (s, 3H), 1.92 (m, 4H), 1.79 (m, 2H), 1.61 (m, 2H); LC-MS: 488.9 (M+H)$^+$.
13		^{1}H-NMR (400 MHz, DMSO-d_6) δ 10.75 (s, 1H), 10.1 (s, 1H), 8.042 (d, J=8.4 Hz, 1H), 7.77 (d, J=8.8 Hz, 2H), 7.82 (s, 1H), 7.76 (d, 2H), 6.89 (s, 1H), 6.79 (s, 1H), 6.61 (s, 1H), 1.90 (m, 4H), 1.73 (m, 2H), 1.58 (m, 2H); LC-MS: 443 (M+H)$^+$.
14		^{1}H-NMR (400 MHz, DMSO-d_6) δ 10.5 (s, 1H), 10.1 (s, 1H), 7.74-7.68 (m, 1H), 7.55-7.50 (m, 1H), 7.23-7.18 (m, 1H), 6.64 (d, J=1.2 Hz, 1H), 6.30-6.29 (d, J=2 Hz, 1H), 1.88 (m, 5H), 1.76 (m, 2H), 1.55 (m, 2H), 0.88 (m, 2H), (m, 2H), 0.40 (m, 2H); LC-MS: 419.2 (M+H)$^+$.
15		^{1}H-NMR (400 MHz, DMSO-d_6) δ 10.5 (s, 1H), 9.8 (s, 1H), 8.561 (d, J=2 Hz, 1H), 7.85-7.82 (m, 1H), 7.446 (d, J=8Hz, 1H), 6.59 (d, J=2.4 Hz, 1H), 6.273 (d, J=2 Hz, 1H), 1.9 (m, 5H), 1.75 (m, 2H), 1.55 (m, 2H), 0.88 (m, 2H), (m, 2H), 0.41 (m, 2H); LC-MS: 398.0 (M+H)$^+$.

16		^{1}H-NMR (300 MHz, DMSO-d_6) δ 10.4 (s, 1H), 9.5 (s, 1H), 7.63 (d, J=7.5 Hz, 1H), 7.57 (t, J=7.2 Hz, 1H), 7.171- (d, J=8.1 Hz, 1H), 7.01-6.96 (t, J=7.5 Hz, 1H), 6.68 (s, 1H), 3.88 (s, 3H), 1.9-1.86 (m, 7H), 1.5-1.4 (m, 2H), 0.85 (m, 2H), 0.4 (m, 2H); LC-MS: 413.2 (M+H)$^+$.
17		^{1}H-NMR (300 MHz, DMSO-d_6) δ 10.44 (s, 1H), 10.05 (s, 1H), 8.75 (d, J=4.2 Hz, 1H), 8.04-7.99 (m, 1H), 7.82 (d, J=8.1 Hz, 1H), 7.66-7.62(m, 1H), 6.67 (d, J=1.5 Hz, 1H)), 6.330 (d, J=1.5 Hz, 1H) , 1.9-1.86 (m, 7H), 1.5-1.4 (m, 2H), 0.85 (m, 2H), 0.41 (m, 2H); LC-MS: 383.95 (M+H)$^+$.
18		^{1}H-NMR (300 MHz, DMSO-d_6) δ 10.66 (s, 1H), 10.31 (s, 1H) 8.62-8.61 (m, 1H), 8.04-8.01 (m, 1H), 7.76-7.74 (d, J=6 Hz, 1H), 7.022 (s, 1H), 6.81 (s, 1H), 2-1.92 (m, 4H), 1.9-1.7(m, 2H), 1.65-1.62 (m, 2H); LC-MS: 458.2 (M+2H)$^+$.

Example-II: Synthesis of 2-(4-chlorophenyl)-N-(2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl) propanamide: (Compound-19)

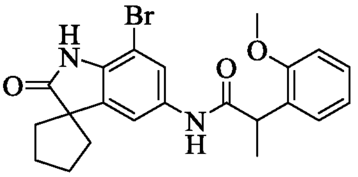


Intermediate-2 **Compound-19**

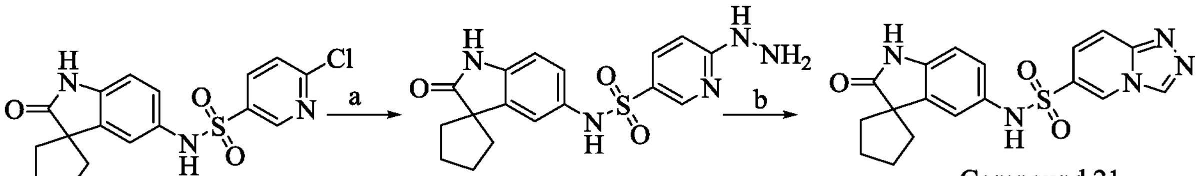
To a stirred solution of 5'-aminospiro[cyclopentane-1,3'-indolin]-2'-one (0.05 g, 0.25 mmol, Intermediate-2) in DCM (5 mL), were added DIPEA (0.11 ml, 0.62 mmol), EDC.HCl (0.058 g, 0.3 mmol), HOBt (0.037 g, 0.27 mmol) and 2-(4-chlorophenyl)propanoic acid (0.046 g, 0.25 mmol) at 0-5 °C.The reaction mixture was stirred for 16h at RT. Then the reaction mixture was diluted with DCM (50 mL), washed with saturated sodium bicarbonate solution, brine solution and dried over Na_2SO_4, the organic layer was concentrated to obtain the crude compound. The obtained crude was purified by silica gel chromatography using a mixture of

50% ethyl acetate/hexane as an eluent to get the title compound as white solid (0.020g, 25%). ^{1}H-NMR (400 MHz, DMSO-d$_6$) δ 10.2 (s, 1H), 9.95 (s, 1H), 7.52 (s, 1H), 7.39 (s, 4H), 7.34 (d, J=8.4 Hz, 1H), 6.74 (d, J=8 Hz, 1H), 3.79 (m, 1H), 1.91 (m, 6H), 1.7 (m, 2H), 1.40-1.38 (d, J=6.8 Hz, 3H); LC-MS: 369.1 (M+H)$^+$.

The below compound was prepared by procedure similar to the one described in Example-II with appropriate variations in reactants, quantities of reagents and reaction conditions. The physiochemical characteristics of the compounds are summarized herein below table.

Comp No.	Structure	Analytical Data
20		^{1}H-NMR (400 MHz, DMSO-d$_6$) δ 10.3 (s, 1H), 9.4 (s, 1H), 7.74 (d, J=1.6 Hz, 1H), 7.47 (d, J=2 Hz, 1H), 7.27-7.21 (m, 2H), 6.997 (d, J=8 Hz, 1H), 6.94 (m, 1H), 4.06 (m, 1H), 3.81(s, 3H), 1.99-1.87 (m, 6H), 1.75-1.71 (m, 2H), 1.355 (d, J=7.2 Hz, 3H); LC-MS: 443.3 (M+H)$^+$.

Example-III: Synthesis of N-(2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-[1,2,4]triazolo[4,3-a]pyridine-6-sulfonamide: (Compound 21)



Compound 21

Step-a: Synthesis of 6-hydrazinyl-N-(2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)pyridine-3-sulfonamide:

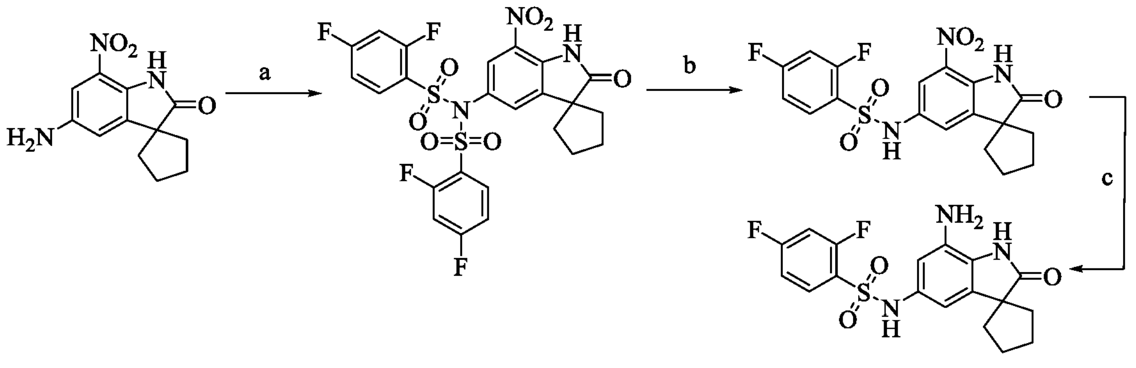
A solution of 6-chloro-N-(2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)pyridine-3-sulfonamide (0.150 g, 0.397 mmol, Compound-1) with hydrazine hydrate (3 mL) was heated to 120 °C for 4h. The reaction mixture was then cooled to room temperature and concentrated to obtain the residue. The residue was then washed with diethyl ether to get the title compound as an off white solid (0.1 g, 67%). LC-MS: *m/z* 374.5 (M+H)$^+$.

Step-b: Synthesis of N-(2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-[1,2,4]triazolo[4,3-a]

pyridine-6-sulfonamide:

To a stirred solution of 6-hydrazinyl-N-(2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)pyridine-3-sulfonamide (0.1 g, 0.278 mmol) in formic acid (5 mL) was heated to 100 °C for 3h. The reaction mixture was then cooled to room temperature and concentrated to get the residue. The residue was purified by column chromatography (Silica gel-60/120) using eluent 10% methanol in DCM e to afford the title compound as a white solid (0.028 g, 26%). ^{1}H-NMR (400 MHz, DMSO-d_6) δ 10.2 (s, 1H), 10.1 (s, 1H), 9.3 (s, 1H), 9.0 (s, 1H), 7.98 (d, J=10 Hz, 1H), 7.49 (d, J=9.6 Hz, 1H), 6.89-6.87 (m, 1H), 6.8 (s, 1H), 6.72 (d, J=8 Hz, 1H), 1.9-1.8 (m, 4H), 1.8-1.6 (m, 2H), 1.52-1.50 (m, 2H); LC-MS: *m/z* 384.1 $(M+H)^+$.

