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(54) **Title**: SUBSTITUTED OXINDOLE CB2 AGONISTS

(57) **Abstract**: Provided are substituted compounds, or pharmaceutically acceptable salts thereof, wherein: R^1 is selected from -(CH_2)nR^a, -CH(OH)R^a, -CH(OR^b)R^a, and -C(O)R^a, or is selected from OR^a, SR^a, SOR^a, SO_2R^a and NR^aR^b; R^2 and R^3 are independently selected from H, halogen, OH, OR^a, OWR^a, C_{1-6} alkyl, and WC $_{1-6}$ alkyl, wherein C_{1-6} alkyl or OR^a, is optionally substituted with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-8}cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; or R^2 and R^3, together with the carbon atom to which they are attached, join to form a ring selected from 3-8 membered cycloalkyl, 3-8 membered heterocycloalkyl, C_5-C_7 oxycycloalkyl, C_{5-7} dioxycycloalkyl and oxazolidinyl ring, each ring optionally substituted with 1, 2, or 3 substituents independently selected from halogen, CN, OH, 0R^a, C_{1-6}alkyl, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{6-10}aryl and C_{4-10} heteroaryl; R^4 is independently selected from H.C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6}alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, -$(CH_2)_n$-benzodioxane, -$(CH_2)_n$- oxazolidinone and -$(CH_2)_n$-C_{1-6} haloalkyl, each of which is optionally substituted with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{1-6} haloalkyl, $C_{3.8}$ cycloalkyl, $WC_{3.8}$ cycloalkyl, C_{6-10} aryl and $C_{4.10}$ heteroaryl; which are agonists of the CB2 receptor, pharmaceutical compositions containing the same, and methods of treatment related to CB2-mediated disorders (eg., pain, cancer etc.) using the substituted oxindole compounds and compositions described herein.

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SUBSTITUTED OXINDOLE CB2 AGONISTS

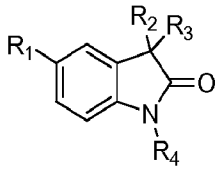
BACKGROUND

CB1 and CB2 receptors, two subtypes of the cannabinoid receptor, both belong to the G-protein-coupled receptor (GPCR) superfamily. The CB1 receptor is predominantly expressed in brain to mediate inhibition of transmitter release and affects many neurological and psychological phenomena, such as mood, appetite, emesis control, memory, spatial coordination muscle tone, and analgesia, as described by Goutopoulos et al., in the publication Pharmacol Ther (2002) 95:103. The CB2 receptor is primarily expressed in immune cells to modulate immune response. Activation of the CB2 receptor is known to induce analgesic effects in inflammatory models involved in neurodegeneration diseases, and plays a role in the maintenance of bone density and progression of atherosclerotic lesions. It has been known that CB2 agonists are potential drug candidates for reducing pain (such as chronic inflammatory pain, post surgical pain, neuropathic pain, and bone pain) and for treating a host of diseases including osteoarthritis, atherosclerosis, osteoporosis, and cancer (e.g., glioma), as described by Malan et al., in the publication Pain (2001) 93:239.

Accordingly, there is an ongoing need for new and improved compounds that modulate the CB2 receptor and can function as therapeutics for the treatment of various CB2 receptor-modulated diseases and disorders such as pain. The invented compounds disclosed herein provide a solution to this need.

SUMMARY OF THE INVENTION

In one aspect, the invention relates to a compound of Formula I:



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or pharmaceutically acceptable salt thereof, wherein the variables are defined herein.

In another aspect, the invention relates to a pharmaceutical composition comprising one or more of the above-described substituted oxindole compounds of the invention, or pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

In another aspect, the invention relates to a method of treating a CB2-mediated disorder by administering to a subject in need of this treatment a therapeutically effective amount of one or more of the compounds described above. CB2-mediated disorders include, but are not limited to, pain (such as chronic inflmmartory pain, post surgical pain, neuropathic pain, bone pain), osteoarthritis, atherosclerosis, osteoporosis, and cancer (e.g., glioma).

In another aspect, the invention relates to a compound of the invention, or pharmaceutically acceptable salt thereof, for use in therapy.

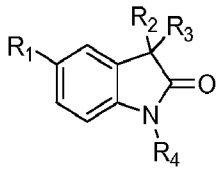
In another aspect, the invention relates to a compound of the invention, or pharmaceutically acceptable salt thereof, for use in the treatment of a CB2-mediated disorder such as pain (e.g., chronic inflmmartory pain, post surgical pain, neuropathic pain, bone pain), osteoarthritis, atherosclerosis, osteoporosis, or cancer (e.g., glioma).

In another aspect, the invention relates to a compound of the invention, or pharmaceutically acceptable salt thereof, for use in the preparation of a medicament for use in the treatment of one or more CB2-mediated disorders.

The details of one or more embodiments of the invention are set forth in the accompanying description below. Other features, objects, and advantages of the invention will be apparent from the description and drawings, and from the claims.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides substituted oxindole compounds, that function as CB2 agonists, of Formula I:



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or pharmaceutically acceptable salts thereof, wherein:

R^1 is selected from $-(CH_2)_nR^a$, $-CH(OH)R^a$, $-CH(OR^b)R^a$, and $-C(O)R^a$, or is selected from OR^a, SR^a, SOR^a, SO_2R^a and NR^aR^b;

R^2 and R^3 are independently selected from H, halogen, OH, OR^a, OWR^a, C_{1-6} alkyl, and WC_{1-6} alkyl, wherein C_{1-6} alkyl or OR^a, is optionally substituted with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl;

or R^2 and R^3, together with the carbon atom to which they are attached, join to form a ring selected from 3-8 membered cycloalkyl, 3-8 membered heterocycloalkyl, C_5-C_7 oxycycloalkyl, C_{5-7} dioxycycloalkyl and oxazolidinyl ring, each ring optionally substituted with 1, 2, or 3 substituents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl;

R^4 is independently selected from H, C_1-$_6$ alkyl, C_2-$_6$ alkenyl, C_2-$_6$ alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n$-benzodioxane, $-(CH_2)_n$- oxazolidinone and $-(CH_2)_n$-C_{1-6} haloalkyl, each of which is optionally substituted with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, WC_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl;

at each occurrence W is $-(CH_2)_n$- or -C(O)-;

at each occurrence, R^a and R^b are independently selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, C_{3-8} cycloalkyl, C_{3-8} heterocycloalkyl, C_{3-8}

heterocycloalkenyl C_{7-14} arylalkyl, C_{4-14} heteroarylalkyl, C_{5-12} cycloalkylalkyl and C_{5-12} heterocycloalkylalkyl, each of which is optionally substituted with OR^a, cyano, amino, halo, C_{1-6} alkyl, C_{6-10} aryl, C_{4-10} heteroaryl, C_{3-8} cycloalkyl, C_{3-8} heterocycloalkyl, C_{3-8} heterocycloalkenyl C_{7-14} arylalkyl, C_{4-14} heteroarylalkyl, C_{5-12} cycloalkylalkyl and C_{5-12} heterocycloalkylalkyl;

at each occurrence, halogen is selected from F, Cl, Br and I; and

at each occurrence, n is 0, 1, 2, or 3.

According to one embodiment, the invented compounds selected from:

5'-benzoyl-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2-fluorobenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(3-fluorobenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(4-fluorobenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[3-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[3-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[4-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2-methoxybenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(3-methoxybenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(4-methoxybenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(2-chlorobenzoyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(3-chlorobenzoyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(4-chlorobenzoyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(3-methylbenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(4-methylbenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[3-(trifluoromethoxy)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[4-(trifluoromethoxy)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(3-furoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(3-thienylcarbonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2-methylbenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[4-fluoro-2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[5-fluoro-2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-[4-chloro-2-(trifluoromethyl)benzoyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2,3-difluorobenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(cyclopropylmethyl)-5'-(2,5-difluorobenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(3-chloro-4-fluorobenzoyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2,3-dichlorobenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2,5-dichlorobenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(3,4-dichlorobenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2,3-dimethoxybenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2-methoxy-5-

methylbenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(5-chloro-2-methoxybenzoyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(5-fluoro-2-methoxybenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2,3-dimethylbenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2,6-dimethylbenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(5-chloro-2-methylbenzoyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[2-(trifluoromethoxy)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2,4-difluorobenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2,6-dimethoxybenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[hydroxy(phenyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[(2-fluorophenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[(3-fluorophenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[(4-fluorophenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 2-[5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}-2'-oxospiro[1,3-dioxane-2,3'- indol]-1'(2'H)-yl]benzonitrile, (-)-2-[5'-{(S)-hydroxy[2-(trifluoromethyl)phenyl]methyl}-2'-oxospiro[1,3-dioxane- 2,3'-indol]-1'(2'H)-yl]benzonitrile, (+)2-[5'-{(R)-hydroxy[2-(trifluoromethyl)phenyl]methyl}-2'-oxospiro[1,3-dioxane- 2,3'-indol]-1'(2'H)-yl]benzonitrile, (+)-1'-(3,4-difluorophenyl)-5'-{(R)-hydroxy[2-(trifluoromethyl)phenyl]-methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, (-)-1'-(3,4-difluorophenyl)-5'-{(S)-hydroxy[2-(trifluoromethyl)phenyl]-methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(cyclopropylmethyl)-5'-{1-hydroxy-1-[2-(trifluoromethyl)phenyl]ethyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(3,4-difluorophenyl)-5'-{1-hydroxy-1-[2-(trifluoromethyl)phenyl]ethyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(cyclopropylmethyl)-5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-{hydroxy[3-(trifluoromethyl)phenyl]methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-{hydroxy[4-(trifluoromethyl)phenyl]methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[hydroxy(2-methoxyphenyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[hydroxy(3-methoxyphenyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[hydroxy(4-methoxyphenyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-[(2-chlorophenyl)(hydroxy)methyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-[(3-chlorophenyl)(hydroxy)methyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-[(4-chlorophenyl)(hydroxy)methyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[hydroxy(3-methylphenyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[hydroxy(4-methylphenyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-{hydroxy[3-(trifluoromethoxy)phenyl]methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-{hydroxy[4-(trifluoromethoxy)phenyl]methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[3-furyl(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[hydroxy(3-thienyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[hydroxy(2-methylphenyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-

(cyclopropylmethyl)-5'-{[4-fluoro-2-(trifluoromethyl)phenyl](hydroxy)methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-{[5-fluoro-2-(trifluoromethyl)phenyl](hydroxy)methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-{[4-chloro-2-(trifluoromethyl)phenyl](hydroxy)methyl}-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[(2,3-difluorophenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[(2,5-difluorophenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-[(3-chloro-4-fluorophenyl)(hydroxy)methyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[(2,3-dichlorophenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[(2,5-dichlorophenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[(3,4-dichlorophenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[(2,3-dimethoxyphenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[hydroxy(2-methoxy-5-methylphenyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-[(5-chloro-2-methoxyphenyl)(hydroxy)methyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[(5-fluoro-2-methoxyphenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[(2,3-dimethylphenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[(2,6-dimethylphenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-[(5-chloro-2-methylphenyl)(hydroxy)methyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-{hydroxy[2-(trifluoromethoxy)phenyl]methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[(2,4-difluorophenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-benzyl-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2-fluorobenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(3-fluorobenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(4-fluorobenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[3-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[4-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2-methoxybenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(3-methoxybenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(4-methoxybenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(2-chlorobenzyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(3-chlorobenzyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(4-chlorobenzyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(3-methylbenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(4-methylbenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[4-(trifluoromethoxy)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(3-thienylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2-

methylbenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[4-fluoro-2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[5-fluoro-2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-[4-chloro-2-(trifluoromethyl)benzyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2,3-difluorobenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2,5-difluorobenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(3-chloro-4-fluorobenzyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2,3-dichlorobenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2,5-dichlorobenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(3,4-dichlorobenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2,3-dimethoxybenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2-methoxy-5-methylbenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(5-chloro-2-methoxybenzyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(5-fluoro-2-methoxybenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2,3-dimethylbenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(5-chloro-2-methylbenzyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[2-(trifluoromethoxy)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2,4-difluorobenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one,

1'-phenyl-5'-[2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-benzoyl-1'-phenylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(2-fluorobenzoyl)-1'-phenylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(2-methoxybenzoyl)-1'-phenylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(2-chlorobenzoyl)-1'-phenylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(2-methylbenzoyl)-1'-phenylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 2-(5'-benzoyl-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl)benzonitrile, 2-[5'-(2-fluorobenzoyl)-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl]benzonitrile, 2-{2'-oxo-5'-[2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl}benzonitrile, 2-[5'-(2-methoxybenzoyl)-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl]benzonitrile, 2-[5'-(2-chlorobenzoyl)-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl]benzonitrile, 5'-benzoyl-1'-(3,4-difluorophenyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(3,4-difluorophenyl)-5'-(2-fluorobenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(3,4-difluorophenyl)-5'-[2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(3,4-difluorophenyl)-5'-(2-methoxybenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(2-chlorobenzoyl)-1'-(3,4-difluorophenyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(3,4-difluorophenyl)-5'-(2-methylbenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(2,5-difluorophenyl)-5'-[2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(2-chlorobenzoyl)-1'-(2,5-difluorophenyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(3-thienyl)-5'-[2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(2-chlorobenzoyl)-1'-(3-thienyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 2-[5'-(2-methylbenzoyl)-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl]benzonitrile,

5'-benzoyl-1'-(3,3,3-trifluoropropyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-propyl-5'-[2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(3,4-Difluorophenyl)-5'-phenethylspiro[[1,3]dioxane-2,3'-indolin]-2'-one, 5'-(Benzylamino)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(2-furylmethyl)amino]spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(2-thienylmethyl)amino]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 5'-{[(5-Chloro-2-thienyl)methyl]amino}-1'-(cyclopropylmethyl)spiro[1,3-dioxane- 2,3'-indol]-2'(1'H)-one, 5'-{[(2-Butyl-1-benzofuran-3-yl)methyl]amino}-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 5'-[(4-Chlorobenzyl)amino]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(4-methoxybenzyl)amino]spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(4-methylbenzyl)amino]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(3,4-dichlorobenzyl)amino]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 5'-[(3-Chlorobenzyl)amino]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-{[4-(trifluoromethyl)benzyl]amino}spiro[1,3-dioxane- 2,3'-indol]-2'(1'H)-one, 5'-{[4-Chloro-3-(trifluoromethyl)benzyl]amino}-1'-(cyclopropylmethyl)spiro[1,3- dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(1-naphthylmethyl)amino]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(2,3-dihydro-1,4-benzodioxin-6- ylmethyl)amino]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(4-fluorobenzyl)amino]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 5'-[(1-Benzothiophen-2-ylmethyl)amino]-1'-(cyclopropylmethyl)spiro[1,3-dioxane- 2,3'-indol]-2'(1'H)-one,

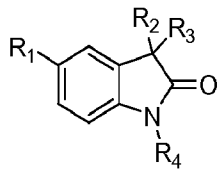
5'-[Bis(cyclohexylmethyl)amino]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(dimethylamino)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-Butyl-5'-(methylamino)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[methyl(phenyl)amino]spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-piperidin-1-ylspiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 5'-(Phenylthio)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 5'-(Phenylsulfinyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 5'-(Phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 5'-(Phenylthio)spiro[1,3-dioxolane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(phenylthio)spiro[1,3-dioxolane-2,3'-indol]-2'(1'H)-one, 5'-(Phenylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(phenylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]- 2'(1'H)-one, 1'-Phenyl-5'-(phenylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'H)-one, 5'-(Phenylsulfonyl)-1'-[3-(trifluoromethyl)phenyl]spiro[1,3-dioxolane-2,3'- indol]-2'(1'H)-one, 1'-(3,4-Difluorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'H)-one, 1'-Phenyl-5'-(phenylthio)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-Phenyl-5'-(phenylthio)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(3,4-Difluorophenyl)-5'-(phenylthio)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-Phenyl-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 5'-(Phenylsulfonyl)-1'-[3-(trifluoromethyl)phenyl]spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 1'-(3,4-difluorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(2,5-difluorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(3-fluorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(3,5-dichlorophenyl)-5'-