Example-IV: Synthesis of N-(7'-amino-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2,4-difluorobenzenesulfonamide: (Compound-22)



Compound-22

Step-a: Synthesis of N-((2,4-difluorophenyl)sulfonyl)-2,4-difluoro-N-(7'-nitro-2'-oxospiro [cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide:

To an ice cooled solution of 5'-amino-7'-nitrospiro[cyclopentane-1,3'-indolin]-2'-one (1.0 g, 4.04 mmol, intermediate-7) in DCM (10 mL) was added TEA (2.2 mL, 16.16 mmol) followed by 2,4-difluorobenzenesulfonyl chloride (0.81 mL,6.06 mmol) drop wise and stirred at RT for 16 h. The reaction mixture was diluted with DCM (100 mL) and washed with water (100 mL), brine (100 mL), dried over sodium sulphate and concentrated under reduced pressure to afford title compound as brown oil (2.0 g). LC-MS: *m/z* 598.0 $(M-H)^-$.

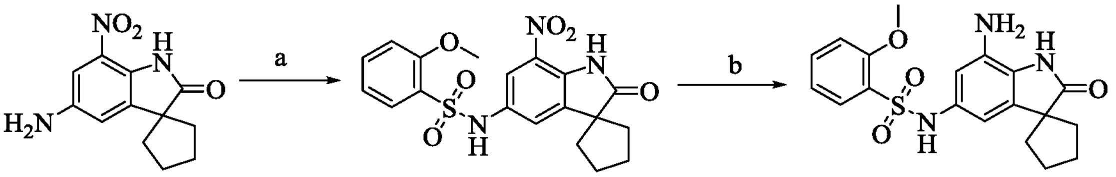
Step-b: Synthesis of 2,4-difluoro-N-(7'-nitro-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl) benzenesulfonamide:

To a solution of N-((2,4-difluorophenyl)sulfonyl)-2,4-difluoro-N-(7'-nitro-2'-oxospiro [cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide (2.0 g, 3.33 mmol) in THF (20 mL) was added 3N NaOH (20 mL) and heated to 80 °C for 16h. Then the reaction mixture was concentrated under reduced pressure, the residue was diluted with water, neutralized with 1N HCl, extracted with EtOAc (100 mL X 2), the organic layer was dried over sodium sulphate and concentrated under reduced pressure to afford the title compound as brown oil (2.0 g). LC-MS: *m/z* 422.1 $(M-H)^-$.

Step-c: Synthesis of N-(7'-amino-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2,4-difluoro benzenesulfonamide:

To a solution of 2,4-difluoro-N-(7'-nitro-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide (2.0 g, 4.72 mmol) in EtOH (40 mL) and H_2O (20 mL) were added iron powder (1.3 g, 23.6 mmol) and NH_4Cl (2.5 g, 47.2 mmol) and heated to 100 °C for 2h. Then the reaction mixture was cooled to room temperature, filtered through Celite ®, washed with EtOAc the combined filtrate was concentrated to obtain the residue, the residue was diluted with water, extracted with EtOAc (200 mL X 2), washed with brine solution (200 mL), dried over sodium sulphate, concentrated under reduced pressure and purified by column chromatography to afford the title compound as pale brown solid (1.0 g, 53%). ^1H NMR (400 MHz, DMSO-d_6): δ 9.99 (s, 1H), 9.72 (s, 1H), 7.77-7.71 (m, 1H), 7.52 (t, J=8.8 Hz, 1H), 7.22 (t, J=6.8 Hz, 1H), 6.27 (s, 1H), 6.15 (s, 1H), 4.94 (s, 2H), 1.87-1.75 (m, 6H), 1.60-1.45 (m, 2H); LC-MS: *m/z* 394.0 $(M+H)^+$.

Example-V: Synthesis of N-(7'-amino-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-methoxy benzenesulfonamide: (Compound-23)



Compound-23

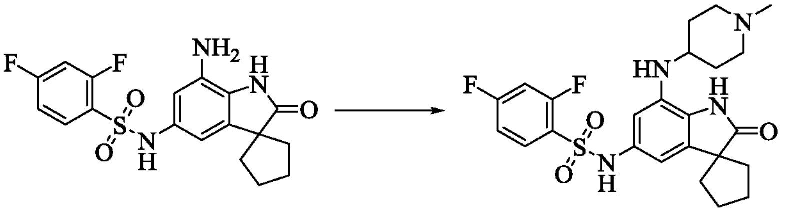
Step-a: Synthesis of 2-methoxy-N-(7'-nitro-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl) benzenesulfonamide:

The process for this step was depicted in example-I by using 5'-amino-7'-nitrospiro[cyclopentane-1,3'-indolin]-2'-one (Intermediate-7) and 2-methoxybenzene-1-sulfonyl chloride as starting materials. The desired product obtained as yellow solid (0.8 g). LC-MS: *m/z* 416.0 $(M-H)^-$.

Step-b: Synthesis of N-(7'-amino-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-methoxy benzenesulfonamide:

The process for this step was depicted in step-c of example-IV by using 2-methoxy-N-(7'-nitro-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide as starting material. The desired product obtained as brown solid. ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 9.66 (s, 1H), 9.33 (s, 1H), 7.63 (d, J=7.3 Hz, 1H), 7.54 (t, J=7.4 Hz, 1H), 7.16 (d, J=8.3 Hz, 1H), 6.98 (t, J=7.4 Hz, 1H), 6.29 (s, 1H), 6.17 (s, 1H), 4.86 (s, 2H), 3.90 (s, 3H), 1.86-1.74 (m, 6H), 1.47-1.44 (m, 2H); LC-MS: m/z 388.1 (M+H)$^+$.

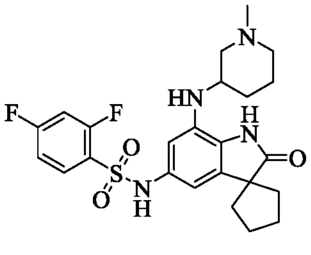
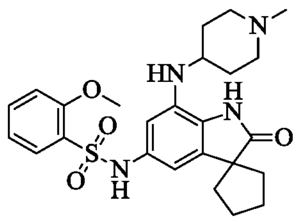
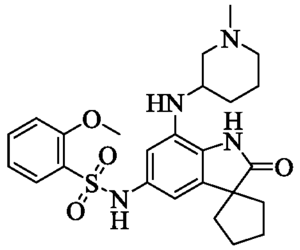
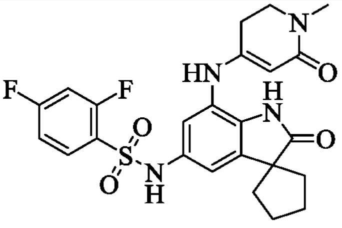
Example-VI: Synthesis of 2,4-difluoro-N-(7'-((1-methylpiperidin-4-yl) amino)-2'-oxospiro [cyclopentane-1,3'-indolin]-5'-yl) benzenesulfonamide: (Compound-24)



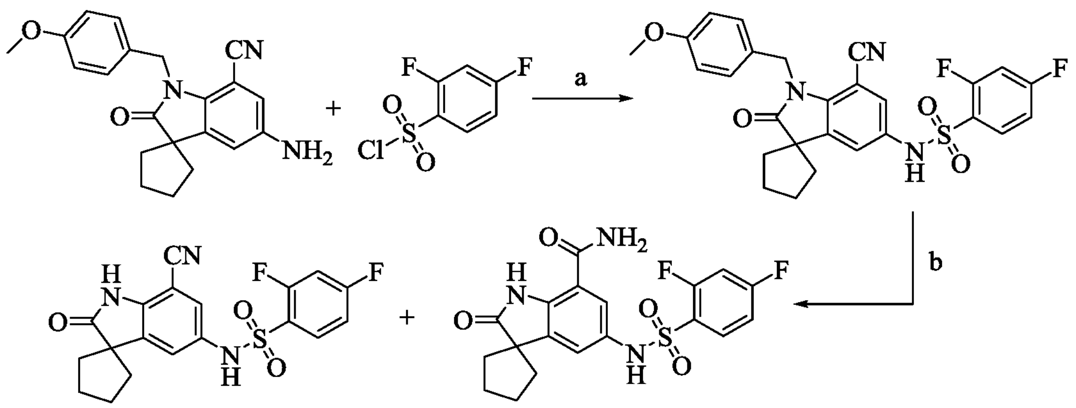
Compound-24

To a stirred suspension of N-(7'-amino-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2,4-difluoro benzenesulfonamide (0.15 g, 0.38 mmol, Compound-22) in titanium isopropoxide (1.5 mL) was added 1-methylpiperidine-4-one (0.07 g, 0.57 mmol) and stirred at room temperature for 16h. Then the reaction mixture was cooled to 0 °C, added MeOH (5 mL) followed by sodium borohydride (0.03 g, 0.76 mmol) and stirred at RT for 3h. After completion of the reaction, the reaction mixture was diluted with EtOAc (100 mL) washed with aqueous ammonia (100 mL), water (100 mL), dried over sodium sulphate and concentrated under reduced pressure to obtain the crude compound. The crude compound was purified by column chromatography to afford the title compound as brown solid (0.04 g, 21%). ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 9.90 (bs, 1H), 9.81 (s, 1H), 7.78-7.72 (m, 1H), 7.57-7.51 (m, 1H), 7.25-7.20 (m, 1H), 6.20 (s, 1H), 6.11 (s, 1H), 4.78 (d, J=7.3 Hz, 1H), 2.96-2.85 (m, 1H), 2.75-2.73 (m, 2H), 2.61-2.50 (m, 2H), 2.20 (s, 3H), 2.05-1.95 (m, 2H), 1.88-1.77 (m, 6H), 1.56-1.53 (m, 2H), 1.34-1.26 (m, 2H); LC-MS: m/z 491.2 (M+H)$^+$.