(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(3-chloro-4-fluorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(4-chlorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 5'-(phenylsulfonyl)-1'-[2-(trifluoromethyl)phenyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(2-methoxyphenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(4-fluorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(2,3-difluorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(phenylsulfinyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 5'-(Phenylthio)-1'-(2,2,2-trifluoroethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(phenylthio)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(2-fluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(2-methoxyphenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 5'-[(2-Chlorophenyl)sulfonyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 5'-[(3-Chlorophenyl)sulfonyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(2-methylphenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(3-fluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(4-fluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-{[2-(trifluoromethyl)phenyl]sulfinyl}spiro[1,3- dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(2,5-dichlorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 5'-[(4-Chlorophenyl)sulfonyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(3-methoxyphenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(3,4-dichlorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(3-methylphenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(4-methoxyphenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 5'-(1,3-Benzothiazol-2-ylsulfonyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(3,4-difluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(pyridin-4-ylthio)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(3,4-dichlorophenyl)thio]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(3,4-difluorophenyl)thio]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-{[3-(trifluoromethyl)phenyl]sulfanyl}spiro[1,3- dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(pyridin-2-ylsulfanyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(pyridin-4-ylsulfinyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(pyridin-2-ylsulfinyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(3,4-difluorophenyl)sulfinyl]-spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(pyridin-3-ylsulfanyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(4-methylphenyl)sulfanyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-{[4-(trifluoromethyl)phenyl]sulfanyl}spiro[1,3- dioxane-2,3'-indol]-2'(1'H)-one,

5'-[(3-Chloro-4-fluorophenyl)sulfanyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane- 2,3'-indol]-2'(1'H)-one, 5'-[(6-Chloropyridin-3-yl)sulfanyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane- 2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(naphthalen-1-ylsulfanyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(thiophen-2-ylsulfanyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(5-methyl-2-thienyl)thio]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 5'-[(5-Acetyl-2-thienyl)thio]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 5'-[(2-Chloropyridin-4-yl)thio]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(3,5-dichlorophenyl)thio]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(3,5-dichloropyridin-4-yl)thio]spiro[1,3-dioxane- 2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(2,4-dichlorophenyl)thio]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(2,5-dichlorophenyl)thio]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 5'-[(4-Chloro-2-fluorophenyl)thio]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(2,4-difluorophenyl)thio]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(pyridin-3-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-{[3-(trifluoromethyl)phenyl]sulfonyl}spiro[1,3- dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(4-methylphenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-{[4-(trifluoromethyl)phenyl]sulfonyl}spiro[1,3- dioxane-2,3'-indol]-2'(1'H)-one, 5'-[(3-Chloro-4-fluorophenyl)sulfonyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane- 2,3'-indol]-2'(1'H)-one, 5'-[(6-Chloropyridin-3-yl)sulfonyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane- 2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(naphthalen-1-ylsulfonyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(thiophen-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(5-methyl-2-thienyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 5'-[(5-Acetyl-2-thienyl)sulfonyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 5'-[(2-Chloropyridin-4-yl)sulfonyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane- 2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(3,5-dichlorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(3,5-dichloropyridin-4-yl)sulfonyl]spiro[1,3-dioxane- 2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(2,4-dichlorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 5'-[(4-Chloro-2-fluorophenyl)sulfonyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane- 2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(2,4-difluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(4-methoxyphenoxy)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(4-methoxyphenoxy)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(2,6-difluoropyridin-4-yl)oxy]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(2,3,5,6-tetrafluoropyridin-4-yl)oxy]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-[(3-Chloro-2,5,6-trifluoropyridin-4-yl)oxy]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(Cyclopropylmethyl)-5'-[(3,5-difluoro-2,6-dimethoxypyridin-4-yl)oxy]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-[(3-Chloro-5-fluoro-2,6-dimethoxypyridin-4-yl)oxy]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(Cyclopropylmethyl)-5'-[(2,3,5-

trifluoro-6-methoxypyridin-4-yl)oxy]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one and pharmaceutically acceptable salts thereof.

According to one embodiment, the invented compounds are certain substituted oxindole compounds of Formula I:



I

or pharmaceutically acceptable salts thereof, wherein:

R^1 is selected from -Y-R^a, -Y-Cy and -Y-Ar;

Y is a divalent carbon radical selected from -$(CH_2)_n$-, -CH(OH)-, -CH(OR^a)-, and -C(O)-, or Y is a heteroatom selected from O, S, SO, SO_2 and NR^aR^b;

Ar is independently selected from C_{6-10} aryl, C_{4-10} heteroaryl, C_{7-14} arylalkyl and C_{4-14} heteroarylalkyl, wherein each of said C_{6-10} aryl, C_{4-10} heteroaryl, C_{7-14} arylalkyl or C_{4-14} heteroarylalkyl is optionally substituted with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, OR^a-W, C_{1-6} alkyl, C_{1-6} W-alkyl, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{3-8} W-cycloalkyl, -C(O)-C_{1-6} alkyl, -C(O)-C_{6-10} aryl, C_{6-10} aryl and C_{4-10} heteroaryl;

Cy is independently selected from C_{3-8} cycloalkyl, C_{3-8} heterocycloalkyl, C_{3-8} heterocycloalkenyl, C_{4-12} W-cycloalkyl, C_{4-12} W-heterocycloalkyl and C_{3-8} W-heterocycloalkenyl, wherein each of said C_{3-8} cycloalkyl, C_{3-8} heterocycloalkyl, C_{3-8} heterocycloalkenyl, C_{4-12} W-cycloalkyl, C_{4-12} W-heterocycloalkyl or C_{3-8} W-heterocycloalkenyl, is optionally substituted with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, OR^a-W, C_{1-6} alkyl, C_{1-6} W-alkyl, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{3-8} W-cycloalkyl, -C(O)-C_{1-6} alkyl, -C(O)-C_{6-10} aryl, C_{6-10} aryl and C_{4-10} heteroaryl;

at each occurrence W is a linker selected from -$(CH_2)_n$- and -C(O)-;

R^2 and R^3 are independently selected from H, halogen, OH, OR^a, OR^a-W, C_{1-6} alkyl, C_{1-6} W-alkyl, wherein C_{1-6} alkyl or OR^a, is optionally substituted with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl;

or R^2 and R^3, together with the carbon atom to which they are attached, join to form a ring selected from 3-8 membered cycloalkyl, 3-8 membered heterocycloalkyl or C_5-C_7 oxycycloalkyl, C_{5-7} dioxycycloalkyl and oxazolidinyl ring, each ring optionally substituted with 1, 2, or 3 substituents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl;

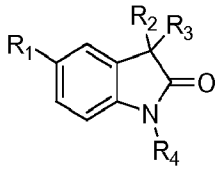
R^4 is independently selected from H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, -$(CH_2)_n$-benzodioxane, -$(CH_2)_n$- oxazolidinone and -$(CH_2)_n$-C_{1-6} haloalkyl, wherein each of said C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, -$(CH_2)_n$-benzodioxane, -$(CH_2)_n$-oxazolidinone is optionally substituted with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl;

at each occurrence, R^a is independently selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-6} haloalkyl, C_{6-10} aryl, C_{4-10} heteroaryl, C_{3-8} cycloalkyl, C_{3-8} heterocycloalkyl, C_{3-8} heterocycloalkenyl C_{7-14} arylalkyl, C_{4-14} heteroarylalkyl, C_{5-12} cycloalkylalkyl and C_{5-12} heterocycloalkylalkyl, wherein said C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, C_{3-8} cycloalkyl, C_{3-8} heterocycloalkyl, C_{3-8} heterocycloalkenyl C_{7-14} arylalkyl, C_{4-14} heteroarylalkyl, C_{5-12} cycloalkylalkyl or C_{5-12} heterocycloalkylalkyl, is optionally substituted with OR^a, cyano, amino, halo, C_{1-6} alkyl, C_{6-10} aryl, C_{4-10} heteroaryl, C_{3-8} cycloalkyl, C_{3-8} heterocycloalkyl, C_{3-8} heterocycloalkenyl C_{7-14} arylalkyl, C_{4-14} heteroarylalkyl, C_{5-12} cycloalkylalkyl and C_{5-12} heterocycloalkylalkyl;

halogen is selected from F, Cl, Br and I; and

n is 0, 1, 2, or 3.

According to a separate embodiment, the invented compounds are substituted oxindole compounds of Formula I:



I

or pharmaceutically acceptable salts thereof, wherein:

R^1 is selected from $-(CH_2)_nR^a$, $-CH(OH)R^a$, $-CH(OR^b)R^a$, and $-C(O)R^a$, or is selected from OR^a, SR^a, SOR^a, SO_2R^a and NR^aR^b;

R^2 and R^3 are independently selected from H, halogen, OH, OR^a, OWR^a, C_{1-6} alkyl, and WC_{1-6} alkyl, wherein C_{1-6} alkyl or OR^a, is optionally substituted with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl;

or R^2 and R^3, together with the carbon atom to which they are attached, join to form a ring selected from 3-8 membered cycloalkyl, 3-8 membered heterocycloalkyl, C_5-C_7 oxycycloalkyl, C_{5-7} dioxycycloalkyl and oxazolidinyl ring, each ring optionally substituted with 1, 2, or 3 substituents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl;

R^4 is independently selected from H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n$-benzodioxane, $-(CH_2)_n$- oxazolidinone and $-(CH_2)_n$-C_{1-6} haloalkyl, each of which is optionally substituted with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, WC_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl;

at each occurrence W is $-(CH_2)_n$- or -C(O)-;

at each occurrence, R^a and R^b are independently selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, C_{3-8} cycloalkyl, C_{3-8} heterocycloalkyl, C_{3-8}

heterocycloalkenyl C_{7-14} arylalkyl, C_{4-14} heteroarylalkyl, C_{5-12} cycloalkylalkyl and C_{5-12} heterocycloalkylalkyl, each of which is optionally substituted with OR^a, cyano, amino, halo, C_{1-6} alkyl, C_{6-10} aryl, C_{4-10} heteroaryl, C_{3-8} cycloalkyl, C_{3-8} heterocycloalkyl, C_{3-8} heterocycloalkenyl C_{7-14} arylalkyl, C_{4-14} heteroarylalkyl, C_{5-12} cycloalkylalkyl and C_{5-12} heterocycloalkylalkyl;

at each occurrence, halogen is selected from F, Cl, Br and I; and

at each occurrence, n is 0, 1, 2, or 3.

In some embodiments, R^1 is $-N(R^a)R^b$; R^2 and R^3, together with the carbon atom to which they are attached, join to form a ring selected from 3-8 membered cycloalkyl, 3-8 membered heterocycloalkyl, C_5-C_7 oxycycloalkyl, C_{5-7} dioxycycloalkyl and oxazolidinyl ring, each ring optionally substituted with 1, 2, or 3 substituents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-8} cycloalkyl, WC_{3-8} cycloalkyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n$-benzodioxane, $-(CH_2)_n$-oxazolidinone and $-(CH_2)_n$-C_{1-6} haloalkyl, each of which is optionally substituted with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl.

In some embodiments, R^1 is $-N(R^a)R^b$ and at least one of R^a and R^b are hydrogen or R^a and R^b, together with the N atom to which they are attached, join to form a 4-6 memebered heterocycloalkyl ring.

In some embodiments, R^1 is a methylene radical $-(CH_2)_n$- further attached to substituents selected from C_{6-10} aryl, C_{4-10} heteroaryl, benzodioxanyl, oxazolidinonyl, $-(CH_2)_n$-C_{1-6} haloalkyl, C_{3-8} cycloalkyl and C_{1-6} haloalkyl, each of which is optionally substituted with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, and C_{1-6} haloalkyl, C_{3-8} cycloalkyl, WC_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl.

In some embodiments, R^1 is $-OR^a$; R^2 and R^3, together with the carbon atom to which they are attached, join to form a ring selected from 3-8 membered cycloalkyl, 3-8 membered heterocycloalkyl, C_5-C_7 oxycycloalkyl, C_{5-7} dioxycycloalkyl and oxazolidinyl ring, each ring optionally substituted with 1, 2, or 3 substituents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{6-10} heteroaryl, $-(CH_2)_n$-benzodioxane, $-(CH_2)_n$- oxazolidinone, $-(CH_2)_n$-C_{1-6} haloalkyl, $-(CH_2)_n$- C_{3-8} cycloalkyl and C_{1-6} haloalkyl, each of which is optionally substituted with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl.

In some embodiments, R^1 is -O-, substituted with substituents selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n$-benzodioxane, $-(CH_2)_n$-oxazolidinone, each of which is optionally substituted with 1, 2, 3 or 4 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n$- C_{3-8} cycloalkyl, $-(CH_2)_n$- C_{3-8} heterocycloalkyl, $-(CH_2)_n$-C_{1-6} haloalkyl, $-(CH_2)_n$- and C_{1-6} haloalkyl.

In some embodiments, R^1 is -SR^a; R^2 and R^3, together with the carbon atom to which they are attached, join to form a ring selected from 3-8 membered cycloalkyl, 3-8 membered heterocycloalkyl, C_5-C_7 oxycycloalkyl, C_{5-7} dioxycycloalkyl and oxazolidinyl ring, each ring optionally substituted with 1, 2, or 3 substituents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, -$(CH_2)_n$-benzodioxane, -$(CH_2)_n$- oxazolidinone, -$(CH_2)_n$-C_{1-6} haloalkyl, -$(CH_2)_n$- C_{3-8} cycloalkyl and C_{1-6} haloalkyl, each of which is optionally substituted with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl.

In some embodiments, R^1 is -S-, substituted with substituents selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, -$(CH_2)_n$-benzodioxane, -$(CH_2)_n$-oxazolidinone, each of which is optionally substituted with 1, 2, 3 or 4 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{6-10} aryl, C_{4-10} heteroaryl, -$(CH_2)_n$- C_{3-8} cycloalkyl, -$(CH_2)_n$- C_{3-8} heterocycloalkyl, -$(CH_2)_n$-C_{1-6} haloalkyl, -$(CH_2)_n$- and C_{1-6} haloalkyl.

In some embodiments, R^1 is -S(=O)R^a; R^2 and R^3, together with the carbon atom to which they are attached, join to form a ring selected from 3-8 membered cycloalkyl, 3-8 membered heterocycloalkyl, C_5-C_7 oxycycloalkyl, C_{5-7} dioxycycloalkyl and oxazolidinyl ring, each ring optionally substituted with 1, 2, or 3 substituents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, -$(CH_2)_n$-benzodioxane, -$(CH_2)_n$- oxazolidinone, -$(CH_2)_n$-C_{1-6} haloalkyl, -$(CH_2)_n$- C_{3-8} cycloalkyl and C_{1-6} haloalkyl, each of which is optionally substituted with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl.

In some embodiments, R^1 is -S(=O)-, substituted with substituents selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, -$(CH_2)_n$-benzodioxane, -$(CH_2)_n$-oxazolidinone, each of which is optionally substituted with 1, 2, 3 or 4 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{6-10} aryl, C_{4-10} heteroaryl, -$(CH_2)_n$- C_{3-8} cycloalkyl, -$(CH_2)_n$- C_{3-8} heterocycloalkyl, -$(CH_2)_n$-C_{1-6} haloalkyl, -$(CH_2)_n$- and C_{1-6} haloalkyl.

In some embodiments, R^1 is –S(=O)(O)R^a; R^2 and R^3, together with the carbon atom to which they are attached, join to form a ring selected from 3-8 membered cycloalkyl, 3-8 membered heterocycloalkyl, C_5-C_7 oxycycloalkyl, C_{5-7} dioxycycloalkyl and oxazolidinyl ring, each ring optionally substituted with 1, 2, or 3 substituents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, -$(CH_2)_n$-benzodioxane, -$(CH_2)_n$- oxazolidinone, -$(CH_2)_n$-C_{1-6} haloalkyl, -$(CH_2)_n$- C_{3-8} cycloalkyl and C_{1-6} haloalkyl, each of which is optionally substituted with 1,

2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl.

In some embodiments, R^1 is -S(=O)(O)-, substituted with substituents selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n$-benzodioxane, $-(CH_2)_n$-oxazolidinone, each of which is optionally substituted with 1, 2, 3 or 4 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n$- C_{3-8} cycloalkyl, $-(CH_2)_n$- C_{3-8} heterocycloalkyl, $-(CH_2)_n$- C_{1-6} haloalkyl, $-(CH_2)_n$- and C_{1-6} haloalkyl.

In some embodiments, R^1 is $-C(=O)R^a$; R^2 and R^3, together with the carbon atom to which they are attached, join to form a ring selected from 3-8 membered cycloalkyl, 3-8 membered heterocycloalkyl, C_5-C_7 oxycycloalkyl, C_{5-7} dioxycycloalkyl and oxazolidinyl ring, each ring optionally substituted with 1, 2, or 3 substituents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n$-benzodioxane, $-(CH_2)_n$- oxazolidinone, $-(CH_2)_n$-C_{1-6} haloalkyl, $-(CH_2)_n$- C_{3-8} cycloalkyl and C_{1-6} haloalkyl, each of which is optionally substituted with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl.