The below compounds were prepared by procedure like the one described in Example-VI with appropriate variations in reactants, quantities of reagents and reaction conditions. The physiochemical characteristics of the compounds are summarized herein below table.

Comp No.	Structure	Analytical Data
25		^{1}H NMR (400 MHz, DMSO-d_6): δ 10.00 (bs, 1H), 9.86 (s, 1H), 7.76-7.74 (m, 1H), 7.53-7.51 (m, 1H), 7.25-7.21 (m, 1H), 6.20 (s, 1H), 6.18 (s, 1H), 4.81 (d, J=7.8 Hz, 1H), 3.22-3.18 (m, 1H), 2.18 (s, 3H), 1.91-1.67 (m, 11H), 1.54-1.52 (m, 3H), 1.20-1.10 (m, 2H); LC-MS: m/z 491.2 (M+H)$^+$.
26		^{1}H NMR (400 MHz, DMSO-d_6): δ 9.73 (s, 1H), 9.32 (s, 1H), 7.62 (dd, J=1.4 Hz & 7.8 Hz, 1H), 7.56-7.52 (m, 1H), 7.16 (d, J=8.3 Hz, 1H), 6.98 (t, J=7.8 Hz, 1H), 6.23 (d, J=1.5 Hz, 1H), 6.16 (d, J=1.5 Hz, 1H), 4.70 (d, J=7.4 Hz, 1H), 3.90 (s, 3H), 2.98-2.94 (m, 1H), 2.80-2.70 (m, 2H), 2.21 (s, 3H), 2.10-1.99 (m, 2H), 1.87-1.76 (m, 8H), 1.52-1.49 (m, 2H), 1.32-1.26 (m, 2H); LC-MS: m/z 485.2 (M+H)$^+$.
27		^{1}H NMR (400 MHz, DMSO-d_6): δ 9.78 (s, 1H), 9.34 (s, 1H), 7.63 (d, J=7.3 Hz, 1H), 7.54 (t, J=8.3 Hz, 1H), 7.16 (d, J=8.3 Hz, 1H), 6.98 (t, J=7.8 Hz, 1H), 6.23 (s, 1H), 6.22 (s, 1H), 4.72 (d, J=7.8 Hz, 1H), 3.91 (s, 3H), 3.21-3.15 (m, 1H), 2.80-2.58 (m, 2H), 2.17 (s, 3H), 1.87-1.67 (m, 11H), 1.51-1.42 (m, 3H); LC-MS: m/z 485.2 (M+H)$^+$.
28		^{1}H NMR (400 MHz, DMSO-d_6): δ 10.29 (s, 1H), 10.06 (s, 1H), 7.81-7.72 (m, 2H), 7.55-7.51 (m, 1H), 7.26-7.22 (m, 1H), 6.75 (s, 2H), 4.36 (s, 1H), 2.77 (s, 3H), 2.67-2.49 (m, 2H), 1.92-1.81 (m, 7H), 1.61-1.59 (m, 3H); LC-MS: m/z 503.0 (M+H).

Example-VII: Synthesis of N-(7'-cyano-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2,4-difluorobenzenesulfonamide (Compound-29) & 5'-(2,4-difluorophenylsulfonamido)-2'-oxospiro[cyclopentane-1,3'-indoline]-7'-carboxamide: (Compound-30)



Compound-29 **Compound-30**

Step-a: Synthesis of N-(7'-cyano-1'-(4-methoxybenzyl)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2,4-difluorobenzenesulfonamide:

The process for this step was depicted in example-I by using 5'-amino-1'-(4-methoxybenzyl)-2'-oxospiro[cyclopentane-1,3'-indoline]-7'-carbonitrile (Intermediate-8) and 2,4-difluorobenzene-1-sulfonyl chloride as starting materials. LC-MS 524 $(M+H)^+$.

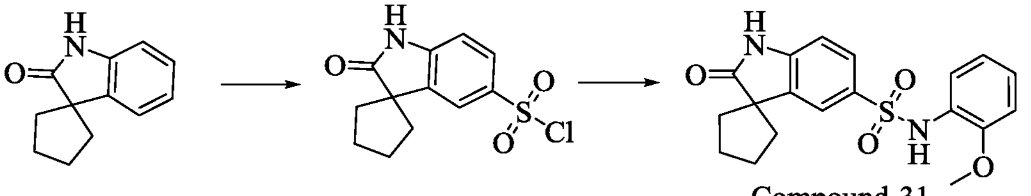
Step-b: Synthesis of N-(7'-cyano-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2,4-difluoro benzene sulfonamide & 5'-((2,4-difluorophenyl) sulfonamido)-2'-oxospiro[cyclopentane-1,3'-indoline]-7'-carboxamide:

To a stirred solution of N-(7'-cyano-1'-(4-methoxybenzyl)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2,4-difluorobenzenesulfonamide (1.1 g, 2.1 mmol) in toluene (20 mL) was added trifluoroacetic acid (5.5 mL) and heated to 100 °C for1h. After completion of the reaction, the reaction mixture was cooled to RT and concentrated to obtain the residue. The obtained residue was purified by preparative TLC to get title compounds-29 and 30.

Compound-29: ^{1}H-NMR (400 MHz, CD_3OD) δ 7.88-7.86 (m, 1H), 7.25-7.2 (m, 2H), 7.17-7.12(m, 2H), 2.15-2.0 (m, 6H), 1.77-1.75 (m, 2H); LC-MS: *m/z* 404.1 $(M+H)^+$.

Compound-30: ^{1}H-NMR (400 MHz, CD_3OD) δ 7.84-7.78 (m, 1H), 7.397-7.393 (d, J=1.6Hz, 1H), 7.26-7.20 (m, 1H), 7.10-7.06 (m, 2H), 2.09-2.03 (m, 4H), 1.96-1.91 (m, 2H), 1.73-1.69(m, 2H); LC-MS: *m/z* 420.1 $(M-H)^-$.

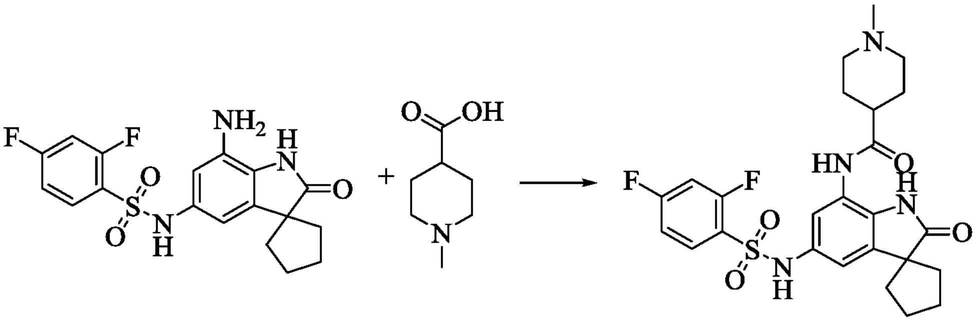
Example-VIII: Synthesis of N-(2-methoxyphenyl)-2'-oxospiro[cyclopentane-1,3'-indoline]-5'-sulfonamide: (Compound-31)



Compound-31

A mixture of spiro[cyclopentane-1,3'-indolin]-2'-one (0.2 g, 1.06 mmol, step-b product of intermediate-2) in chloro sulphonic acid (2.5 mL) was stirred at RT for 1h. Then the reaction mixture was poured into cold water. The precipitate formed was filtered and dried under reduced pressure to get the solid. The obtained solid (2'-oxospiro[cyclopentane-1,3'-indoline]-5'-sulfonyl chloride) (0.15 g, 0.525 mmol) was dissolved in DCM and added pyridine (1 mL), 2-methoxy aniline (0.071 g, 0.577 mmol). The reaction mixture was stirred at RT for 16h. After completion of the reaction, the reaction mixture was evaporated completely to get the residue, and which was purified by preparative TLC (0.04 g, 10%). ^{1}H-NMR (400 MHz, CD_3OD) δ 7.53-7.49 (m, 1H), 7.389-7.383 (d, 1H), 7.25-7.22 (m, 1H), 7.10-7.0 (m, 1H), 6.90-6.87 (m, 3H), 3.47(s, 3H), 1.99-1.93 (m, 4H), 1.84-1.75 (m, 2H), 1.70-1.64 (m, 2H); LC-MS: *m/z* 371.1 $(M-H)^-$.

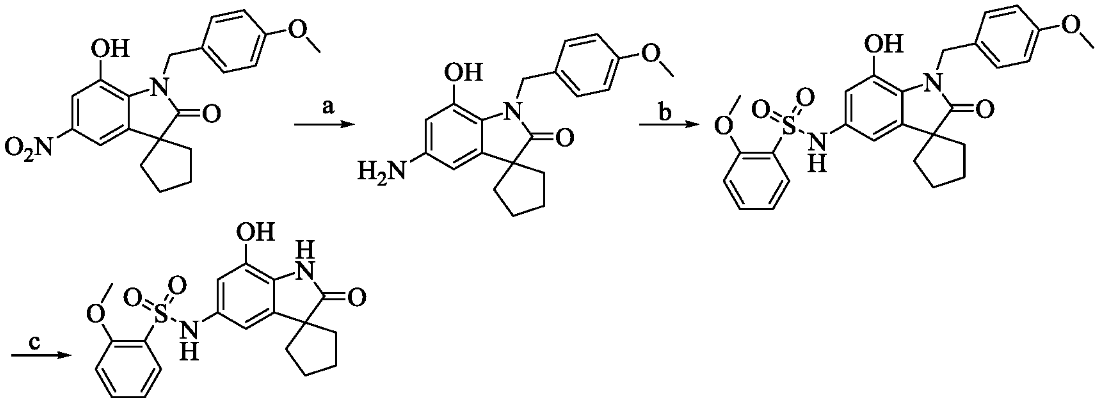
Example-IX: Synthesis of N-(5'-((2,4-difluorophenyl) sulfonamido)-2'-oxospiro[cyclopentane-1,3'-indolin]-7'-yl)-1-methylpiperidine-4-carboxamide: (Compound-32)



Compound-32

To a solution of N-(7'-amino-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2,4-difluoro benzenesulfonamide (compound-22) (0.2 g, 0.51 mmol) in DCM (4 mL) were added 1-methylpiperidine-4-carboxylic acid (0.22 g, 1.53 mmol), triethyl amine (0.35 mL, 2.55 mmol) and PyBOP (1.3 g, 2.55 mmol), and stirred at room temperature for 16h. The reaction mixture was diluted with EtOAc, washed with water and brine, the organic layer was dried over sodium sulphate and concentrated under reduced pressure. The residue was purified by preparative HPLC to afford the title compound as off white solid (0.015 g). ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.30-10.21 (bs, 1H), 9.88 (s, 1H), 9.18 (s, 1H), 7.78-7.76 (m, 1H), 7.53-7.50 (m, 1H), 7.28 (s, 1H), 7.22-7.21 (m, 1H), 6.67 (d, *J*=1.5 Hz, 1H), 2.83-2.80 (m, 2H), 2.22-2.14 (m, 1H), 2.16 (s, 3H), 1.91-1.61 (m, 10H), 1.60-1.56 (m, 4H); LC-MS: m/z 519.0 (M+H).

Example-X: Synthesis of N-(7'-hydroxy-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-methoxy benzenesulfonamide: (Compound-33)



Compound-33

Step-a: Synthesis of 5'-amino-7'-hydroxy-1'-(4-methoxybenzyl) spiro[cyclopentane-1,3'-indolin]-2'-one:

To a solution of 7'-hydroxy-1'-(4-methoxybenzyl)-5'-nitrospiro[cyclopentane-1,3'-indolin]-2'-one (0.15 g, 0.41 mmol) in EtOH (5 mL) and H_2O (1 mL) were added iron powder (0.11 g, 2.05 mmol) and NH_4Cl (0.11 g, 2.05 mmol) and heated to 100 °C for 2h. The reaction mixture was cooled to room temperature, filtered through Celite®, washed with EtOAc combined filtrate was concentrated, the residue was diluted with water and extracted with EtOAc, washed with brine, dried over sodium sulphate and concentrated under reduced pressure. The residue was purified by CombiFlash® to afford the title compound as brown gummy mass (0.07 g, 51 %). ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.21 (s, 1H), 7.16 (d, J=8.8 Hz, 2H), 6.84 (d, J=8.3 Hz, 2H), 6.04 (d, *J*=1.9 Hz, 1H), 5.95 (d, J=2.0 Hz, 1H), 4.91 (s, 2H), 4.80-4.70 (bs, 2H), 3.69 (s, 3H), 1.94-1.90 (m, 6H), 1.75-1.65 (m, 2H).

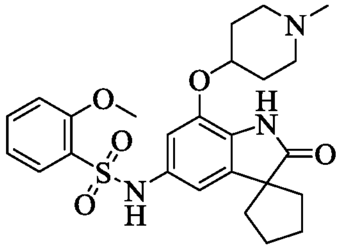
Step-b: Synthesis of N-(7'-hydroxy-1'-(4-methoxybenzyl)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-methoxybenzenesulfonamide:

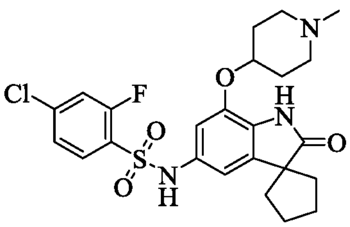
To an ice cooled solution of 5'-amino-7'-hydroxy-1'-(4-methoxybenzyl) spiro [cyclopentane-1,3'-indolin]-2'-one (0.07 g, 0.21 mmol) in DCM (3 mL) were added pyridine (0.05 mL, 0.63 mmol) followed by 2-methoxybenzenesulfonyl chloride (0.05 g, 0.23 mmol) and stirred at RT for 2 h. Reaction mixture was diluted with DCM and washed with aqueous $NaHCO_3$, brine, dried over sodium sulphate and concentrated under reduced pressure. The residue was purified by CombiFlash® to afford title compound as pale brown gummy mass (0.06 g, 57 %.). ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.71 (s, 1H), 9.57 (s, 1H), 7.67-7.65 (m, 1H), 7.54-7.52 (m, 1H), 7.15 (d, J=8.3 Hz, 1H), 7.10 (d, J=8.3 Hz, 2H), 7.00 (t, J=7.8 Hz, 1H), 6.81 (d, *J*=8.3 Hz, 2H), 6.52 (d, J=2.0 Hz, 1H), 6.44 (d, J=2.0 Hz, 1H), 4.90 (s, 2H), 3.87 (s, 3H), 3.68 (s, 3H), 1.90-1.79 (m, 6H), 1.53-1.49 (m, 2H); LC-MS: m/z 509.0 (M+H).

Step-c: Synthesis of N-(7'-hydroxy-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-methoxy benzenesulfonamide:

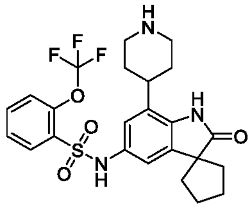
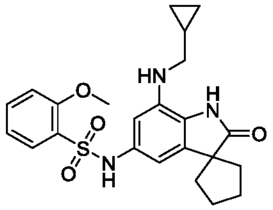
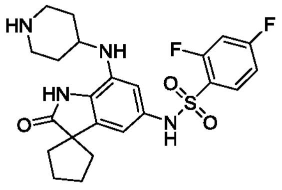
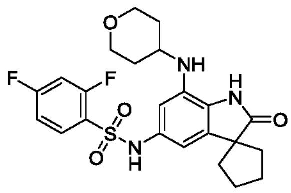
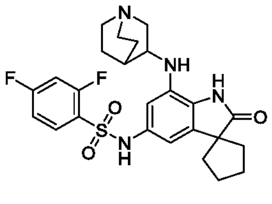
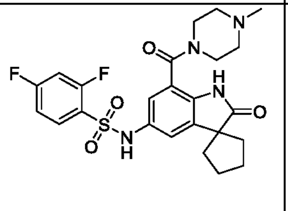
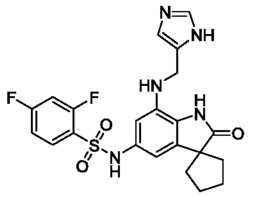
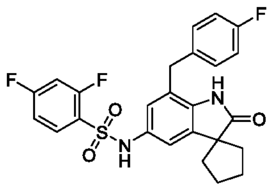
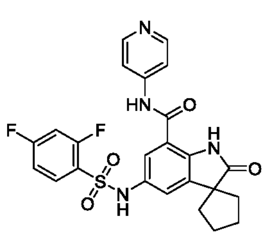
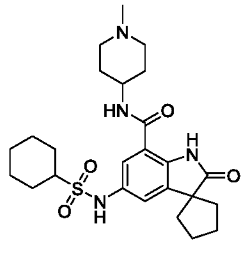
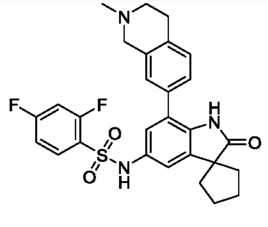
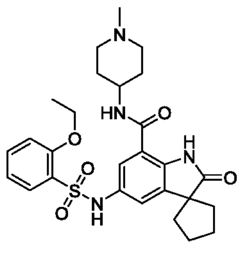
To a cold solution of 2 N-(7'-hydroxy-1'-(4-methoxybenzyl)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-methoxybenzenesulfonamide (0.06 g, 0.12 mmol) in DCM (3 mL) was added TFA (1 mL) followed by trifluoromethanesulfonic acid (0.1 mL) and the reaction mixture stirred at room temperature for 3h. The reaction mixture was slowly poured in to aqueous $NaHCO_3$ and extracted with DCM, the organic layer was dried over Na_2SO_4, concentrated under reduced pressure and purified by CombiFlash® to afford title compound as white solid (0.015 g, 32%). ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.88 (s, 1H), 9.50 (s, 1H), 9.47 (s, 1H), 7.65-7.63 (m, 1H), 7.54-7.52 (m, 1H), 7.16 (d, J=8.3 Hz, 1H), 6.98 (t, J=7.8 Hz, 1H), 6.51 (d, J=1.4 Hz, 1H), 6.39 (s, 1H), 3.89 (s, 3H), 1.86-1.76 (m, 6H), 1.48-1.45 (m, 2H); LC-MS: m/z 389.0 (M+H).