In some embodiments, R^1 is -C(=O)- , substituted with substituents selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n$-benzodioxane, $-(CH_2)_n$-oxazolidinone, each of which is optionally substituted with 1, 2, 3 or 4 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n$- C_{3-8} cycloalkyl, $-(CH_2)_n$- C_{3-8} heterocycloalkyl, $-(CH_2)_n$- C_{1-6} haloalkyl, $-(CH_2)_n$- and C_{1-6} haloalkyl.

In some embodiments, R^4 is $-(CH_2)_n$-C_{3-7} cycloalkyl or C_{6-10} aryl and C_{4-10} heteroaryl, wherein each of C_{6-10} aryl and C_{4-10} heteroaryl is substituted with 1-4 substituents selected from H, CN, OH, OR^a, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{6-10} heteroaryl, $-(CH_2)_n$-C_{1-6} haloalkyl, $-(CH_2)_n$-, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{6-10} heteroaryl.

In some embodiments, R^4 is $-(CH_2)$-cyclopropyl, OR^a, C_{6-10} aryl, C_{4-10} heteroaryl, substituted C_{6-10} aryl, or substituted C_{4-10} heteroaryl.

In some embodiments, R^4 is C_{6-10} aryl or C_{6-10} heteroaryl substituted with 1, 2, 3 or 4 substitutents independently selected from halogen, CN, OH, OR^a and C_{1-6} alkyl.

In some embodiments, R^a is C_{1-6} haloalkyl.

In some embodiments, halogen or halogen of C_{1-6} haloalkyl is fluoro.

20. In some embodiments, R^a is CF_3 or OCF_3.

In some embodiments, R^1 is $-CH(OH)R^a$; R^2 and R^3, together with the carbon atom to which they are attached, join to form a ring selected from 3-8 membered cycloalkyl, 3-8 membered heterocycloalkyl, C_5-C_7 oxycycloalkyl, C_{5-7} dioxycycloalkyl and oxazolidinyl ring, each ring optionally substituted with 1, 2, or 3 substituents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10}

aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, -$(CH_2)_n$-benzodioxane, -$(CH_2)_n$- oxazolidinone, -$(CH_2)_n$-C_{1-6} haloalkyl, -$(CH_2)_n$- C_{3-8} cycloalkyl and C_{1-6} haloalkyl, each of which is optionally substituted with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl.

In some embodiments, R^1 is -CH(OH)-, substituted with substituents selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, -$(CH_2)_n$-benzodioxane, -$(CH_2)_n$-oxazolidinone, each of which is optionally substituted with 1, 2, 3 or 4 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{6-10} aryl, C_{4-10} heteroaryl, -$(CH_2)_n$- C_{3-8} cycloalkyl, -$(CH_2)_n$- C_{3-8} heterocycloalkyl, -$(CH_2)_n$-C_{1-6} haloalkyl, -$(CH_2)_n$- and C_{1-6} haloalkyl.

In some embodiments, R^4 is -$(CH_2)_n$-C_{3-7} cycloalkyl, C_{6-10} aryl or C_{4-10} heteroaryl, wherein each of C_{6-10} aryl and C_{4-10} heteroaryl is substituted with 1-4 substituents selected from H, CN, OH, OR^a, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{6-10} heteroaryl, -$(CH_2)_n$-C_{1-6} haloalkyl, -$(CH_2)_n$-, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{6-10} heteroaryl.

In some embodiments, R^4 is -(CH_2)-cyclopropyl, OR^a, C_{6-10} aryl, C_{4-10} heteroaryl, substituted C_{6-10} aryl, or substituted C_{4-10} heteroaryl.

In some embodiments, R^4 is C_{6-10} aryl or C_{6-10} heteroaryl substituted with 1, 2, 3 or 4 substitutents independently selected from halogen, CN, OH, OR^a and C_{1-6} alkyl.

In some embodiments, R^a is C_{1-6} haloalkyl.

In some embodiments, halogen or halogen of C_{1-6} haloalkyl is fluoro.

In some embodiments, R^a is CF_3 or OCF_3.

In some embodiments, R^1 is -CH(OR^b)R^a; R^2 and R^3, together with the carbon atom to which they are attached, join to form a ring selected from 3-8 membered cycloalkyl, 3-8 membered heterocycloalkyl, C_5-C_7 oxycycloalkyl, C_{5-7} dioxycycloalkyl and oxazolidinyl ring, each ring optionally substituted with 1, 2, or 3 substituents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, -$(CH_2)_n$-benzodioxane, -$(CH_2)_n$- oxazolidinone, -$(CH_2)_n$-C_{1-6} haloalkyl, -$(CH_2)_n$- C_{3-8} cycloalkyl and C_{1-6} haloalkyl, each of which is optionally substituted with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl.

In some embodiments, R^1 is -CH(OR^a)-, substituted with substituents selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, -$(CH_2)_n$-benzodioxane, -$(CH_2)_n$-oxazolidinone, each of which is optionally substituted with 1, 2, 3 or 4 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{6-10} aryl, C_{4-10} heteroaryl, -$(CH_2)_n$- C_{3-8} cycloalkyl, -$(CH_2)_n$- C_{3-8} heterocycloalkyl, -$(CH_2)_n$-C_{1-6} haloalkyl, -$(CH_2)_n$- and C_{1-6} haloalkyl.

In some embodiments, R^1 is -$(CH_2)_n$-; R^2 and R^3, together with the carbon atom to which they are attached, join to form a ring selected from 3-8 membered cycloalkyl, 3-8 membered heterocycloalkyl, C_5-C_7 oxycycloalkyl, C_{5-7} dioxycycloalkyl and oxazolidinyl ring, each ring optionally substituted with 1, 2, or 3 substituents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, -$(CH_2)_n$-benzodioxane, -$(CH_2)_n$- oxazolidinone, -$(CH_2)_n$-C_{1-6} haloalkyl, -$(CH_2)_n$- C_{3-8} cycloalkyl and C_{1-6} haloalkyl, each of which is optionally substituted with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl.

In some embodiments, R^1 is -$(CH_2)_n$-, substituted with substituents selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, -$(CH_2)_n$-benzodioxane, -$(CH_2)_n$-oxazolidinone, each of which is optionally substituted with 1, 2, 3 or 4 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{6-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{6-10} aryl, C_{4-10} heteroaryl, -$(CH_2)_n$- C_{3-8} cycloalkyl, -$(CH_2)_n$- C_{3-8} heterocycloalkyl, -$(CH_2)_n$-C_{1-6} haloalkyl, -$(CH_2)_n$- and C_{1-6} haloalkyl.

In some embodiments, R^4 is -$(CH_2)_n$-C_{3-7} cycloalkyl or C_{6-10} aryl and C_{6-10} heteroaryl, wherein each of C_{6-10} aryl and C_{6-10} heteroaryl is substituted with 1-4 substituents selected from H, CN, OH, OR^a, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, -$(CH_2)_n$-C_{1-6} haloalkyl, -$(CH_2)_n$-, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl.

In some embodiments, R^4 is -(CH_2)-cyclopropyl, OR^a, C_{6-10} aryl, C_{4-10} heteroaryl, substituted C_{6-10} aryl, or substituted C_{4-10} heteroaryl.

In some embodiments, R^4 is C_{6-10} aryl or C_{4-10} heteroaryl substituted with 1, 2, 3 or 4 substitutents independently selected from halogen, CN, OH, OR^a and C_{1-6} alkyl.

In some embodiments, R^a is C_{1-6} haloalkyl.

In some embodiments, halogen or halogen of C_{1-6} haloalkyl is fluoro.

In some embodiments, R^a is CF_3 or OCF_3.

At various places in the present specification, substituents of compounds of the invention are disclosed in groups or in ranges. It is specifically intended that the invention include each and every individual subcombination of the members of such groups and ranges. For example, the term "C_{1-6} alkyl" is specifically intended to individually disclose methyl, ethyl, C_3 alkyl, C_4 alkyl, C_5 alkyl, and C_6 alkyl.

It is further intended that the compounds of the invention are stable. As used herein "stable" refers to a compound that is sufficiently robust to survive isolation to a useful degree of purity from a reaction mixture, and preferably capable of formulation into an efficacious therapeutic agent.

It is further appreciated that certain features of the invention, which are, for clarity, described in the context of separate embodiments, can also be provided in combination in a single embodiment. Conversely, various features of the invention, which are for brevity, described in the context of a single embodiment, can also be provided separately or in any suitable subcombination.

As used herein, the term "alkyl" is meant to refer to a saturated hydrocarbon group, which is straight-chained or branched. Example alkyl groups include methyl (Me), ethyl (Et), propyl (*e.g.*, n-propyl and isopropyl), butyl (*e.g.*, n-butyl, isobutyl, t-butyl), pentyl (e.g., n-pentyl, isopentyl, neopentyl), and the like. An alkyl group can contain from 1 to about 20, from 2 to about 20, from 1 to about 10, from 1 to about 8, from 1 to about 6, from 1 to about 4, or from 1 to about 3 carbon atoms.

As used herein, "alkenyl" refers to an alkyl group having one or more double carbon-carbon bonds. Example alkenyl groups include ethenyl, propenyl, and the like.

As used herein, "alkynyl" refers to an alkyl group having one or more triple carbon-carbon bonds. Example alkynyl groups include ethynyl, propynyl, and the like.

As used herein, "haloalkyl" refers to an alkyl group having one or more halogen substituents. Example haloalkyl groups include CF_3, C_2F_5, CHF_2, CCl_3, $CHCl_2$, C_2Cl_5, and the like.

As used herein, "aryl" refers to monocyclic or polycyclic (e.g., having 2, 3 or 4 fused rings) aromatic hydrocarbons such as, for example, phenyl, naphthyl, anthracenyl, phenanthrenyl, and the like. In some embodiments, aryl groups comprise from 6 to about 20 carbon atoms, including comprising from 6 to 10 carbon atoms.

As used herein, "arylalkyl" refers to an alkyl group substituted by an aryl group. Examplary arylalkyl groups include, but are not limited to, benzyl and phenethyl.

As used herein, "cycloalkyl" refers to non-aromatic carbocycles including cyclized alkyl, alkenyl, and alkynyl groups. Cycloalkyl groups can include mono- or polycyclic (e.g., having 2, 3 or 4 fused rings) ring systems, including spirocycles. In some embodiments, cycloalkyl groups comprise from 3 to 20 carbon atoms, including comprising from 3 to 14 carbon atoms, 3 to 10 carbon atoms, 3 to 8 carbon atoms or 3 to 6 carbon atoms. Cycloalkyl groups can further comprise 0, 1 or 2 double bonds and/or 0, 1, or 2 triple bonds. Also included in the definition of cycloalkyl are moieties that have one or more aromatic rings fused (i.e., having a bond in common with) to the cycloalkyl ring, for example, benzo derivatives of pentane, pentene, hexane, and the like. A cycloalkyl group having one or more fused aromatic rings can be attached though either the aromatic or non-aromatic portion. One or more ring-forming carbon atoms of a cycloalkyl group can be oxidized, for example, having an oxo or sulfido substituent. Example cycloalkyl groups include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclopentenyl, cyclohexenyl, cyclohexadienyl, cycloheptatrienyl, norbornyl, norpinyl, norcarnyl, adamantyl, and the like.

As used herein, a "cycloalkylalkyl" group refers to an alkyl group substituted by a cycloalkyl group. An examplary cycloalkylalkyl group includes, but is not limited to cyclopentylmethyl and cyclohexylmethyl.

As used herein, a "heteroaryl" group refers to an aromatic heterocycle comprising at least one heteroatom ring member selected from sulfur, oxygen and nitrogen. Heteroaryl groups include monocyclic and fused, polycyclic (e.g., heteroaryl comprising 2, 3 or 4 fused rings) systems. Any ring-forming N atom in a heteroaryl group can also be oxidized to form an N-oxo moiety or can be functionalized to form an N-functionalized group (e.g. N-alkyl or N-aryl). Examples of heteroaryl groups

include without limitation, pyridyl, N-oxopyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazinyl, furyl, quinolyl, isoquinolyl, thienyl, imidazolyl, thiazolyl, indolyl, pyrryl, oxazolyl, benzofuryl, benzothienyl, benzthiazolyl, isoxazolyl, pyrazolyl, triazolyl, tetrazolyl, indazolyl, 1,2,4-thiadiazolyl, isothiazolyl, benzothienyl, purinyl, carbazolyl, benzimidazolyl, indolinyl, and the like. In some embodiments, the heteroaryl group comprises from 3 to 20 carbon atoms, and in further embodiments comprises from about 4 to 10 carbon atoms. In some embodiments, the heteroaryl group contains 6 to about 10 ring-forming atoms. In some embodiments, the heteroaryl group comprises from 1 to 4 heteroatoms, including comprising from 1 to 3 heteroatoms or 1 to 2 heteroatoms.

As used herein, a "heteroarylalkyl" group refers to an alkyl group substituted by a heteroaryl group. An example of a heteroarylalkyl group is pyridylmethyl.

As used herein, "heterocycloalkyl" refers to a non-aromatic heterocycle where one or more of the ring-forming atoms comprises a heteroatom selected from O, N and S. As used herein, "heterocycloalkenyl" refers to a partially-unsaturated heterocycle or a heterocycle comprising at least one unsaturated bonding of carbon atoms or carbon and heteroatoms, where one or more of the ring-forming atoms comprises a heteroatom selected from O, N and S. Heterocycloalkyl groups can include mono- or polycyclic (e.g., having 2, 3 or 4 fused rings) ring systems as well as spirocycles. Examplary "heterocycloalkyl" groups include, but are not limited to, morpholino, thiomorpholino, piperazinyl, tetrahydrofuranyl, tetrahydrothienyl, 2,3-dihydrobenzofuryl, 1,3-benzodioxole, benzo-1,4-dioxane, piperidinyl, pyrrolidinyl, isoxazolidinyl, isothiazolidinyl, pyrazolidinyl, oxazolidinyl, thiazolidinyl, imidazolidinyl, and the like. Also included in the definition of heterocycloalkyl are moieties that have one or more aromatic rings fused (i.e., having a bond in common with) to the nonaromatic heterocyclic ring, for example phthalimidyl, naphthalimidyl, and benzo derivatives of heterocycles. A heterocycloalkyl group having one or more fused aromatic rings can be attached though either the aromatic or non-aromatic portion. Also included in the definition of heterocycloalkyl are moieties where one or more ring-forming atoms is substituted by 1 or 2 oxo or sulfido groups. In some embodiments, the heterocycloalkyl group comprises from 4 to 20 carbon atoms, and in further embodiments from 5 to 10 carbon atoms. In some embodiments, the heterocycloalkyl group comprises 5 to 20, 5 to 14, 5 to 12, or 5 to 10 ring-forming atoms. In some embodiments, the heterocycloalkyl group further comprises 1 to 4 heteroatoms, including comprising from 1 to 3, or 1 to 2 heteroatoms. In some embodiments, the heterocycloalkyl group further comprises 0 to 2 double bonds. In some embodiments, the heterocycloalkyl group comprises 0 to 2 triple bonds.

As used herein, "heterocycloalkylalkyl" refers to an alkyl group substituted by a heterocycloalkyl group.

As used herein, "halo" or "halogen" includes fluoro, chloro, bromo, and iodo.

As used herein, "haloalkyl" refers to an alkyl group substituted by one or more halogen atoms. Examples of haloalkyl groups include CF_3 and CF_2CF_3.

As used herein, "alkoxy" refers to an –O-alkyl group. Example alkoxy groups include methoxy, ethoxy, propoxy (*e.g.*, n-propoxy and isopropoxy), t-butoxy, and the like.

The compounds described herein can be asymmetric (e.g., having one or more stereocenters). All stereoisomers, such as enantiomers and diastereomers, are intended unless otherwise indicated. Compounds of the present invention that comprise asymmetrically substituted carbon atoms can be isolated in optically active or racemic forms. Methods on how to prepare optically active forms from optically active starting materials are known in the art, such as by resolution of racemic mixtures or by stereoselective synthesis. Many geometric isomers of olefins, C=N double bonds, and the like can also be present in the compounds described herein, and all such stable isomers are contemplated in the present invention. Cis and trans geometric isomers of the compounds of the present invention are described and may be isolated as a mixture of isomers or as separated isomeric forms.