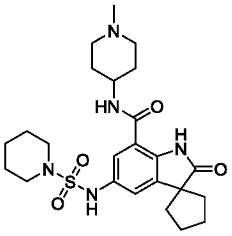
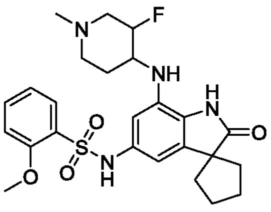
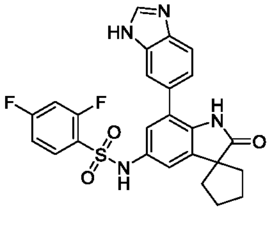
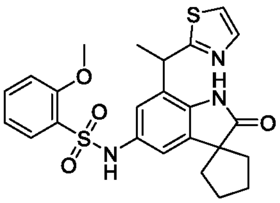
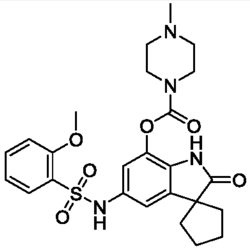
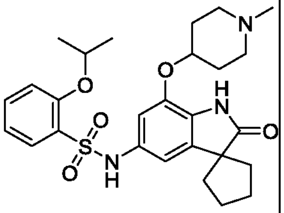
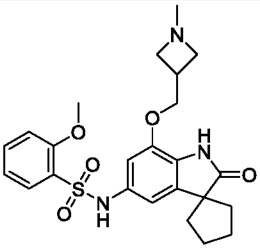
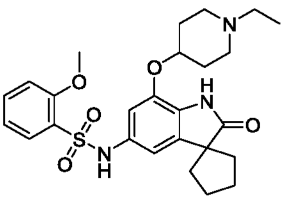
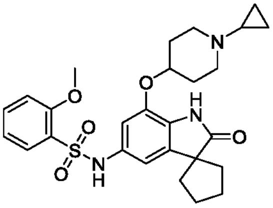
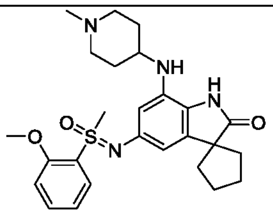
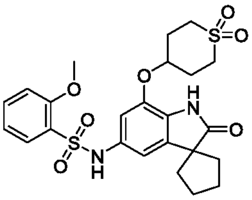
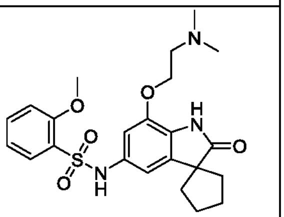
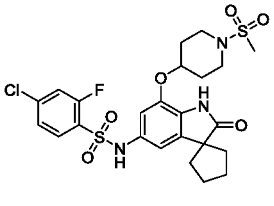
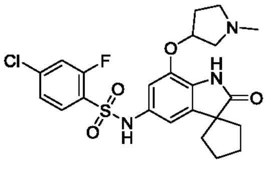
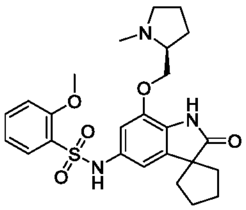
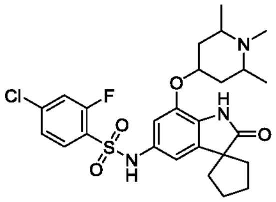
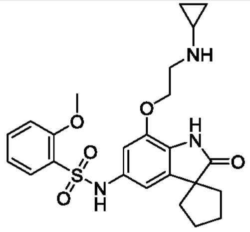
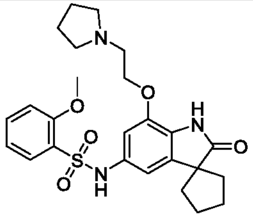
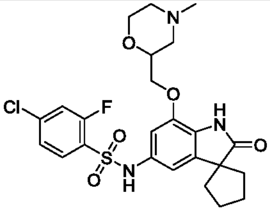
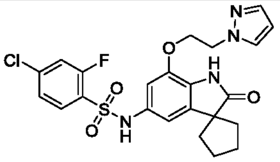
The below compounds were prepared by procedure similar to the one described in two steps of Example-X with appropriate variations in reactants, quantities of reagents and reaction conditions. The physiochemical characteristics of the compounds are summarized herein below table.

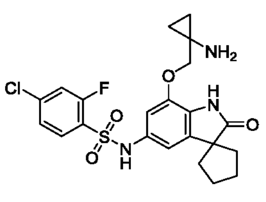
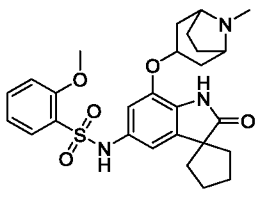
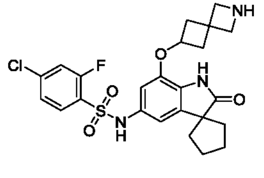
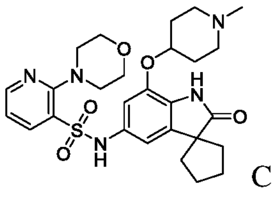
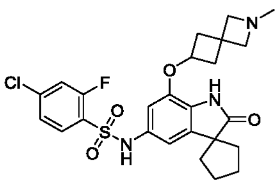
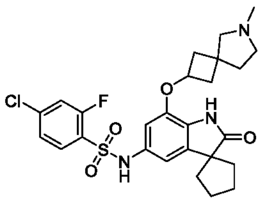
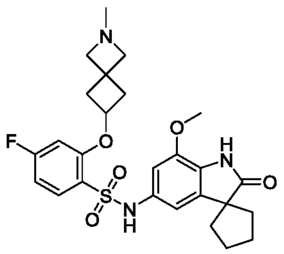
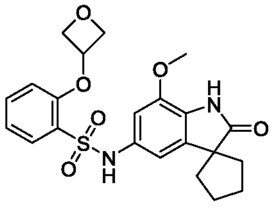
Comp No.	Structure	Analytical Data
34		^{1}H NMR (400 MHz, DMSO-d_6): δ 10.17 (s, 1H), 9.52 (s, 1H), 7.65-7.63 (m, 1H), 7.54-7.52 (m, 1H), 7.16 (d, J=8.3 Hz, 1H), 6.98 (t, J=7.8 Hz, 1H), 6.56 (d, *J*=1.5 Hz, 1H), 6.53 (d, *J*=1.5 Hz, 1H), 4.15-4.05 (m, 1H), 3.89 (s, 3H), 2.75-2.65 (m, 2H), 2.25-2.20 (m, 5H), 1.88-1.79 (m, 8H), 1.58-1.49 (m, 4H); LC-MS: m/z 486.1 (M+H).

35		^{1}H NMR (400 MHz, DMSO-d_6): δ 10.28 (s, 1H), 10.15-10.05 (bs, 1H), 7.74-7.66 (m, 2H), 7.43 (d, J=8.3 Hz, 1H), 6.53 (s, 1H), 6.50 (s, 1H), 4.15-4.11 (m, 1H), 2.75-2.70 (m, 2H), 2.30-2.25 (m, 5H), 1.90-1.78 (m, 8H), 1.62-1.56 (m, 4H); LC-MS: m/z 509.0 (M+2H).

Although the present application has been illustrated by certain of the preceding examples, it is not to be construed as being limited thereby; but rather, the present application encompasses the generic area as hereinbefore disclosed. Various modifications and embodiments can be made without departing from the spirit and scope thereof. For example, the following compounds which can be prepared by following similar procedure as described above with suitable modifications known to the one ordinary skilled in the art are also included in the scope of the present application.

 Compound No: 36	 Compound No: 37	 Compound No: 38	 Compound No: 39
 Compound No: 40	 Compound No: 41	 Compound No: 42	 Compound No: 43
 Compound No: 44	 Compound No: 45	 Compound No: 46	 Compound No: 47

 Compound No: 48	 Compound No: 49	 Compound No: 50	 Compound No: 51
 Compound No:52	 Compound No: 53	 Compound No: 54	 Compound No: 55
 Compound No: 56	 Compound No: 57	 Compound No: 58	 Compound No: 59
 Compound No: 60	 Compound No: 61	 Compound No: 62	 Compound No: 63
 Compound No: 64	 Compound No: 65	 Compound No: 66	 Compound No: 67

 Compound No: 68	 Compound No: 69	 Compound No: 70	 Compound No: 71
 Compound No: 72	 Compound No: 73	 Compound No:74, and	 Compound No: 75

BIOLOGICAL DATA:

In-Vitro Biochemical data of spiro[cyclopentane-1,3'-indolin]-2'-one derivatives in time-resolved fluorescence resonance energy transfer (TR-FRET) assay.

The Bet bromodomain TR-FRET assay has been used to identify compounds that bind to bet bromodomain and prevent its interaction with acetylated histone peptides.

In the assay, optimized concentration of in-house Bet bromodomain protein and 300nM of acetyl histone peptide substrate were diluted in assay buffer (50 mM HEPES, pH: 7.5, 50 mM NaCl, 500 µM CHAPS) and were added to the positive control and test control wells in a 384 well plate. Substrate control wells have 300 nM of acetyl histone peptide substrate diluted in assay buffer. Buffer blank wells were added with assay buffer. The reaction mixture was allowed for incubation at room temperature for 30mins. Stock solutions of test compounds at 20mM DMSO are prepared. Compounds are serially diluted and added to the test wells in 384-well polypropylene plates. The reaction mixture was further incubated for 30mins at room temperature on a plate shaker. 1 nM of Europium labeled streptavidn and 5nM of XL-665 labeled antibody diluted in detection buffer (50 mM HEPES, pH: 7.5, 50 mM NaCl, 500 µM CHAPS and 800 mM KF) were added to all the wells excluding the buffer blank wells. The reaction plate was incubated for additional 60mins at room temperature on plate shaker. The plate was read in Perkin Elmer WALLAC 1420 Multilabel Counter Victor 5 (Ex: 340 nm Em:

615 and 665 nm). The amount of displacement of the peptide was measured as ratio of specific 665 nm energy transfer signal to 615 nm signals. The compounds IC_{50} was determined by fitting the dose response data to sigmoid curve fitting equation using Graph Pad Prism software V7.

The compounds were screened in the above-mentioned assay and the results (IC_{50}) are summarized in the table-1 below; wherein group "A" refers to an IC_{50} value of less than or equal to 1 µM and group "B" refers to IC_{50} value in range of 1 to 10 µM

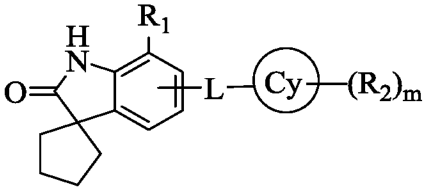
Table-1: IC_{50} values for BRD4 activity for selected compounds

Comp. No	% inhibition @1µM	% inhibition @10µM	BRD4 Full IC50(µM)
1.	97	100	A
2.	26	80	B
3.	69	72	A
4.	29	92	B
5.	20	66	-
6.	55	96	A
7.	17	66	-
8.	89	99	A
9.	30	84	B
10.	35	84	B
11.	67	98	A
12.	43	93	B
13.	44	97	B
14.	92	99	A
15.	73	99	A
16.	94	99	A
17.	60	96	A
18.	46	94	B
19.	1	27	-
20.	27	60	B

21.	5	30	-
22.	53	95	A
23.	67	98	A
24.	84	99	A
25.	46	92	B
26.	93	99	A
27.	60	99	A
28.	5	93	B
29.	6	52	B
30.	14	67	B
31.	0	26	-
32.	0	27	-
33.	71	97	A
34.	96	102	A
35.	95	102	A

We Claim:

1. A compound of formula(I):



(I)

or a pharmaceutically acceptable salt or a stereoisomer thereof;

wherein;

Cy is a 3-12 membered monocyclic or bicyclic ring containing 0-4 hetero atoms or groups independently selected from N, O, S, NH or C(O);

L represents a linker selected from $-NHS(O)_2-$, $-S(O)_2NH-$, $-NHS(O)_2CH(R_3)-$, $-N=S(O)(R_3)-$ or $-NHC(O)CH(R_3)-$;

R_1 is hydrogen, cyano, nitro, halogen, C_{1-7} alkyl, haloalkyl, $-OR_a$, $-COR_a$, $-COOR_a$, $-O(CO)R_a$, $-CONR_aR_b$, $-NHCOR_a$, $-NR_aR_b$, $-SR_3$, $-S(O_2)R_3$, optionally substituted alkylamino, optionally substituted C_{3-10} cycloalkyl, optionally substituted C_{3-10} cycloalkylalkyl, optionally substituted aryl, optionally substituted arylalkyl, optionally substituted heterocyclyl or optionally substituted heterocyclylalkyl; wherein the optional substitution at each occurrence is independently 1-3 substituents selected from halogen, C_{1-7} alkyl, C_{1-7} alkoxy, haloalkyl or C_{3-10} cycloalkyl;

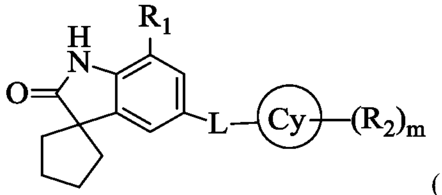
R_2 is halogen, C_{1-7} alkyl, $-OR_a$, haloalkyl, amino, alkylamino, cyano, nitro, $-COOR_3$, $-SR_3$, $-S(O_2)R_3$, optionally substituted C_{3-10} cycloalkyl, optionally substituted aryl or optionally substituted heterocyclyl; wherein the optional substitution at each occurrence is independently 1-3 substituents selected from halogen, cyano, nitro, amino, oxo, hydroxy, alkylamino, $-COOR_3$, $-SR_3$, $-S(O_2)R_3$, C_{1-7} alkyl, C_{1-7} alkoxy, C_{3-10} cycloalkyl, aryl or heterocyclyl;

R_3 is hydrogen or C_{1-7} alkyl;

R_a and R_b are independently selected from hydrogen, C_{1-7} alkyl, haloalkyl, optionally substituted alkylamino, optionally substituted C_{3-10} cycloalkyl, optionally substituted C_{3-10} cycloalkylalkyl , optionally substituted heterocyclyl , optionally substituted heterocyclylalkyl, optionally substituted C_{3-12} spiroheterocyclyl, optionally substituted aryl or optionally substituted arylalkyl; wherein the optional substitution at each occurrence is independently 1-3 substituents selected from halogen, cyano, nitro, amino, oxo, hydroxy, alkylamino, -COOR$_3$, -SR$_3$, -S(O$_2$)R$_3$, C$_{1-7}$ alkyl, C$_{1-7}$ alkoxy, C$_{3-10}$ cycloalkyl, aryl or heterocyclyl; and

'm' is 0, 1, 2 or 3.

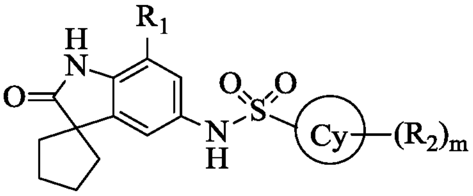
2. A compound according to claim 1, wherein the compound is represented by formula(IA):



(IA),

or a pharmaceutically acceptable salt or a stereoisomer thereof; wherein, R$_1$, R$_2$, L, Cy and 'm' are same as defined in claim 1.

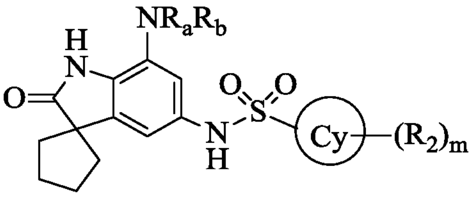
3. A compound according to claim 1or 2, wherein the compound is represented by formula(IB):



(IB),

or a pharmaceutically acceptable salt or a stereoisomer thereof; wherein, R$_1$, R$_2$, Cy and 'm' are same as defined in claim 1.

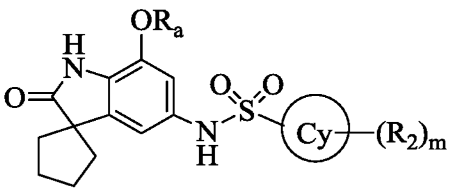
4. A compound according to claim 1or 2, wherein the compound is represented by formula(IC):



(IC),

or a pharmaceutically acceptable salt or a stereoisomer thereof; wherein, R$_2$, Cy, R$_a$, R$_b$ and 'm' are same as defined in claim 1.

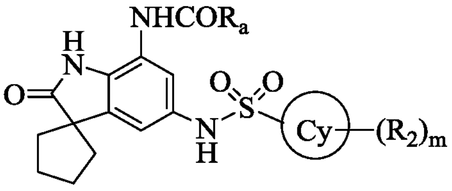
5. A compound according to claim 1or 2, wherein the compound is represented by formula(ID):



(ID),

or a pharmaceutically acceptable salt or a stereoisomer thereof; wherein, R$_2$, Cy, R$_a$ and 'm' are same as defined in claim 1.

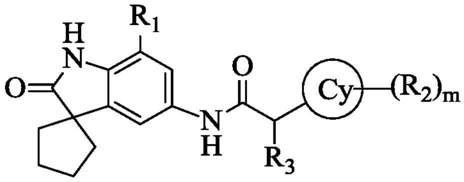
6. A compound according to claim 1or 2, wherein the compound is represented by formula (IE):



(IE),

or a pharmaceutically acceptable salt or a stereoisomer thereof; wherein, R_2, Cy, R_a and 'm' are same as defined in claim 1.

7. A compound according to claim 1or 2, wherein the compound is represented by formula (IF):



(IF),

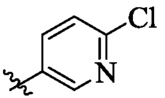
or a pharmaceutically acceptable salt or a stereoisomer thereof; wherein, R_1, R_2, R_3, Cy and 'm' are same as defined in claim 1.

8. A compound according to any of claims 1 to 7, wherein Cy is a 3-8 membered monocyclic ring or 8-12 membered bicyclic ring containing 0-3 heteroatoms independently selected from N, NH, O or C(O).

9. A compound according to claim 8, wherein Cy is cyclohexyl, phenyl, piperidinyl, pyridinyl, 1,4-benzodioxanyl, 2-oxobicyclo[2.2.1]heptane, [1,2,4]triazolo[4,3-a]pyridine, 1,2,3,4-tetrahydro isoquinoline or quinoline.

10. A compound according to any of claims 1 to 9, wherein R_2 is selected from halogen, $-OR_a$, C_{1-7}alkyl, C_{1-7}alkoxy or 4-10 membered heterocyclic ring containing 1-3 heteroatoms independently selected from O, N, NH or C(O); wherein the heterocyclic ring is optionally substituted with 1-2 substituents selected from halogen or C_{1-7} alkyl; R_a is selected from haloalkyl, heterocyclyl, C_{1-7} alkyl substituted C_{3-12} spiroheterocyclyl; and 'm' is 0, 1, 2 or 3.