Compounds of the invention also include tautomeric forms. Tautomeric forms result from the swapping of a single bond with an adjacent double bond together with the concomitant migration of a proton. Tautomeric forms include prototropic tautomers which are isomeric protonation states having the same empirical formula and total charge. Example prototropic tautomers include ketone – enol pairs, amide - imidic acid pairs, lactam – lactim pairs, amide - imidic acid pairs, enamine – imine pairs, and annular forms where a proton can occupy two or more positions of a heterocyclic system, for example, 1H- and 3H-imidazole, 1H-, 2H- and 4H- 1,2,4-triazole, 1H- and 2H- isoindole, and 1H- and 2H-pyrazole. Tautomeric forms can be in equilibrium or sterically locked into one form by appropriate substitution.

Compounds of the invention can also include all isotopes of atoms occurring in the intermediates or final compounds. Isotopes include those atoms having the same atomic number but different mass numbers. For example, isotopes of hydrogen include tritium and deuterium.

The term, "compound," as used herein is meant to include all stereoisomers, geometric iosomers, tautomers, and isotopes of the structures depicted.

All compounds, and pharmaceuticaly acceptable salts thereof, are also meant to include solvated or hydrated forms.

In some embodiments, the compounds of the invention, and salts thereof, are substantially isolated. By "substantially isolated" is meant that the compound is at least partially or substantially separated from the environment in which it was formed or detected. Partial separation can include, for example, a composition enriched in the compound of the invention. Substantial separation can include compositions comprising at least 50%, at least about 60%, at least about 70%, at least about 80%, at least about 90%, at least about 95%, at least about 97%, or at least about 99% by weight of the compound of the invention, or salt thereof. Methods for isolating compounds and their salts are routine in the art.

The present invention also includes pharmaceutically acceptable salts of the compounds described herein. As used herein, "pharmaceutically acceptable salts" refers to derivatives of the disclosed compounds wherein the parent compound is modified by converting an existing acid or base moiety to its salt form. Examples of pharmaceutically acceptable salts include, but are not limited to, mineral or organic acid salts of basic residues such as amines; alkali or organic salts of acidic residues such as carboxylic acids; and the like. The pharmaceutically acceptable salts of the present invention include the

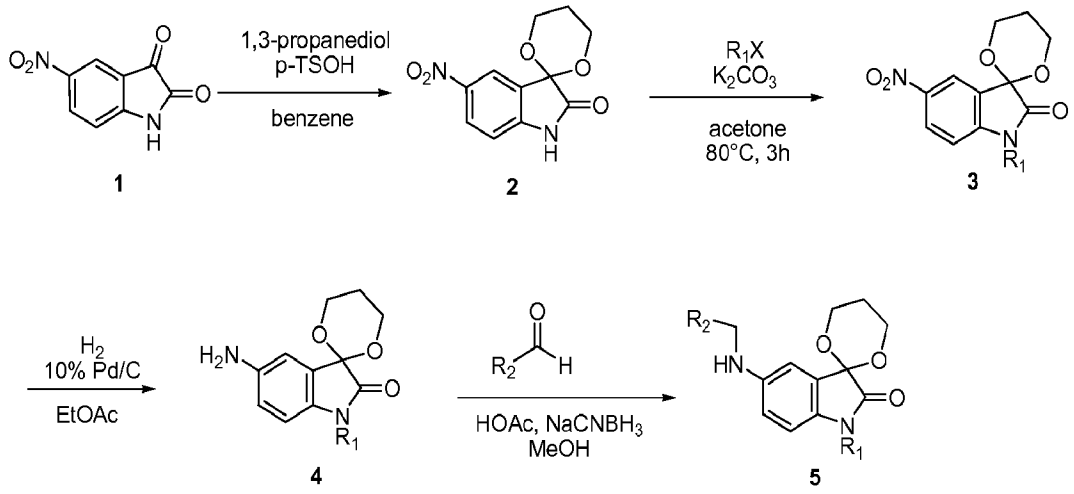
conventional non-toxic salts of the parent compound formed, for example, from non-toxic inorganic or organic acids. The pharmaceutically acceptable salts of the present invention can be synthesized from the parent compound, which comprises a basic or acidic moiety by conventional chemical methods. Generally, such salts can be prepared by reacting the free acid or base forms of these compounds with a stoichiometric amount of the appropriate base or acid in water or in an organic solvent, or in a mixture of the two; generally, non-aqueous media like ether, ethyl acetate, ethanol, isopropanol, or acetonitrile are preferred. Lists of suitable salts are found in *Remington's Pharmaceutical Sciences*, 17th ed., Mack Publishing Company, Easton, Pa., 1985, p. 1418 and *Journal of Pharmaceutical Science*, 66, 2 (1977).

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

Synthesis

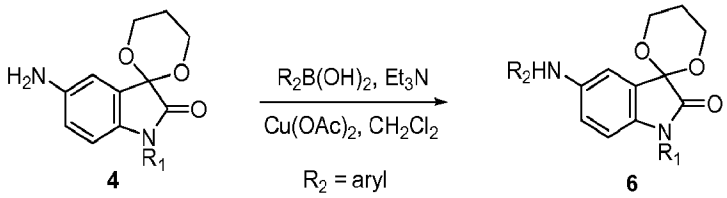
The compounds of the present invention can be prepared from readily available starting materials in a variety of ways known to one skilled in the art of organic synthesis. For example, they can be synthesized via the reaction pathways and techniques as described below.

Scheme 1



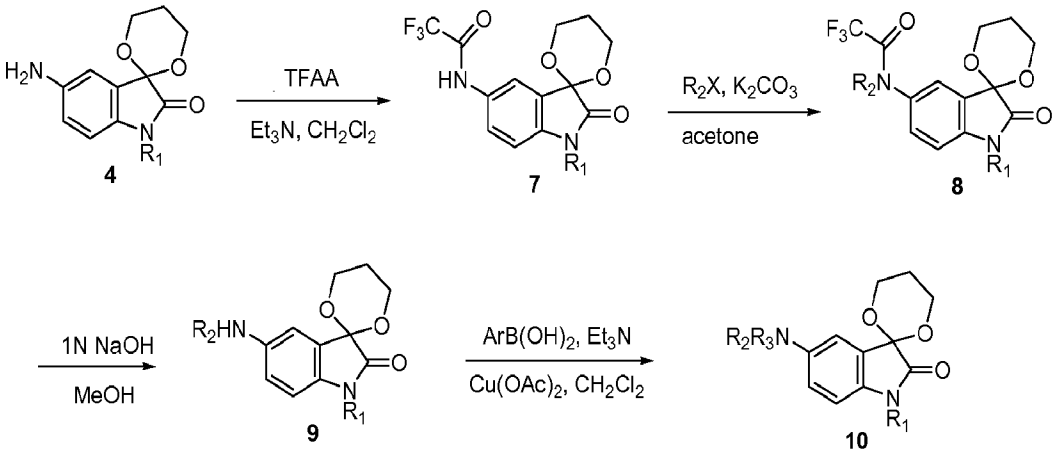
Certain invented benzyl amine compounds **5** were prepared according to Scheme 1. 5-Nitroisatin (**1**) was converted to the corresponding cyclic acetal **2** using 1,3-propanediol and *p*-TsOH in benzene. Alkylation of the oxindole nitrogen with organohalides produced nitro acetal compound **3**. Reduction of the NO_2 group to the corresponding amine compound **4** was accomplished by catalytic hydrogenation using H_2/10% Pd/C. Functionalization of the amine **4** with benzaldehydes under reductive amination conditions produced invented benzyl amine compounds **5**.

Scheme 2



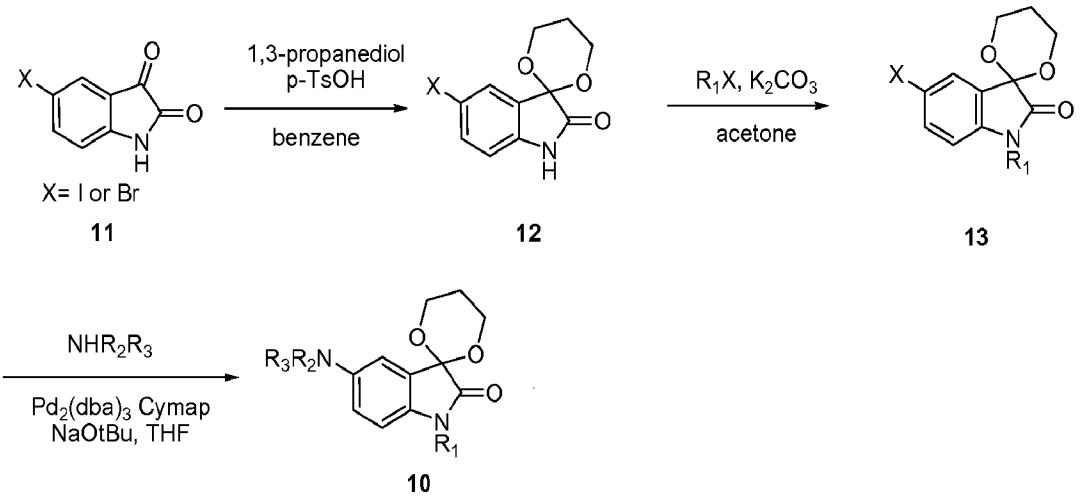
Certain invented 5-Aryl amine compounds **6** were prepared from amine compounds **4** using aryl boronic acids, copper acetate, amine bases such as Et_3N in aprotic solvents, such as CH_2Cl_2, as summarized in Scheme 2.

Scheme 3



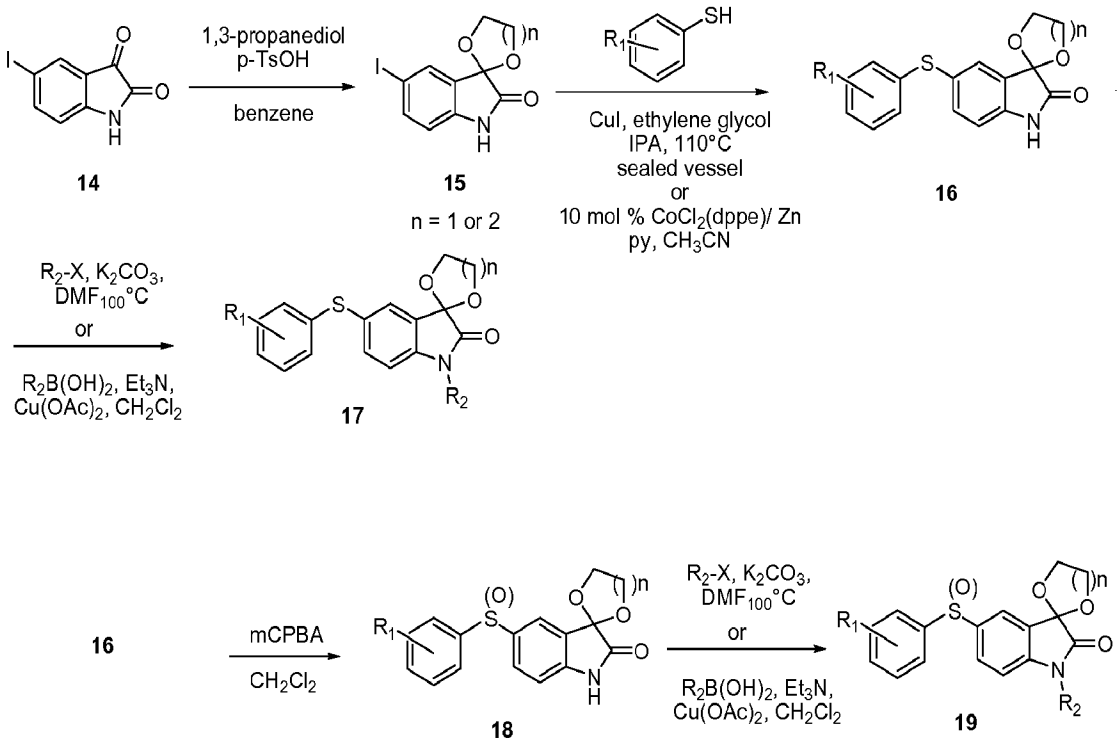
Certain invented disubstituted amino compounds were prepared according to Scheme 3. Amine compound **4** was protected as the trifluoroacetamide compound **7** by treatment with trifluoroacetic anhydride and Et_3N in CH_2Cl_2. Alkylation of the nitrogen of compound **7** with organohalides produced compound **8,** which can be deprotected under basic conditions to provide deprotected compound **9.** Invented compounds (**10**) were then prepared from aryl boronic acids, copper acetate, amine bases such as Et_3N in aprotic solvents such as CH_2Cl_2.

Scheme 4



Other invented 5-amino compounds (**10**) were also prepared according to Scheme 4. 5-Iodo- or 5-bromo isatin compounds **11** were converted to the corresponding cyclic acetal compounds **12** using 1,3-propanediol and *p*-TsOH in benzene. Alkylation of the oxindole nitrogen of compounds **12** with organohalides produced compounds **13**. Amidation was accomplished via Buchwald amination conditions with an amine in the presence of a catalyst, such as $Pd_2(dba)_3$ and a ligand such as cymap, to provide other examples of invented 5-amino compounds **10**.

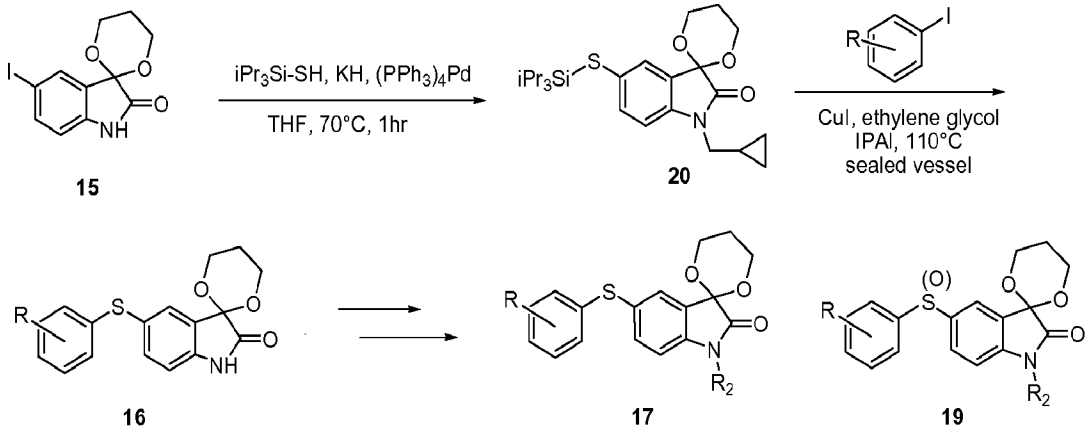
Scheme 5



Certain invented sulfides, sulfoxides and sulfone compounds (**17** and **19**, respectively) were prepared according to Scheme 5. 5-Iodo-isatin (**14**) was converted to the corresponding cyclic acetal

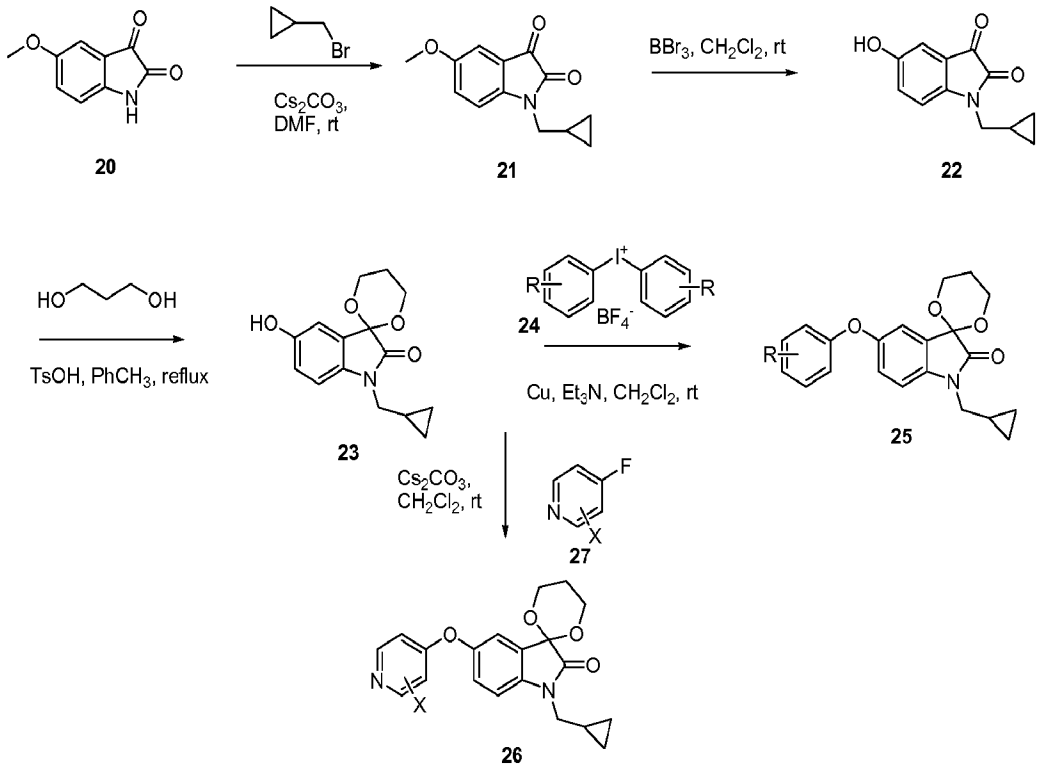
compounds **15** using 1,3-propanediol or ethylene glycol and *p*-TsOH in benzene with heating. Aryl sulfide compounds **16** were prepared from corresponding compounds **15** using aryl thiols, in the presence of CuI and ethylene glycol in isopropanol (*Org. Lett.* **2002**, *4*, 3517) or $CoCl_2$(dppe), zinc and pyridine in acetonitrile (*Org. Lett.* **2006**, *8*, 5613). Oxidation to corresponding sulfoxide or sulfone compounds (**18**) was accomplished with *m*-CPBA. N-Alkyl oxindole compounds **17** or **19**, respectively were prepared from corresponding compounds **16** or **18** using organohalides and K_2CO_3 in DMF with heating. Corresponding N-Aryl oxindole compounds **17** or **19** were prepared from respective compounds **16** or **18** using aryl boronic acids, copper acetate, amine bases such as Et_3N in aprotic solvents such as CH_2Cl_2.