11. A compound according to any of claims 1 to 10, wherein Cy-$(R_2)_m$ is selected from one of the following groups or tautomer's thereof;



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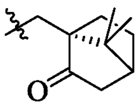

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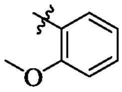

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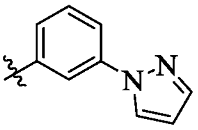

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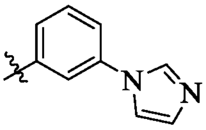

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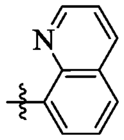

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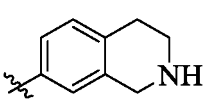

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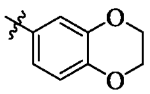

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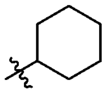
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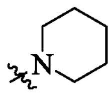

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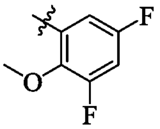

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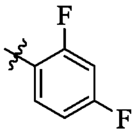

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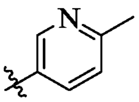

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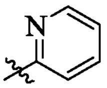

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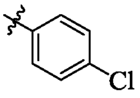

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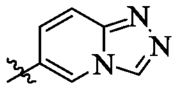

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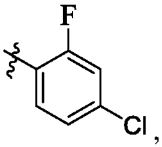

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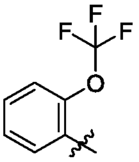

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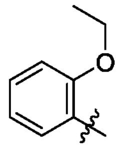

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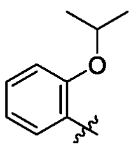

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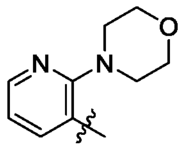

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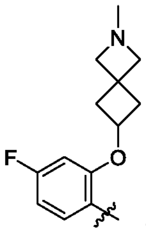
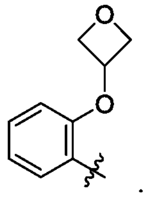


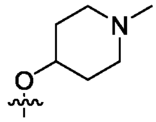
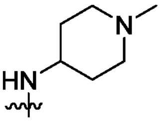
or


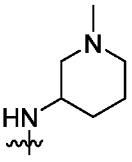
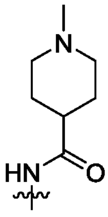
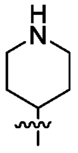
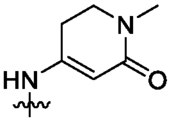
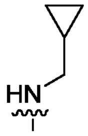
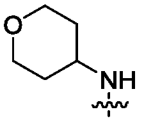
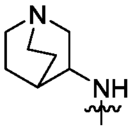
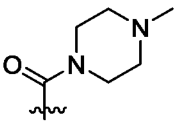
.

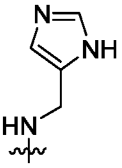
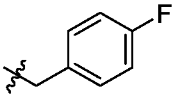
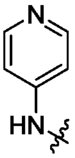
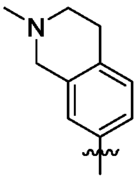
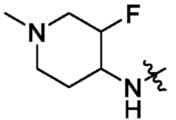
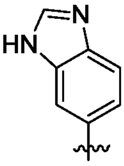
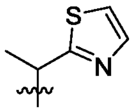
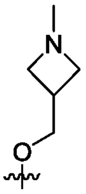
12. A compound according to any of claims 1 to 11, wherein R_1 is selected from hydrogen, cyano, halogen, C_{1-7} alkyl, -OR_a, -COR_a, -$O(CO)R_a$, -$CONR_aR_b$, -$NHCOR_a$, -NR_aR_b, optionally substituted C_{3-10} cycloalkyl, optionally substituted arylalkyl, optionally substituted heterocyclyl or optionally substituted heterocyclylalkyl; wherein the optional substitution is selected from halogen or C_{1-7} alkyl; and heterocyclyl group is a 3-10 membered mono or bicyclic ring containing 1-3 heteroatoms independently selected from N, NH, O, S or C(O).

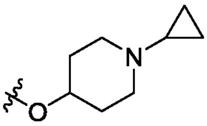
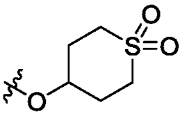
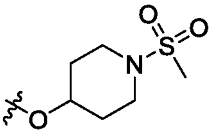
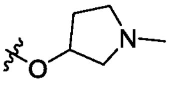
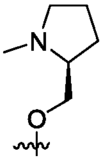
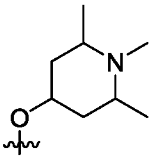
13. A compound according to claim 12, wherein R_a and R_b are independently selected from hydrogen, optionally substituted alkylamino, optionally substituted C_{3-10} cycloalkylalkyl, optionally substituted heterocyclyl, optionally substituted heterocyclylalkyl or optionally substituted C_{3-12} spiroheterocyclyl; wherein the optional substitution is selected from halogen, amino, oxo, -$S(O_2)R_3$, C_{1-7} alkyl or C_{3-10} cycloalkyl; and heterocyclyl group is a 3-10 membered mono or bicyclic ring containing 1-3 heteroatoms independently selected from N, NH, O, S or C(O).

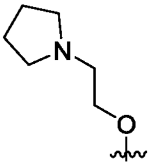
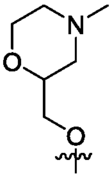
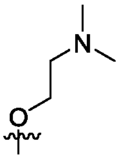
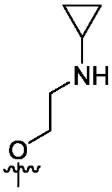
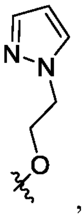
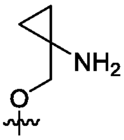
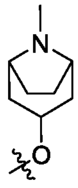
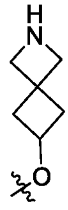
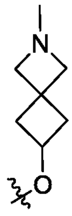
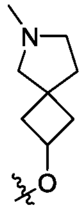
14. A compound according to any of claims 1 to 13, wherein R_1 is hydrogen, hydroxyl,

amino, bromo, chloro, cyano, methyl, CONH$_2$, cyclopropyl,  ,  ,

 ,  ,  ,  ,  ,  ,  ,  ,

 ,  ,  ,  ,  ,  ,  ,  ,

 ,  ,  ,  ,  ,  ,

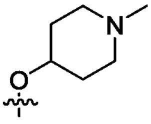
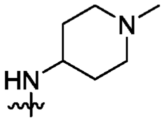
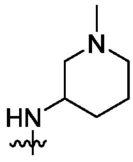
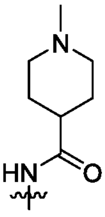
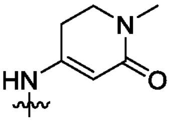
 ,  ,  ,  ,  ,  ,  ,  ,  or  .

15. A compound according to any of claims 1 to 14, wherein L is a linker selected from -NHS(O)$_2$-, -S(O)$_2$NH-, -N=S(O)(CH$_3$)-, -NHS(O)$_2$CH$_2$- or -NHC(O)CH(CH$_3$)-.

16. A compound according to any of claims 1 to 15, wherein Cy is cyclohexyl, phenyl, piperidinyl, pyridinyl, 1,4-benzodioxanyl, 2-oxobicyclo[2.2.1]heptane, [1,2,4]triazolo[4,3-a]pyridine, 1,2,3,4-tetrahydroisoquinoline or quinoline;

L is -NHS(O)$_2$-;

R$_1$ is hydrogen, hydroxyl, amino, bromo, chloro, cyano, methyl, CONH$_2$, cyclopropyl,

 ,  ,  ,  or  ;

R_2 is halogen, C_{1-7} alkyl or C_{1-7} alkoxy.

17. A compound according to claim1 is selected from the group consisting of:

Comp No	IUPAC name
1.	6-chloro-N-(2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)pyridine-3-sulfonamide;
2.	1-((1R)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl)-N-(2'-oxospiro[cyclo pentane-1,3'-indolin]-5'-yl)methanesulfonamide;
3.	2-methoxy-N-(2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
4.	N-(2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-3-(1H-pyrazol-1-yl)benzene sulfonamide;
5.	3-(1H-imidazol-1-yl)-N-(2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)benzene sulfonamide;
6.	N-(2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)quinoline-8-sulfonamide;
7.	N-(2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-1,2,3,4-tetrahydroisoquinoline-7-sulfonamide;
8.	N-(7'-bromo-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2,3-dihydrobenzo[b] [1,4]dioxine-6-sulfonamide;
9.	N-(2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)cyclohexanesulfonamide;
10.	N-(2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)piperidine-1-sulfonamide;
11.	6-chloro-N-(7'-methyl-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)pyridine-3-sulfonamide;
12.	N-(7'-bromo-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-3,5-difluoro-2-methoxybenzene sulfonamide;
13.	N-(7'-chloro-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-3-(1H-pyrazol-1-yl) benzene sulfonamide;
14.	N-(7'-cyclopropyl-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2,4-difluoro benzene sulfonamide;
15.	N-(7'-cyclopropyl-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-6-methylpyridine -3 sulfonamide;
16.	N-(7'-cyclopropyl-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-methoxy benzene sulfonamide;

17.	N-(7'-cyclopropyl-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)pyridine-2-sulfonamide;
18.	N-(7'-bromo-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-6-chloropyridine-3-sulfonamide;
19.	2-(4-chlorophenyl)-N-(2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)propanamide;
20.	N-(7'-bromo-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-(2-methoxyphenyl) propanamide;
21.	N-(2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-[1,2,4]triazolo[4,3-a]pyridine-6-sulfonamide;
22.	N-(7'-amino-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2,4-difluorobenzene sulfonamide;
23.	N-(7'-amino-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-methoxybenzene sulfonamide;
24.	2,4-difluoro-N-(7'-((1-methylpiperidin-4-yl)amino)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
25.	2,4-difluoro-N-(7'-((1-methylpiperidin-3-yl)amino)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
26.	2-methoxy-N-(7'-((1-methylpiperidin-4-yl)amino)-2'-oxospiro[cyclopentane-1,3' indolin]-5'-yl)benzenesulfonamide;
27.	2-methoxy-N-(7'-((1-methylpiperidin-3-yl)amino)-2'-oxospiro[cyclopentane-1,3' indolin]-5'-yl)benzenesulfonamide;
28.	2,4-difluoro-N-(7'-((1-methyl-6-oxo-1,2,3,6-tetrahydropyridin-4-yl)amino)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
29.	N-(7'-cyano-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2,4-difluorobenzene sulfonamide;
30.	5'-(2,4-difluorophenylsulfonamido)-2'-oxospiro[cyclopentane-1,3'-indoline]-7'-carboxamide;
31.	N-(2-methoxyphenyl)-2'-oxospiro[cyclopentane-1,3'-indoline]-5'-sulfonamide;
32.	N-(5'-((2,4-difluorophenyl)sulfonamido)-2'-oxospiro[cyclopentane-1,3'-indolin]-7'-yl)-1-methylpiperidine-4-carboxamide;

33.	N-(7'-hydroxy-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-methoxybenzene sulfonamide;
34.	2-methoxy-N-(7'-((1-methylpiperidin-4-yl)oxy)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide; and
35.	4-chloro-2-fluoro-N-(7'-((1methylpiperidin4yl)oxy)-2'-oxospiro[cyclopentane-1,3'-indolin]5'-yl)benzenesulfonamide;

or a pharmaceutically acceptable salt or a stereoisomer thereof.