Scheme 6



Other invented sulfides and sulfone compounds **17** and **19**, respectively, were alternately prepared according to Scheme 6. TIPS-protected thiol compounds **20** were prepared from protected 5-iodoisatin compound **15** by the treatment with appropriate triisopropylthiols, KH and $Pd(PPh_3)_4$ in THF (*J.Med. Chem.* **2001**, *44*, 4393). Aryl sulfide compounds were prepared from compound **20** using appropriate aryl iodides in the presence of CuI and ethylene glycol in isopropanol. Oxidation, arylation or alkylation to respective compounds **17** or **19**, can be accomplished, as summarized in Scheme 5.

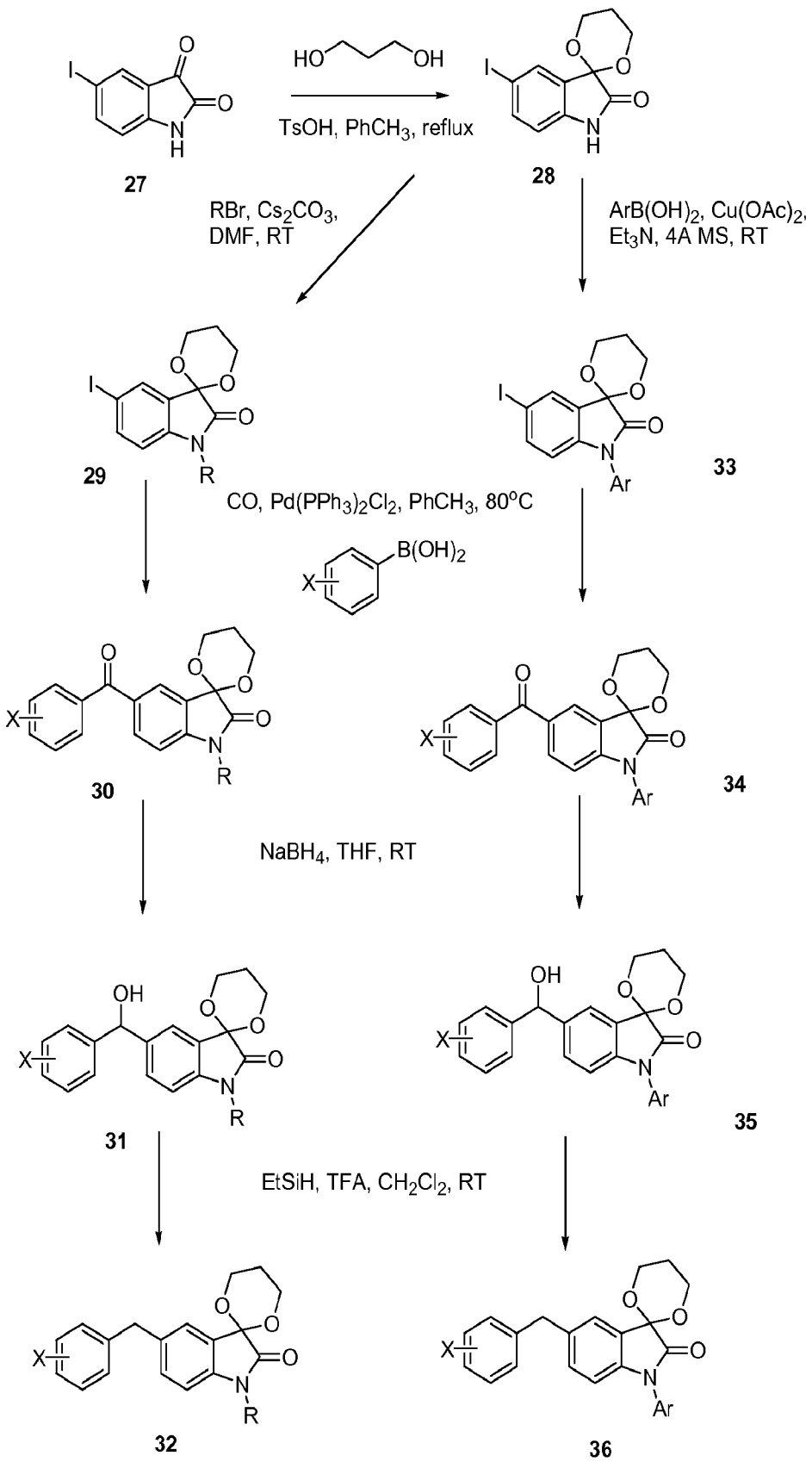
Scheme 7



Certain invented 5-Aryl ether compounds (**25**) were prepared according to the procedure of Scheme 7. 5-methoxyisatin (**20**) was converted to compound **22** via alkylation with cyclopropylmethyl bromide followed by demethylation of compound **21** with boron tribromide in dichloromethane. Compound **22** was then converted to compound **23** with 1,3-propanediol and *p*-TsOH in toluene. Reaction of compound **23** with an iodonium tetrafluoroborate salt (**24**) in presence of copper and triethylamine in dichloromethane produced invented 5-Aryl ether compounds **25**.

Alternatively, reaction of compound **23** with a substituted fluoropyridine (**27**) in presence of cesium carbonate in dichloromethane also produced other invented 5-Aryl ether compounds (**26**).

Scheme 8

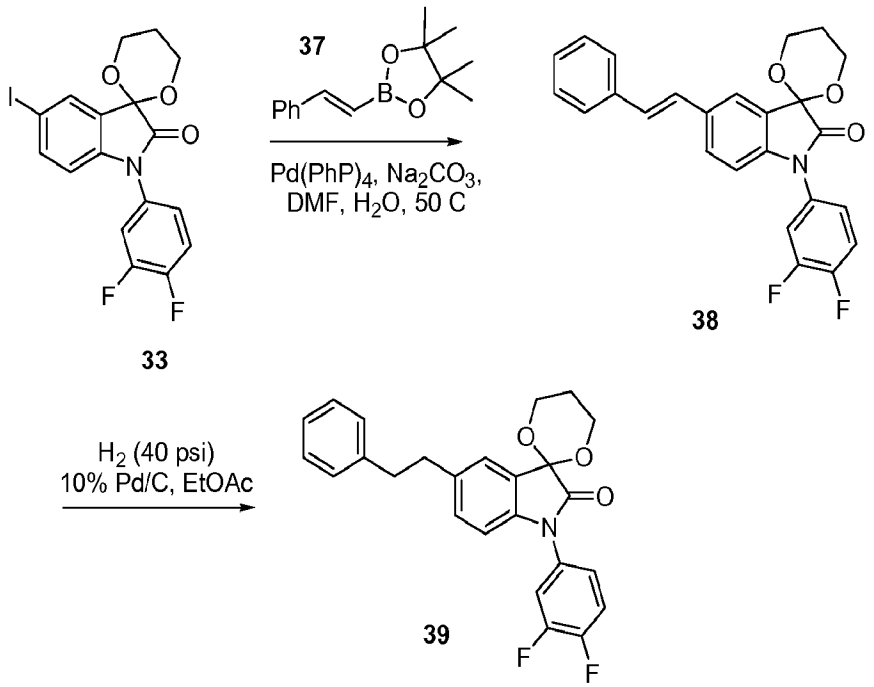


Certain invented substituted oxindole compounds (**32**) were prepared according to the procedure of Scheme 8. Thus 5-iodoisatin (**27**) was converted to acetal compound (**28**) with 1,3-propanediol and *p*-TsOH in toluene. Alkylation of N1 was accomplished using organohalides with Cs_2CO_3 in DMF at 60

°C, and produced N-functionalized ketone componds (**29**). Carbonylation of N-functionalized compounds **29** in presence of substituted boronic acid, carbon monoxide and dichloro-bis-triphenylphosphinepallidium in toluene produced ketone compounds (**30**). Sodium borohydride reduction of ketone compounds **30** produced hydroxyl compounds (**31**). Deoxygenation of hydroxyl compounds **31** with triethylsilane and trifluoroacetic acid in dichloromethane produced methylene bridged compounds (**32**).

Alternatively, other substituted oxindole compounds (**36**) were prepared as shown in Scheme 8. Oxindole compound (**28**) was converted to compound (**33**) via reaction with appropriate arylboronic acids in presence of copper acetate, triethylamine and 4 Å molecular sieves in dichloromethane. Carbonylation of compound **33** in presence of substituted boronic acids, carbon monoxide and dichloro-bis-triphenylphosphinepallidium in toluene produced ketone compounds (**34**). Sodium borohydride reduction of ketone compounds **34** produced hydroxyl compounds (**35**). Deoxygenation of hydroxyl compounds **35** with triethylsilane and trifluoroacetic acid in dichloromethane produced methylene bridged compounds (**36**).

Scheme 9



Other invented substituted oxindole compounds (**39**) were synthesized according to Scheme 9. Thus oxindole compounds **38** were synthesized by reaction of N-functionalized compounds **33** with an appropriate borate **37** in DMF in presence of tetrakis(triphenylphosphine)palladium and sodium carbonate. Subsequent catalytic hydrogenation of the alkene group in compound **38** in a Parr apparatus at 40 psi of hydrogen produced the other invented 1, 3, 5-substituted oxindole compounds **39**.

Conventional synthetic reagents and conditions were employed in accordance with methods for preparing compounds of the invention. It will be appreciated that where typical or preferred process conditions (i.e., reaction temperatures, times, mole ratios of reactants, solvents, pressures, etc.) are given; other process conditions can also be used unless otherwise stated. Optimum reaction conditions may vary with the particular reactants or solvent used, however, alteration of such conditions may be determined and adjusted by persons skilled in the art.

The processes described herein can be monitored according to any suitable method known in the art. For example, product formation can be monitored by spectroscopic means, such as nuclear magnetic resonance spectroscopy (e.g., ^{1}H or ^{13}C) infrared spectroscopy, spectrophotometry (e.g., UV-visible), or mass spectrometry, or by chromatography such as high performance liquid chromatograpy (HPLC) or thin layer chromatography.

Preparation of compounds can involve the protection and deprotection of various chemical groups. The need for protection and deprotection of certain functional groups attached to the oxoindole core of the invented compounds, and selection of appropriate protecting groups may be determined by one skilled in the art. The chemistry of protecting groups is described, for example, in Greene, et al., *Protective Groups in Organic Synthesis*, 2d. Ed., Wiley & Sons, 1991.

The reactions of the processes described herein can be carried out in suitable solvents, which can be readily selected by one of skill in the art of organic synthesis. Suitable solvents can be substantially non-reactive with the starting materials (reactants), the intermediates, or products at the temperatures at which the reactions are carried out, i.e., temperatures, which can range from the solvent's freezing temperature to the solvent's boiling temperature. A given reaction can be carried out in one solvent or a mixture of more than one solvent. Depending on the particular reaction step, suitable solvents for a particular reaction step can be selected.

Resolution of racemic mixtures of compounds can be carried out by any of numerous methods known in the art. An example method includes fractional recrystallization using a "chiral resolving acid" which is an optically active, salt-forming organic acid. Suitable resolving agents for fractional recrystallization methods are, for example, optically active acids, such as the D and L forms of tartaric acid, diacetyltartaric acid, dibenzoyltartaric acid, mandelic acid, malic acid, lactic acid or the various optically active camphorsulfonic acids. Resolution of racemic mixtures can also be carried out by elution on a column packed with an optically active resolving agent (e.g., dinitrobenzoylphenylglycine). The selection of a suitable elution solvent composition may be determined by one skilled in the art.

Methods of Use

Compounds of this invention are able to interact with the CB2 receptor and therefore modulate the receptor's activity. The term "modulate" is meant to refer to an ability to increase or decrease activity of an the receptor. Modulation can occur in vitro or in vivo. Modulation can further occur in a cell. Accordingly, compounds of the invention can be used in methods of modulating the activity of the CB2 receptor, by contacting the receptor with one or more of the compounds or compositions described herein.

As used herein, the term "contacting" refers to bringing together of indicated moieties in an *in vitro* system or an *in vivo* system. For example, "contacting" a compound of the invention with the CB2 receptor includes the administration of a compound of the present invention to an individual or patient, such as a human, as well as, for example, introducing a compound of the invention into a sample comprising a cellular or purified preparation of the receptor.

As used herein, the term "individual" or "patient," used interchangeably, refers to any animal, including mammals, preferably mice, rats, other rodents, rabbits, dogs, cats, swine, cattle, sheep, horses, or primates, and most preferably humans.

The compounds of the present invention can act as CB2 receptor agonists. Thus, these compounds can be used to treat CB2-mediated disorders, such as CB2 agonists are potential drug candidates for reducing treating pain (e.g., chronic inflmmartory pain, post surgical pain, neuropathic pain, bone pain), osteoarthritis, atherosclerosis, osteoporosis, and cancer (e.g., glioma). The treatment includes administration of a therapeutically effective amount of one or more of the invented 3-substituted oxindole compounds described above to a patient in need thereof.

As used herein, the phrase "therapeutically effective amount" refers to the amount of active compound or pharmaceutical agent that elicits the biological or medicinal response that is being sought in a tissue, system, animal, individual or human by a researcher, veterinarian, medical doctor or other clinician.

As used herein, the term "treating" or "treatment" refers to one or more of (1) preventing the disease; for example, preventing a disease, condition or disorder in an individual who may be predisposed to the disease, condition or disorder but does not yet experience or display the pathology or symptomatology of the disease; (2) inhibiting the disease; for example, inhibiting a disease, condition or disorder in an individual who is experiencing or displaying the pathology or symptomatology of the disease, condition or disorder; and (3) ameliorating the disease; for example, ameliorating a disease, condition or disorder in an individual who is experiencing or displaying the pathology or symptomatology of the disease, condition or disorder (i.e., reversing the pathology and/or symptomatology) such as decreasing the severity of disease.

Examplary cancers treatable by the invented compounds herein include, but are not limited to, glioma, bladder cancer, breast cancer, cervical cancer, cholangiocarcinoma cancer, colorectal cancer, esophageal cancer, gastric cancer, head and neck cancer, cancer of the kidney, liver cancer, lung cancer, nasopharygeal cancer, ovarian cancer, pancreatic cancer, prostate cancer, thyroid cancer, osteosarcoma, synovial sarcoma, rhabdomyosarcoma, MFH/fibrosarcoma, leiomyosarcoma, Kaposi's sarcoma, multiple myeloma, lymphoma, adult T cell leukemia, acute myelogenous leukemia, chronic myeloid leukemia. glioblastoma, astrocytoma, melanoma, mesothelioma, or Wilm's tumor, and the like.

Combination Therapy

One or more additional pharmaceutical agents or treatment methods can be used in combination with the compounds of the present invention for treatment of the diseases, disorders or conditions

described herein. For example, one or more of the above-described 3-substituted oxindole compounds can be used together with an anti-inflammatory agent, an anti-cancer agent, an analgesic, or other therapeutic agent useful in treating pain, cancer, osteoarthritis, atherosclerosis, osteoporosis or other disease. The agents or therapies can be administered together with the compounds of the invention (e.g., combined into a single dosage form), or the agents or therapies and may be administered simultaneously or sequentially by separate routes of administration.

Pharmaceutical Formulations and Dosage Forms

When employed as pharmaceuticals, the compounds of the invention can be administered in the form of pharmaceutical compositions, which is a combination of a compound of the invention, or pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier. These compositions can be prepared in a manner well known in the pharmaceutical art, and can be administered by a variety of routes, depending upon whether local or systemic treatment is desired and upon the area to be treated. Administration may be topical (including ophthalmic and to mucous membranes including intranasal, vaginal and rectal delivery), pulmonary (e.g., by inhalation or insufflation of powders or aerosols, including by nebulizer; intratracheal, intranasal, epidermal and transdermal), ocular, oral or parenteral. Methods for ocular delivery can include topical administration (eye drops), subconjunctival, periocular or intravitreal injection or introduction by balloon catheter or ophthalmic inserts surgically placed in the conjunctival sac. Parenteral administration includes intravenous, intraarterial, subcutaneous, intraperitoneal or intramuscular injection or infusion; or intracranial, e.g., intrathecal or intraventricular, administration. Parenteral administration can be in the form of a single bolus dose, or may be, for example, by a continuous perfusion pump. Pharmaceutical compositions and formulations for topical administration may include transdermal patches, ointments, lotions, creams, gels, drops, suppositories, sprays, liquids and powders. Conventional pharmaceutical carriers, aqueous, powder or oily bases, thickeners and the like may be necessary or desirable.

This invention also includes pharmaceutical compositions, which comprise, as the active ingredient, one or more of the compounds of the invention above in combination with one or more pharmaceutically acceptable carriers. In making the compositions of the invention, the active ingredient is typically mixed with an excipient, diluted by an excipient or enclosed within such a carrier in the form of, for example, a capsule, sachet, paper, or other container. When the excipient serves as a diluent, it can be a solid, semi-solid, or liquid material, which acts as a vehicle, carrier or medium for the active ingredient. Thus, the compositions can be in the form of tablets, pills, powders, lozenges, sachets, cachets, elixirs, suspensions, emulsions, solutions, syrups, aerosols (as a solid or in a liquid medium), ointments comprising, for example, up to 10 % by weight of the active compound, soft and hard gelatin capsules, suppositories, sterile injectable solutions, and sterile packaged powders.

In preparing a formulation, the active compound can be milled to provide the appropriate particle size prior to combining with the other ingredients. If the active compound is substantially insoluble, it can be milled to an average particle size of less than 200 mesh. If the active compound is substantially water-

soluble, the particle size can be adjusted by milling to provide a substantially uniform distribution in the formulation, e.g. an average particle size of about 40 mesh.

The compounds of the invention may be milled using known milling procedures such as wet milling to obtain a particle size appropriate for tablet formation and for other formulation types. Finely divided (nanoparticulate) preparations of the compounds of the invention can be prepared by methods described in International Patent Application No. WO 2002/000196.

Some examples of suitable excipients include lactose, dextrose, sucrose, sorbitol, mannitol, starches, gum acacia, calcium phosphate, alginates, tragacanth, gelatin, calcium silicate, microcrystalline cellulose, polyvinylpyrrolidone, cellulose, water, syrup, and methyl cellulose. The formulations can additionally include: lubricating agents such as talc, magnesium stearate, and mineral oil; wetting agents; emulsifying and suspending agents; preserving agents such as methyl- and propylhydroxy-benzoates; sweetening agents; and flavoring agents. The compositions of the invention can be formulated so as to provide quick, sustained or delayed release of the active ingredient after administration to the patient by employing procedures known in the art.

The compositions can be formulated in a unit dosage form, each dosage containing from about 5 to about 100 mg, more usually about 10 to about 30 mg, of the active ingredient. The term "unit dosage forms" refers to physically discrete units suitable as unitary dosages for human subjects and other mammals, each unit comprising a predetermined quantity of active material calculated to produce the desired therapeutic effect, in association with a suitable pharmaceutical excipient.

The active compound can be effective over a wide dosage range and is generally administered in a pharmaceutically effective amount. It will be understood, however, that the amount of the compound actually administered will usually be determined by a physician, according to the relevant circumstances, including the condition to be treated, the chosen route of administration, the actual compound administered, the age, weight, and response of the individual patient, the severity of the patient's symptoms, and the like.

For preparing solid compositions such as tablets, the principal active ingredient is mixed with a pharmaceutical excipient to form a solid preformulation composition containing a homogeneous mixture of a compound of the present invention. When referring to these preformulation compositions as homogeneous, the active ingredient is typically dispersed evenly throughout the composition so that the composition can be readily subdivided into equally effective unit dosage forms such as tablets, pills and capsules. This solid preformulation is then subdivided into unit dosage forms of the type described above comprising from, for example, 0.1 to about 500 mg of the active ingredient of the present invention.

The tablets or pills of the present invention can be coated or otherwise compounded to provide a dosage form affording the advantage of prolonged action. For example, the tablet or pill can comprise an inner dosage and an outer dosage component, the latter being in the form of an envelope over the former. The two components can be separated by an enteric layer, which serves to resist disintegration in the stomach and permit the inner component to pass intact into the duodenum or to be delayed in release. A variety of materials can be used for such enteric layers or coatings, such materials including a number of

polymeric acids and mixtures of polymeric acids with such materials as shellac, cetyl alcohol, and cellulose acetate.

The liquid forms in which the compounds and compositions of the present invention can be incorporated for administration orally or by injection include aqueous solutions, suitably flavored syrups, aqueous or oil suspensions, and flavored emulsions with edible oils such as cottonseed oil, sesame oil, coconut oil, or peanut oil, as well as elixirs and similar pharmaceutical vehicles.

Compositions for inhalation or insufflation include solutions and suspensions in pharmaceutically acceptable, aqueous or organic solvents, or mixtures thereof, and powders. The liquid or solid compositions may comprise suitable pharmaceutically acceptable excipients as described *supra*, and in some embodiments, the compositions are administered by an oral or nasal respiratory route for local or systemic effect. Compositions can be nebulized by use of inert gases. Nebulized solutions may be breathed directly from the nebulizing device or the nebulizing device can be attached to a face masks tent, or intermittent positive pressure breathing machine. Solution, suspension, or powder compositions can be administered orally or nasally from devices, which deliver the formulation in an appropriate manner.

The amount of compound or composition administered to a patient will vary depending upon what is being administered, the purpose of the administration, such as prophylaxis or therapy, the state of the patient, the manner of administration, and the like. In therapeutic applications, compositions can be administered to a patient already suffering from a disease in an amount sufficient to cure or at least partially arrest the symptoms of the disease and its complications. Effective doses will depend on the disease condition being treated as well as by the judgment of the attending clinician depending upon factors such as the severity of the disease, the age, weight and general condition of the patient, and the like.

The compositions administered to a patient can be in the form of pharmaceutical compositions described above. These compositions can be sterilized by conventional sterilization techniques, or may be sterile filtered. Aqueous solutions can be packaged for use as is, or lyophilized, the lyophilized preparation being combined with a sterile aqueous carrier prior to administration. The pH of the compound preparations typically will be between 3 and 11, more preferably from 5 to 9 and most preferably from 7 to 8. It will be understood that use of certain of the foregoing excipients, carriers, or stabilizers will result in the formation of pharmaceutical salts.

The therapeutic dosage of the compounds of the present invention can vary according to, for example, the particular use for which the treatment is made, the manner of administration of the compound, the health and condition of the patient, and the judgment of the prescribing physician. The proportion or concentration of a compound of the invention in a pharmaceutical composition can vary depending upon a number of factors including dosage, chemical characteristics (e.g., hydrophobicity), and the route of administration. For example, the compounds of the invention can be provided in an aqueous physiological buffer solution comprising about 0.1 to about 10% w/v (weight/volume) of the compound for parenteral adminstration. Some typical dose ranges are from about 1 mg/kg to about 1 g/kg of body weight per day. In some embodiments, the dose range is from about 0.01 mg/kg to about 100 mg/kg of

body weight per day. The dosage is likely to depend on such variables as the type and extent of progression of the disease or disorder, the overall health status of the particular patient, the relative biological efficacy of the compound selected, formulation of the excipient, and its route of administration. Effective doses can be extrapolated from dose-response curves derived from *in vitro* or animal model test systems.

Kits

The present invention also includes pharmaceutical kits useful, for example, in the treatment or prevention of diseases, such as pain or cancer and other diseases referred to herein, which include one or more containers comprising a pharmaceutical composition comprising a therapeutically effective amount of a compound of the invention, or pharmaceutically acceptable salt thereof. Such kits can further include, if desired, one or more of various conventional pharmaceutical kit components, such as, for example, containers with one or more pharmaceutically acceptable carriers, additional containers, etc., as will be readily apparent to those skilled in the art. Instructions, either as inserts or as labels, indicating quantities of the components to be administered, guidelines for administration, and/or guidelines for mixing the components, can also be included in the kit.

The invention will be described in greater detail by way of specific examples. The following examples are offered for illustrative purposes, and are not intended to limit the invention in any manner. Those of skill in the art will readily recognize a variety of noncritical parameters, which can be changed or modified to yield essentially the same results. The compounds of the Examples were found to be CB2 agonists according to one or more of the assays provided herein.

EXAMPLES

Analytical LC/MS:

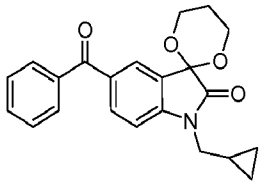
Samples were analyzed on an Agilent LC-1100-MSD. The mass spectrometer, utilized to confirm the integrity of the compound, was a single quadrapole mass filter scanning from 100-1000 Da. The PDA, used to assess compound purity, monitors 254, 215, 230, 280, and 300 nm wavelengths. The compound purity was reported at 254 nm unless stated otherwise. The HPLC mobile phase flow rate was 0.8 ml/min. Eluent A was 0.1% HCO_2H in water and eluent B was 0.1% HCO_2H in ACN. The HPLC mobile phase gradient was initiated at 100% eluent A followed by a linear increase to 100% eluent B in 2.5 minutes. The gradient was held at 100% eluent B for an additional 1.5 minutes (total time 4.0 minutes). The HPLC rapidly equilibrated the column back to 100% eluent A for an additional 1.5 minutes for subsequent injections. The total HPLC/MS run time was 5.5 minutes. Compounds were diluted to ~1.0 mg/mL in DMSO. The analysis injection volume was 5 μL. The HPLC column used was a Thermo Electron Corporation, Aquasil C18, 50 x 2.1 mm, 5 μm particle size.

Preparative reverse-phase HPLC (RP-HPLC):

Compounds were in dissolved in 2 mL of 1:1 DMSO:MeCN, filtered through a 0.45 μm GMF, and purified on a Gilson HPLC, using a Phenomenex LUNA C_{18} column: 60 mm x 21.2 mm I.D., 5 μm particle size: with ACN/H_2O (containing 0.2% TFA) gradient elution (95:5 H_2O:MeCN to 10:90 H_2O:MeCN; 8 minutes running time.

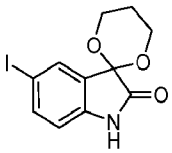
Example 1

5'-benzoyl-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



Step 1

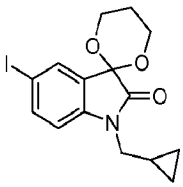
5'-Iodospiro[[1,3]dioxane-2,3'-indolin]-2'-one



A stirred mixture containing 5-iodoisatin (4.06 g, 14.9 mmol), 1,3-propanediol (3.23 mL, 44.6 mmol) and p-toluene sulfonic acid monohydrate (0.565 g, 2.97 mmol) in benzene (149 mL) was heated at reflux temperature for 15 hours. The reaction was cooled to room temperature, washed with saturated aqueous $NaHCO_3$ (3 x), then dried (Na_2SO_4) and concentrated. The crude product was purified on RediSep silica eluting with a 0 to 100% EtOAc/hexane linear gradient to give 4.00 g (81%) of the title compound as a white solid. ^1H NMR (400 MHz, $CDCl_3$): consistent.

Step 2

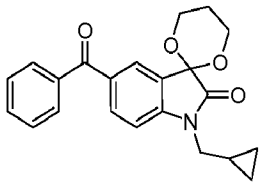
1'-(cyclopropylmethyl)-5'-iodospiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



5'-Iodospiro[[1,3]dioxane-2,3'-indolin]-2'-one (5.10g, 15.40mmol) was dissolved in DMF (150 mL) under a N_2 atmosphere. To this solution was added Cs_2CO_3 (15.06g, 46.21mmol) and cyclopropylmethyl bromide (4.48mL, 46.21mmol), and this mixture was heated to 60° C. After stirring for 1 hour, TLC indicated reaction was complete, so reaction mixture was diluted with EtOAc, then washed with H_2O, followed by brine. The organic layer was dried over Na_2SO_4, then concentrated and purified by flash chromatography on silica gel to afford product as a white solid (5.50g, 93%). ^1H NMR (400 MHz, $CDCl_3$): consistent; MS (ES) *m/z* 385.9 (M+H).

Step 3

5'-benzoyl-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



1'-(cyclopropylmethyl)-5'-iodospiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one (1.00g, 2.59mmol), trans-dichlorobis(triphenylphosphine)palladium(II) (0.054g, 0.078mmol), K_2CO_3 (1.07g, 7.77mmol), and phenyl boronic acid (0.35g, 2.86mmol) were added to a flask fitted with a reflux condenser, a septum inlet, and a magnetic stir bar. The flask was flushed with carbon monoxide and then charged with toluene (20 mL). The mixture was then stirred at 80° C and exposed to an atmosphere of carbon monoxide via a balloon. After stirring overnight, TLC analysis indicated reaction to be complete, so reaction mixture was diluted with EtOAc, then washed with H_2O, followed by brine. The organic layer was dried over Na_2SO_4, concentrated and purified by flash chromatography on silica gel to afford product as a white solid (0.71g, 75%). ^{1}H NMR (400 MHz, $CDCl_3$): consistent; MS (ES) *m/z* 364.1 (M+H).

A procedure similar to that of Example 1, using different boronic acids, provided Examples 2 - 39. The compounds and their analytical data are shown in Table 1.

Table 1: Compounds Prepared According to the Procedure of Example 1.