18. A compound according to claim1 is selected from the group consisting of:

Comp No	IUPAC name
36	N-(2'-oxo-7'-(piperidin-4-yl)spiro[cyclopentane-1,3'-indolin]-5'-yl)-2-(trifluoro methoxy)benzenesulfonamide;
37	N-(7'-((cyclopropylmethyl)amino)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-methoxybenzenesulfonamide;
38	2,4-difluoro-N-(2'-oxo-7'-(piperidin-4-ylamino)spiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
39	2,4-difluoro-N-(2'-oxo-7'-((tetrahydro-2H-pyran-4-yl)amino)spiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
40	2,4-difluoro-N-(2'-oxo-7'-(quinuclidin-3-ylamino)spiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
41	2,4-difluoro-N-(7'-(4-methylpiperazine-1-carbonyl)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
42	N-(7'-(((1H-imidazol-5-yl)methyl)amino)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2,4-difluorobenzenesulfonamide;
43	2,4-difluoro-N-(7'-(4-fluorobenzyl)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl) Benzenesulfonamide;
44	5'-((2,4-difluorophenyl)sulfonamido)-2'-oxo-N-(pyridin-4-yl)spiro[cyclopentane-1,3'-indoline]-7'-carboxamide;
45	5'-(cyclohexanesulfonamido)-N-(1-methylpiperidin-4-yl)-2'-oxospiro[cyclopentane-1,3'-indoline]-7'-carboxamide;
46	2,4-difluoro-N-(7'-(2-methyl-1,2,3,4-tetrahydroisoquinolin-7-yl)-2'-oxospiro

	[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
47	5'-((2-ethoxyphenyl)sulfonamido)-N-(1-methylpiperidin-4-yl)-2'-oxospiro[cyclopentane-1,3'-indoline]-7'-carboxamide;
48	N-(1-methylpiperidin-4-yl)-2'-oxo-5'-(piperidine-1-sulfonamido)spiro[cyclopentane-1,3'-indoline]-7'-carboxamide;
49	N-(7'-((3-fluoro-1-methylpiperidin-4-yl)amino)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-methoxybenzenesulfonamide;
50	N-(7'-(1H-benzo[d]imidazol-6-yl)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2,4-difluorobenzenesulfonamide;
51	2-methoxy-N-(2'-oxo-7'-(1-(thiazol-2-yl)ethyl)spiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
52	5'-((2-methoxyphenyl)sulfonamido)-2'-oxospiro[cyclopentane-1,3'-indolin]-7'-yl 4-methylpiperazine-1-carboxylate;
53	2-isopropoxy-N-(7'-((1-methylpiperidin-4-yl)oxy)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
54	2-methoxy-N-(7'-((1-methylazetidin-3-yl)methoxy)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide
55	N-(7'-((1-ethylpiperidin-4-yl)oxy)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-methoxybenzenesulfonamide;
56	N-(7'-((1-cyclopropylpiperidin-4-yl)oxy)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-methoxybenzenesulfonamide;
57	5'-(((2-methoxyphenyl)(methyl)(oxo)-l6-sulfaneylidene)amino)-7'-((1-methylpiperidin-4-yl)amino)spiro[cyclopentane-1,3'-indolin]-2'-one;
58	N-(7'-((1,1-dioxidotetrahydro-2H-thiopyran-4-yl)oxy)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-methoxybenzenesulfonamide;
59	N-(7'-(2-(dimethylamino)ethoxy)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-methoxybenzenesulfonamide;
60	4-chloro-2-fluoro-N-(7'-((1-(methylsulfonyl)piperidin-4-yl)oxy)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
61	4-chloro-2-fluoro-N-(7'-((1-methylpyrrolidin-3-yl)oxy)-2'-oxospiro[cyclo

	pentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
62	(S)-2-methoxy-N-(7'-((1-methylpyrrolidin-2-yl)methoxy)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
63	4-chloro-2-fluoro-N-(2'-oxo-7'-((1,2,6-trimethylpiperidin-4-yl)oxy)spiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
64	N-(7'-(2-(cyclopropylamino)ethoxy)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-methoxybenzenesulfonamide;
65	2-methoxy-N-(2'-oxo-7'-(2-(pyrrolidin-1-yl)ethoxy)spiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
66	4-chloro-2-fluoro-N-(7'-((4-methylmorpholin-2-yl)methoxy)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
67	N-(7'-(2-(1H-pyrazol-1-yl)ethoxy)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-4-chloro-2-fluorobenzenesulfonamide;
68	N-(7'-((1-aminocyclopropyl)methoxy)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-4-chloro-2-fluorobenzenesulfonamide;
69	2-methoxy-N-(7'-((8-methyl-8-azabicyclo[3.2.1]octan-3-yl)oxy)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
70	N-(7'-((2-azaspiro[3.3]heptan-6-yl)oxy)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-4-chloro-2-fluorobenzenesulfonamide;
71	N-(7'-((1-methylpiperidin-4-yl)oxy)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-morpholinopyridine-3-sulfonamide;
72	4-chloro-2-fluoro-N-(7'-((2-methyl-2-azaspiro[3.3]heptan-6-yl)oxy)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
73	4-chloro-2-fluoro-N-(7'-((6-methyl-6-azaspiro[3.4]octan-2-yl)oxy)-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)benzenesulfonamide;
74	4-fluoro-N-(7'-methoxy-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-((2-methyl-2-azaspiro[3.3]heptan-6-yl)oxy)benzenesulfonamide; and
75	N-(7'-methoxy-2'-oxospiro[cyclopentane-1,3'-indolin]-5'-yl)-2-(oxetan-3-yloxy) Benzenesulfonamide;

or a pharmaceutically acceptable salt or a stereoisomer thereof.

19. A pharmaceutical composition comprising a compound according to any of claims 1-18

or a pharmaceutically acceptable salt or a stereoisomer thereof and at least one pharmaceutically acceptable carrier or diluent.

20. A method for treatment or prevention of diseases or disorders where bromodomain inhibition is desired comprising administering to a subject in need thereof a therapeutically effective amount of a compound of any one of claims 1-18.

21. The method of claim 20, wherein the disease or disorder is an autoimmune disease, an inflammatory disease or cancer.

22. A method of modulating the function of bromodomain in a subject in need thereof by administering to the subject a therapeutically effective amount of a compound of any one of claims 1 to 18.

23. A compound according to any of claims 1-18, for use in the manufacture of a medicament for the treatment or prevention of diseases or disorders where bromodomain inhibition is desired.

24. A compound according to any of claims 1 to 18, for use in the treatment of an immune disorder, an inflammatory disorder or cancer.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2017/057823

A. CLASSIFICATION OF SUBJECT MATTER
C07D401/12 Version=2018.01

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C07D

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Patseer, IPO Internal Database

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO2009124692 (ALMIRALL, S.A.) 15/Oct/2009(15/10/2009) *The whole document*	1-19, 23 & 24
A	WO2009132774 (ALMIRALL, S. A.) 05/Nov/2009(05/11/2009) *The whole document*	1-19, 23 & 24
A	WO2015092118 (ORION CORPORATION) 25/Jun/2015 (25/06/2015) *The whole document*	1-19, 23 & 24

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents:

"A"	document defining the general state of the art which is not considered to be of particular relevance
"E"	earlier application or patent but published on or after the international filing date
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O"	document referring to an oral disclosure, use, exhibition or other means
"P"	document published prior to the international filing date but later than the priority date claimed
"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&"	document member of the same patent family

Date of the actual completion of the international search 06-04-2018	Date of mailing of the international search report 06-04-2018
Name and mailing address of the ISA/ Indian Patent Office Plot No.32, Sector 14,Dwarka,New Delhi-110075 Facsimile No.	Authorized officer Dr. Manmeet Kumar Telephone No. +91-1125300200

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2017/057823

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 20-22
because they relate to subject matter not required to be searched by this Authority, namely:
The subject matter of claims 20-22 relates to a method for treatment of the human, which does not require an international search by the International Searching Authority in accordance with PCT Article 17(2)(a)(i) and [Rule 39.1(iv)].

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

International application No.

PCT/IB2017/057823

Citation	Pub.Date	Family	Pub.Date
WO 2009124692 A1	15-10-2009	EP 2280943 A1	09-02-2011
		JP 2011516512 A	26-05-2011
WO 2009132774 A1	05-11-2009	US 2009132774 A1	24-02-2011
		EP 2113503 A1	04-11-2009