Example	Compound Name	MS
2	1'-(cyclopropylmethyl)-5'-(2-fluorobenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 382.2 (M+H)
3	1'-(cyclopropylmethyl)-5'-(3-fluorobenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 382.2 (M+H)
4	1'-(cyclopropylmethyl)-5'-(4-fluorobenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 382.2 (M+H)
5	1'-(cyclopropylmethyl)-5'-[2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 432.2 (M+H)
6	1'-(cyclopropylmethyl)-5'-[3-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 432.2 (M+H)
7	1'-(cyclopropylmethyl)-5'-[4-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-	(ES) *m/z* 432.1 (M+H)

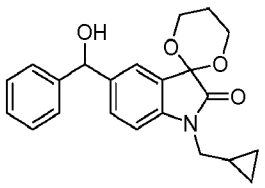
	2'(1'*H*)-one	
8	1'-(cyclopropylmethyl)-5'-(2-methoxybenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 394.2 (M+H)
9	1'-(cyclopropylmethyl)-5'-(3-methoxybenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 394.2 (M+H)
10	1'-(cyclopropylmethyl)-5'-(4-methoxybenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 394.2 (M+H)
11	5'-(2-chlorobenzoyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 398.2 (M+H)
12	5'-(3-chlorobenzoyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 398.2 (M+H)
13	5'-(4-chlorobenzoyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 398.2 (M+H)
14	1'-(cyclopropylmethyl)-5'-(3-methylbenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 378.2 (M+H)
15	1'-(cyclopropylmethyl)-5'-(4-methylbenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 378.2 (M+H)
16	1'-(cyclopropylmethyl)-5'-[3-(trifluoromethoxy)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 448.2 (M+H)
17	1'-(cyclopropylmethyl)-5'-[4-(trifluoromethoxy)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 448.2 (M+H)
18	1'-(cyclopropylmethyl)-5'-(3-furoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 354.2 (M+H)
19	1'-(cyclopropylmethyl)-5'-(3-thienylcarbonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 370.2 (M+H)
20	1'-(cyclopropylmethyl)-5'-(2-	(ES) *m/z* 378.2

	methylbenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(M+H)
21	1'-(cyclopropylmethyl)-5'-[4-fluoro-2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 450.2 (M+H)
22	1'-(cyclopropylmethyl)-5'-[5-fluoro-2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 450.2 (M+H)
23	5'-[4-chloro-2-(trifluoromethyl)benzoyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 466.2 (M+H)
24	1'-(cyclopropylmethyl)-5'-(2,3-difluorobenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	(ES) *m/z* 400.2 (M+H)
25	1'-(cyclopropylmethyl)-5'-(2,5-difluorobenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 400.2 (M+H)
26	5'-(3-chloro-4-fluorobenzoyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 416.2 (M+H)
27	1'-(cyclopropylmethyl)-5'-(2,3-dichlorobenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 432.1 (M+H)
28	1'-(cyclopropylmethyl)-5'-(2,5-dichlorobenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 432.1 (M+H)
29	1'-(cyclopropylmethyl)-5'-(3,4-dichlorobenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 432.1 (M+H)
30	1'-(cyclopropylmethyl)-5'-(2,3-dimethoxybenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 424.2 (M+H)
31	1'-(cyclopropylmethyl)-5'-(2-methoxy-5-methylbenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 408.2 (M+H)
32	5'-(5-chloro-2-methoxybenzoyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-	(ES) *m/z* 428.2 (M+H)

	2'(1'*H*)-one	
33	1'-(cyclopropylmethyl)-5'-(5-fluoro-2-methoxybenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 412.2 (M+H)
34	1'-(cyclopropylmethyl)-5'-(2,3-dimethylbenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 392.2 (M+H)
35	1'-(cyclopropylmethyl)-5'-(2,6-dimethylbenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 392.2 (M+H)
36	5'-(5-chloro-2-methylbenzoyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 412.2 (M+H)
37	1'-(cyclopropylmethyl)-5'-[2-(trifluoromethoxy)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 448.2 (M+H)
38	1'-(cyclopropylmethyl)-5'-(2,4-difluorobenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 400.2 (M+H)
39	1'-(cyclopropylmethyl)-5'-(2,6-dimethoxybenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 424.2 (M+H)

Example 40

1'-(cyclopropylmethyl)-5'-[hydroxy(phenyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



5'-benzoyl-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one (0.30g, 0.83mmol) was dissolved in THF (8 mL) and to this solution was added $NaBH_4$ (0.031g, 0.826mmol). After stirring for 1 hour, TLC analysis indicated reaction to be complete, so reaction mixture was diluted with EtOAc, then washed with H_2O, followed by brine. The organic layer was dried over Na_2SO_4, then concentrated and purified by flash chromatography on silica gel to afford product as a white solid (0.29g, 96%). ^1H NMR (400 MHz, $CDCl_3$): consistent; MS (ES) *m/z* 366.1 (M+H).

A procedure similar to that of Example 40, using Examples 2-39 (see Table 1), provided Examples 41-77. The compounds and their analytical data are shown in Table 2.

Table 2: Compounds Prepared According to the Procedure of Example 40.

Example	Compound Name	MS
41	1'-(cyclopropylmethyl)-5'-[(2-fluorophenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 384.2 (M+H)
42	1'-(cyclopropylmethyl)-5'-[(3-fluorophenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(EI) *m/z* 383 (M+.)
43	1'-(cyclopropylmethyl)-5'-[(4-fluorophenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(APPI) *m/z* 383 (M+.)
44	1'-(cyclopropylmethyl)-5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 434.2 (M+H)
45	1'-(cyclopropylmethyl)-5'-{hydroxy[3-(trifluoromethyl)phenyl]methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 492.2 (M+CH_3COO)-
46	1'-(cyclopropylmethyl)-5'-{hydroxy[4-(trifluoromethyl)phenyl]methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 492.2 (M+CH_3COO)-
47	1'-(cyclopropylmethyl)-5'-[hydroxy(2-methoxyphenyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 396.3 (M+H)
48	1'-(cyclopropylmethyl)-5'-[hydroxy(3-methoxyphenyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 396.2 (M+H)
49	1'-(cyclopropylmethyl)-5'-[hydroxy(4-methoxyphenyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 396.3 (M+H)
50	5'-[(2-chlorophenyl)(hydroxy)methyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 400.2 (M+H)
51	5'-[(3-chlorophenyl)(hydroxy)methyl]-1'-	(ES) *m/z* 400.2

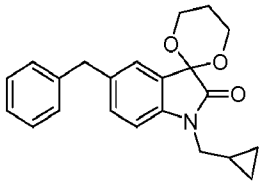
	(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(M+H)
52	5'-[(4-chlorophenyl)(hydroxy)methyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 400.2 (M+H)
53	1'-(cyclopropylmethyl)-5'-[hydroxy(3-methylphenyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 380.3 (M+H)
54	1'-(cyclopropylmethyl)-5'-[hydroxy(4-methylphenyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 380.3 (M+H)
55	1'-(cyclopropylmethyl)-5'-{hydroxy[3-(trifluoromethoxy)phenyl]methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 508.2 (M+CH_3COO)-
56	1'-(cyclopropylmethyl)-5'-{hydroxy[4-(trifluoromethoxy)phenyl]methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 508.2 (M+CH_3COO)-
57	1'-(cyclopropylmethyl)-5'-[3-furyl(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 356.2 (M+H)
58	1'-(cyclopropylmethyl)-5'-[hydroxy(3-thienyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 372.2 (M+H)
59	1'-(cyclopropylmethyl)-5'-[hydroxy(2-methylphenyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 380.2 (M+H)
60	1'-(cyclopropylmethyl)-5'-{[4-fluoro-2-(trifluoromethyl)phenyl](hydroxy)methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 510.1 (M+CH_3COO)-
61	1'-(cyclopropylmethyl)-5'-{[5-fluoro-2-(trifluoromethyl)phenyl](hydroxy)methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 510.1 (M+CH_3COO)-
62	5'-{[4-chloro-2-(trifluoromethyl)phenyl](hydroxy)methyl}-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 526.1 (M+CH_3COO)-
63	1'-(cyclopropylmethyl)-5'-[(2,3-	(ES) *m/z* 460.1

	difluorophenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(M+CH_3COO)-
64	1'-(cyclopropylmethyl)-5'-[(2,5-difluorophenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 460.1 (M+CH_3COO)-
65	5'-[(3-chloro-4-fluorophenyl)(hydroxy)methyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 476.1 (M+CH_3COO)-
66	1'-(cyclopropylmethyl)-5'-[(2,3-dichlorophenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 492.1 (M+CH_3COO)-
67	1'-(cyclopropylmethyl)-5'-[(2,5-dichlorophenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 492.1 (M+CH_3COO)-
68	1'-(cyclopropylmethyl)-5'-[(3,4-dichlorophenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 492.1 (M+CH_3COO)-
69	1'-(cyclopropylmethyl)-5'-[(2,3-dimethoxyphenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 484.2 (M+CH_3COO)-
70	1'-(cyclopropylmethyl)-5'-[hydroxy(2-methoxy-5-methylphenyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 410.2 (M+H)
71	5'-[(5-chloro-2-methoxyphenyl)(hydroxy)methyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 488.2 (M+CH_3COO)-
72	1'-(cyclopropylmethyl)-5'-[(5-fluoro-2-methoxyphenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 414.2 (M+H)
73	1'-(cyclopropylmethyl)-5'-[(2,3-dimethylphenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 394.2 (M+H)
74	1'-(cyclopropylmethyl)-5'-[(2,6-dimethylphenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 392.2 (M-H)-
75	5'-[(5-chloro-2-	(ES) *m/z* 472.2

	methylphenyl)(hydroxy)methyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(M+CH_3COO)-
76	1'-(cyclopropylmethyl)-5'-{hydroxy[2-(trifluoromethoxy)phenyl]methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 508.2 (M+CH_3COO)-
77	1'-(cyclopropylmethyl)-5'-[(2,4-difluorophenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 460.2 (M+CH_3COO)-

Example 78

5'-benzyl-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



1'-(cyclopropylmethyl)-5'-[hydroxy(phenyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one (0.24g, 0.66mmol) was dissolved in methylene chloride (6 mL) and was then treated with Et_3SiH (0.12mL, 0.72mmol). This solution was cooled to 0° C and then TFA (0.15mL, 1.97mmol) was added dropwise. TLC analysis confirmed reaction was complete immediately after the addition of TFA, so the reaction mixture was treated with $NaHCO_3$, and then diluted with methylene chloride. The organic layer was separated, washed with brine, then dried over Na_2SO_4 and purified by flash chromatography on silica gel to afford product as a colorless oil (0.15g, 66%). ^1H NMR (400 MHz, $CDCl_3$): consistent; MS (ES) m/z 350.1 (M+H).

A procedure similar to that of Example 78, using Examples 41-77, provided Examples 79- 112. The compounds and their analytical data are shown in Table 3.

Table 3: Compounds Prepared According to the Procedure of Example 78.

Example	Compound Name	MS
79	1'-(cyclopropylmethyl)-5'-[2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 418.2 (M+H)
80	1'-(cyclopropylmethyl)-5'-(2-fluorobenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 368.2 (M+H)
81	1'-(cyclopropylmethyl)-5'-(3-	(ES) *m/z* 368.2

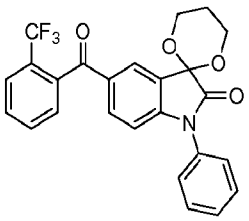
	fluorobenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(M+H)
82	1'-(cyclopropylmethyl)-5'-(4-fluorobenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 368.2 (M+H)
83	1'-(cyclopropylmethyl)-5'-[3-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 418.1 (M+H)
84	1'-(cyclopropylmethyl)-5'-[4-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(APPI) *m/z* 417 (M+.)
85	1'-(cyclopropylmethyl)-5'-(2-methoxybenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 380.2 (M+H)
86	1'-(cyclopropylmethyl)-5'-(3-methoxybenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 380.2 (M+H)
87	1'-(cyclopropylmethyl)-5'-(4-methoxybenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 380.3 (M+H)
88	5'-(2-chlorobenzyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 384.2 (M+H)
89	5'-(3-chlorobenzyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 384.2 (M+H)
90	5'-(4-chlorobenzyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 384.2 (M+H)
91	1'-(cyclopropylmethyl)-5'-(3-methylbenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 364.3 (M+H)
92	1'-(cyclopropylmethyl)-5'-(4-methylbenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 364.3 (M+H)
93	1'-(cyclopropylmethyl)-5'-[4-(trifluoromethoxy)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(APPI) *m/z* 433 (M+.)
94	1'-(cyclopropylmethyl)-5'-(3-thienylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 356.2 (M+H)
95	1'-(cyclopropylmethyl)-5'-(2-	(ES) *m/z* 364.3

	methylbenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(M+H)
96	1'-(cyclopropylmethyl)-5'-[4-fluoro-2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 436.0 (M+H)
97	1'-(cyclopropylmethyl)-5'-[5-fluoro-2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 436.0 (M+H)
98	5'-[4-chloro-2-(trifluoromethyl)benzyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 452.0 (M+H)
99	1'-(cyclopropylmethyl)-5'-(2,3-difluorobenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 386.1 (M+H)
100	1'-(cyclopropylmethyl)-5'-(2,5-difluorobenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 386.1 (M+H)
101	5'-(3-chloro-4-fluorobenzyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 402.0 (M+H)
102	1'-(cyclopropylmethyl)-5'-(2,3-dichlorobenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 418.0 (M+H)
103	1'-(cyclopropylmethyl)-5'-(2,5-dichlorobenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 418.0 (M+H)
104	1'-(cyclopropylmethyl)-5'-(3,4-dichlorobenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 418.0 (M+H)
105	1'-(cyclopropylmethyl)-5'-(2,3-dimethoxybenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 410.1 (M+H)
106	1'-(cyclopropylmethyl)-5'-(2-methoxy-5-methylbenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 394.1 (M+H)
107	5'-(5-chloro-2-methoxybenzyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 414.0 (M+H)
108	1'-(cyclopropylmethyl)-5'-(5-fluoro-2-	(ES) *m/z* 398.1

	methoxybenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(M+H)
109	1'-(cyclopropylmethyl)-5'-(2,3-dimethylbenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 378.1 (M+H)
110	5'-(5-chloro-2-methylbenzyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 398.0 (M+H)
111	1'-(cyclopropylmethyl)-5'-[2-(trifluoromethoxy)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 434.0 (M+H)
112	1'-(cyclopropylmethyl)-5'-(2,4-difluorobenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 386.1 (M+H)

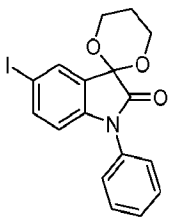
Example 113

1'-phenyl-5'-[2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



Step 1

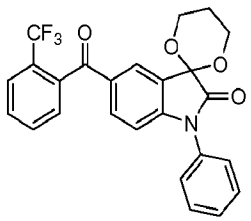
5'-iodo-1'-phenylspiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



5'-Iodospiro[[1,3]dioxane-2,3'-indolin]-2'-one (2.50g, 7.55mmol), phenylboronic acid (2.76g, 22.65mmol), $Cu(OAc)_2$ (2.74g, 15.10mmol), and 4 Angstrom molecular sieves (3.00g) were stirred together in CH_2Cl_2 (75 mL). To this stirring solution was added Et_3N (3.25mL, 22.65mmol) and this mixture was allowed to stir overnight. TLC analysis indicated reaction had occurred, although starting material still persisted after 48 hours of stirring. Reaction was stopped, diluted with CH_2Cl_2 and then filtered through celite. The organic layer was washed with $NaHCO_3$, followed by brine, then was dried over Na_2SO_4, concentrated, and purified by flash chromatography on silica gel to afford product as a white solid (1.82g, 59%). ^{1}H NMR (400 MHz, $CDCl_3$): consistent; MS (ES) *m/z* 407.9 (M+H).

Step 2

1'-phenyl-5'-[2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



5'-iodo-1'-phenylspiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one (0.28g, 0.68mmol), trans-dichlorobis(triphenylphosphine)palladium(II) (0.014g, 0.020mmol), K_2CO_3 (0.282g, 2.04mmol) and 2-(trifluoromethyl)-phenylboronic acid (0.151g, 0.82mmol), were added to a flask fitted with a reflux condenser, a septum inlet, and a magnetic stir bar. The flask was flushed with carbon monoxide and then charged with toluene (20 mL). The mixture was then stirred at 80° C under an atomosphere of carbon monoxide via balloon. After stirring overnight, TLC analysis indicated reaction to be complete, so reaction mixture was diluted with EtOAc, washed with H_2O, then followed by brine. The organic layer was dried over Na_2SO_4, concentrated and purified by flash chromatography on silica gel to afford product as a white solid (0.22g, 72%). ^{1}H NMR (400 MHz, $CDCl_3$): consistent; MS (ES) *m/z* 454.1 (M+H).

A procedure similar to that of Example 113, using different aryl boronic acids for the N-arylation described in step 1, and different aryl boronic acids for the carbonylation described in step 2, provided Examples 114-134. The compounds and their analytical data are shown in Table 4.

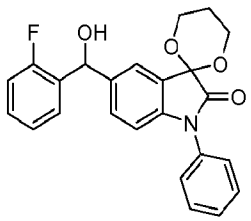
Table 4: Compounds Prepared According to the Procedure of Example 113.

Example	Compound Name	MS
114	5'-benzoyl-1'-phenylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 386.1 (M+H)
115	5'-(2-fluorobenzoyl)-1'-phenylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 404.1 (M+H)
116	5'-(2-methoxybenzoyl)-1'-phenylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 416.1 (M+H)
117	5'-(2-chlorobenzoyl)-1'-phenylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 420.1 (M+H)
118	5'-(2-methylbenzoyl)-1'-phenylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 400.1 (M+H)
119	2-(5'-benzoyl-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl)benzonitrile	(ES) *m/z* 411.1 (M+H)
120	2-[5'-(2-fluorobenzoyl)-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl]benzonitrile	(ES) *m/z* 429.1 (M+H)

121	2-{2'-oxo-5'-[2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl}benzonitrile	(ES) *m/z* 479.1 (M+H)
122	2-[5'-(2-methoxybenzoyl)-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl]benzonitrile	(ES) *m/z* 441.1 (M+H)
123	2-[5'-(2-chlorobenzoyl)-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl]benzonitrile	(ES) *m/z* 445.0 (M+H)
124	5'-benzoyl-1'-(3,4-difluorophenyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 422.1 (M+H)
125	1'-(3,4-difluorophenyl)-5'-(2-fluorobenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(APPI) *m/z* 440 (M+H)
126	1'-(3,4-difluorophenyl)-5'-[2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(APPI) *m/z* 490 (M+H)
127	1'-(3,4-difluorophenyl)-5'-(2-methoxybenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 452.1 (M+H)
128	5'-(2-chlorobenzoyl)-1'-(3,4-difluorophenyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(APPI) *m/z* 456 (M+H)
129	1'-(3,4-difluorophenyl)-5'-(2-methylbenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 436.1 (M+H)
130	1'-(2,5-difluorophenyl)-5'-[2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 490.1 (M+H)
131	5'-(2-chlorobenzoyl)-1'-(2,5-difluorophenyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(APPI) *m/z* 456 (M+H)
132	1'-(3-thienyl)-5'-[2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 460.0 (M+H)
133	5'-(2-chlorobenzoyl)-1'-(3-thienyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 426.0 (M+H)
134	2-[5'-(2-methylbenzoyl)-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl]benzonitrile	(ES) *m/z* 425.0 (M+H)

Example 135

5'-[(2-fluorophenyl)(hydroxy)methyl]-1'-phenylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



5'-(2-fluorobenzoyl)-1'-phenylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one (0.16g, 0.39mmol) was dissolved in THF (4 mL) and to this solution were added $NaBH_4$ (0.044g, 1.17mmol). After stirring for 1 hour, TLC analysis indicated the reaction to be complete, so reaction mixture was diluted with EtOAc, then washed with H_2O, followed by brine. The organic layer was dried over Na_2SO_4, concentrated and then purified by flash chromatography on silica gel to afford product as a white solid (0.10g, 65%). ^1H NMR (400 MHz, $CDCl_3$): consistent; MS (ES) *m/z* 406.2 (M+H).

A procedure similar to that of Example 135, using Examples 114-134 (see Table 4), provided Examples 136-155. The compounds and their analytical data are shown in Table 5.

Table 5: Compounds Prepared According to the Procedure of Example 135.

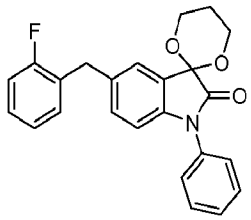
Example	Compound Name	MS
136	5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}-1'-phenylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 456.2 (M+H)
137	5'-[hydroxy(2-methoxyphenyl)methyl]-1'-phenylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 418.2 (M+H)
138	5'-[(2-chlorophenyl)(hydroxy)methyl]-1'-phenylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 422.1 (M+H)
139	2-{5'-[hydroxy(phenyl)methyl]-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl}benzonitrile	(ES) *m/z* 413.2 (M+H)
140	2-{5'-[(2-fluorophenyl)(hydroxy)methyl]-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl}benzonitrile	(ES) *m/z* 431.2 (M+H)
141	2-[5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl]benzonitrile	(ES) *m/z* 481.2 (M+H)

142	2-{5'-[hydroxy(2-methoxyphenyl)methyl]-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl}benzonitrile	(ES) *m/z* 460.2 ($M+NH_4$)
143	2-{5'-[(2-chlorophenyl)(hydroxy)methyl]-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl}benzonitrile	(ES) *m/z* 447.2 (M+H)
144	2-{5'-[hydroxy(2-methylphenyl)methyl]-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl}benzonitrile	(ES) *m/z* 427.2 (M+H)
145	1'-(3,4-difluorophenyl)-5'-[hydroxy(phenyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 427.2 ($M+CH_3COO$)-
146	1'-(3,4-difluorophenyl)-5'-[(2-fluorophenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 500.2 ($M+CH_3COO$)-
147	1'-(3,4-difluorophenyl)-5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 550.2 ($M+CH_3COO$)-
148	1'-(3,4-difluorophenyl)-5'-[hydroxy(2-methoxyphenyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 924.2 ($2M+NH_4$)
149	5'-[(2-chlorophenyl)(hydroxy)methyl]-1'-(3,4-difluorophenyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 516.2 ($M+CH_3COO$)-
150	1'-(3,4-difluorophenyl)-5'-[hydroxy(2-methylphenyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 436.2 (M-H)
151	1'-(2,5-difluorophenyl)-5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 490.2 (M-H)
152	5'-[(2-chlorophenyl)(hydroxy)methyl]-1'-(2,5-difluorophenyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(APPI) *m/z* 457 (M+.)
153	5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}-1'-(3-thienyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 520.1 ($M+CH_3COO$)-
154	5'-[(2-chlorophenyl)(hydroxy)methyl]-1'-(3-	(APPI) *m/z* 427

	thienyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(M+.)
155	5'-[hydroxy(2-methylphenyl)methyl]-1'-phenylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 402.2 (M+H)

Example 156

5'-(2-fluorobenzyl)-1'-phenylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



5'-[(2-fluorophenyl)(hydroxy)methyl]-1'-phenylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one (0.090g, 0.22mmol) was dissolved in methylene chloride (2 mL) and was then treated with Et_3SiH (39μL, 0.24mmol). The mixture was cooled to 0° C and then TFA (0.49μL, 0.66mmol) was added dropwise. TLC analysis confirmed the reaction was complete after 0.5 hour, so the reaction mixture was treated with $NaHCO_3$, and then diluted with methylene chloride. The organic layer was separated, washed with brine, then dried over Na_2SO_4 and purified by flash chromatography on silica gel to afford product as a colorless oil (0.058g, 67%). ^1H NMR (400 MHz, $CDCl_3$): consistent; MS (ES) *m/z* 390.1 (M+H).

A procedure similar to that of Example 156, using Examples 136-155, provided Examples 157-175. The compounds and their analytical data are shown in Table 6.

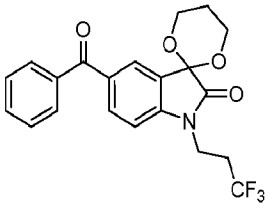
Table 6: Compounds Prepared According to the Procedure of Example 156.

Example	Compound Name	MS
157	1'-phenyl-5'-[2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 440.1 (M+H)
158	5'-(2-methoxybenzyl)-1'-phenylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 402.2 (M+H)
159	5'-(2-chlorobenzyl)-1'-phenylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 406.1 (M+H)
160	5'-(2-methylbenzyl)-1'-phenylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 386.2 (M+H)
161	2-(5'-benzyl-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl)benzonitrile	(ES) *m/z* 397.1 (M+H)
162	2-[5'-(2-fluorobenzyl)-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl]benzonitrile	(ES) *m/z* 415.1 (M+H)

163	2-{2'-oxo-5'-[2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl}benzonitrile	(ES) *m/z* 465.1 (M+H)
164	2-[5'-(2-methoxybenzyl)-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl]benzonitrile	(ES) *m/z* 427.2 (M+H)
165	2-[5'-(2-chlorobenzyl)-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl]benzonitrile	(ES) *m/z* 431.1 (M+H)
166	5'-benzyl-1'-(3,4-difluorophenyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(EI) *m/z* 407 (M+.)
167	1'-(3,4-difluorophenyl)-5'-(2-fluorobenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(EI) *m/z* 425 (M+.)
168	1'-(3,4-difluorophenyl)-5'-[2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 476.1 (M+H)
169	1'-(3,4-difluorophenyl)-5'-(2-methoxybenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(EI) *m/z* 437 (M+.)
170	5'-(2-chlorobenzyl)-1'-(3,4-difluorophenyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(EI) *m/z* 441 (M+.)
171	1'-(3,4-difluorophenyl)-5'-(2-methylbenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 422.1 (M+H)
172	1'-(2,5-difluorophenyl)-5'-[2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(EI) *m/z* 475 (M+.)
173	5'-(2-chlorobenzyl)-1'-(2,5-difluorophenyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 442.1 (M+H)
174	1'-(3-thienyl)-5'-[2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 446.1 (M+H)
175	5'-(2-chlorobenzyl)-1'-(3-thienyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	(ES) *m/z* 412.0 (M+H)

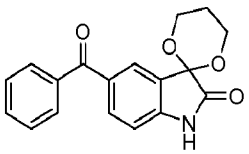
Example 176

5'-benzoyl-1'-(3,3,3-trifluoropropyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



Step 1

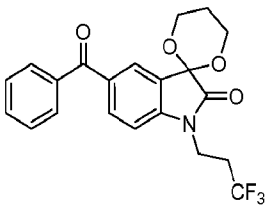
5'-benzoylspiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



5'-Iodospiro[[1,3]dioxane-2,3'-indolin]-2'-one (3.00g, 9.06mmol), trans-dichlorobis-(triphenylphosphine)palladium(II) (0.19g, 0.27mmol), K_2CO_3 (3.75g, 27.18mmol), and phenyl boronic acid (1.33g, 10.87mmol) were added to a flask fitted with a reflux condenser, a septum inlet, and a magnetic stir bar. The flask was flushed with carbon monoxide and then charged with toluene (90 mL). The mixture was then stirred at 80° C under an atmosphere of carbon monoxide via balloon. After stirring overnight, TLC analysis indicated reaction to be complete, so reaction mixture was diluted with EtOAc, then washed with H_2O, followed by brine. The organic layer was dried over Na_2SO_4, concentrated and then purified by flash chromatography on silica gel to afford product as a brown solid (1.20g, 43%). ^1H NMR (400 MHz, $CDCl_3$): consistent; MS (ES) *m/z* 364.1 (M+H).

Step 2

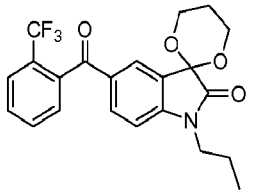
5'-benzoyl-1'-(3,3,3-trifluoropropyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



5'-benzoylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one (0.10g, 0.28mmol) was dissolved in DMF (3.00mL) under a N_2 atmosphere. To this solution was added Cs_2CO_3 (0.27g, 0.83mmol) and 1-trifluoromethylpropyl iodide (0.096mL, 0.83mmol), and this mixture was heated to 60° C. After stirring for 2 days, TLC indicated reaction was still not complete (~40% product), however, reaction was stopped regardless. Reaction mixture was diluted with EtOAc, then washed with H_2O, followed by brine. The organic layer was dried over Na_2SO_4, concentrated and then purified by flash chromatography on silica gel to afford product as a white solid (0.044g, 39%). ^1H NMR (400 MHz, $CDCl_3$): consistent; MS (ES) *m/z* 406.1 (M+H).

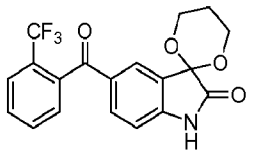
Example 177

1'-propyl-5'-[2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



Step 1

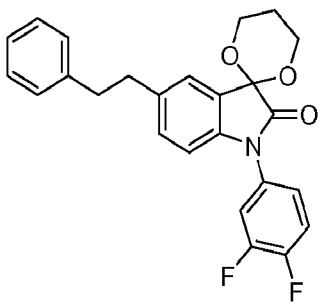
5'-[2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



5'-Iodospiro[[1,3]dioxane-2,3'-indolin]-2'-one (4.00g, 12.08mmol), trans-dichlorobis-(triphenylphosphine)palladium(II) (0.25g, 0.36mmol), K_2CO_3 (5.00g, 36.21mmol), and 2-(trifluoromethyl)-phenylboronic acid (2.66g, 14.50mmol) were added to a flask fitted with a reflux condenser, a septum inlet, and a magnetic stir bar. The flask was flushed with carbon monoxide and then charged with toluene (120 mL). The mixture was then stirred at 80°C under an atmosphere of carbon monoxide via balloon. After stirring overnight, TLC analysis indicated reaction to be complete, so reaction mixture was diluted with EtOAc, then washed with H_2O, followed by brine. The organic layer was dried over Na_2SO_4, concentrated and then purified by flash chromatography on silica gel to afford product as a white solid (1.94g, 43%). ^{1}H NMR (400 MHz, $CDCl_3$): consistent; MS (ES) *m/z* 376.0 (M-H).

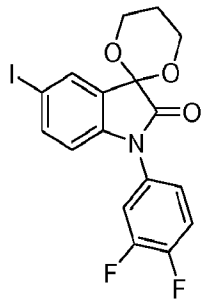
Example 178

1'-(3,4-Difluorophenyl)-5'-phenethylspiro[[1,3]dioxane-2,3'-indolin]-2'-one



Step 1

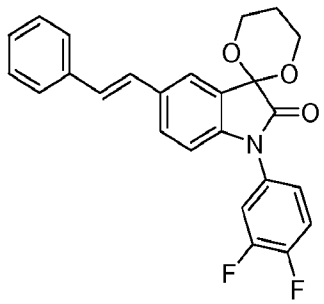
1'-(3,4-Difluorophenyl)-5'-iodospiro[[1,3]dioxane-2,3'-indolin]-2'-one



A suspension consisting of 5'-iodospiro[[1,3]dioxane-2,3'-indolin]-2'-one (1.9 g, 5.7 mmol), 3,4-difluoro-phenylboronic acid (1.8 g, 11.5 mmol), Et_3N (2.4 mL, 17 mmol), $Cu(OAc)_2$ (2.1 g, 11.5 mmol), and 4 Å molecular sieves (2.5 g) in CH_2Cl_2 (100 mL) was stirred at room temperature for 24 hours. The reaction mixture was diluted with CH_2Cl_2 and then treated with aqueous $NaHCO_3$. The organic layer was separated, filtered, concentrated, and then purified by flash chromatography on silica gel (5:1 hexane/EtOAc) to yield 2.1 g of the title compound as a yellow solid. ^1H NMR (400 MHz, $CDCl_3$): consistent; MS (ES^+) *m/z* 443.0 (M+H).

Step 2

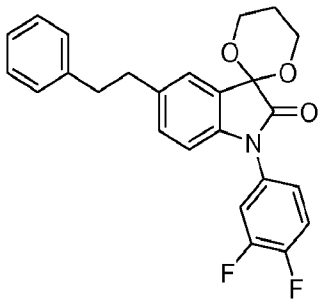
(E)-1'-(3,4-Difluorophenyl)-5'-styrylspiro[[1,3]dioxane-2,3'-indolin]-2'-one



A suspension consisting of 1'-(3,4-Difluorophenyl)-5'-iodospiro[[1,3]dioxane-2,3'-indolin]-2'-one (89 mg, 0.2 mmol), (E)-4,4,5,5-tetramethyl-2-styryl-1,3,2-dioxaborolane (184 mg, 0.8 mmol), $Pd(Ph_3P)_4$ (46 mg, 0.04 mmol), and 2 M Na_2CO_3 (1 mL, 2 mmol) in 3 mL of DMF was stirred at 50° C for 12 hours. The reaction mixture was diluted with EtOAc and then washed with water and brine. The organic layer was dried ($MgSO_4$), filtered, concentrated, and then purified by flash chromatography on silica gel (hexane/EtOAc) to yield 75 mg of the title compound as a tan solid. ^1H NMR (400 MHz, $CDCl_3$): consistent; MS (ES^+) *m/z* 419.1 (M+H).

Step 3

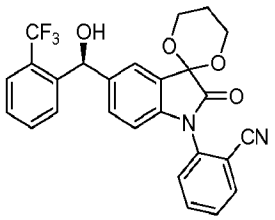
1'-(3,4-Difluorophenyl)-5'-phenethylspiro[[1,3]dioxane-2,3'-indolin]-2'-one



A solution consisting of (E)-1'-(3,4-Difluorophenyl)-5'-styrylspiro[[1,3]dioxane-2,3'-indolin]-2'-one (45 mg, 0.11 mmol) in 10 mL of EtOAc was treated with 10% Pd/C and hydrogenated at 40 psi in a Parr reactor for 2 hours. The suspension was filtered, concentrated, and then purified by flash chromatography on silica gel (CH_2Cl_2) to yield 39 mg of the title compound as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): consistent; MS (ES^+) *m/z* 421.1 (M+H).

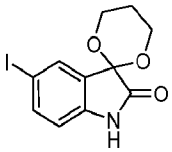
Example 179

(-)-2-[5'-{(S)-hydroxy[2-(trifluoromethyl)phenyl]methyl}-2'-oxospiro[1,3-dioxane- 2,3'-indol]-1'(2'H)-yl]benzonitrile



Step 1

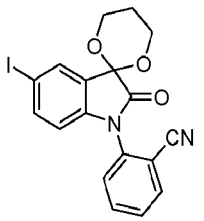
5'-Iodospiro[[1,3]dioxane-2,3'-indolin]-2'-one



A stirred mixture containing 5-iodoisatin (4.06 g, 14.9 mmol), 1,3-propanediol (3.23 mL, 44.6 mmol) and p-toluene sulfonic acid monohydrate (0.565 g, 2.97 mmol) in benzene (149 mL) was heated at reflux temperature for 15 hours. The reaction was cooled to room temperature, then washed with saturated aqueous $NaHCO_3$ (3x), dried (Na_2SO_4) and concentrated. The crude product was purified on RediSep silica eluting with a 0 to 100% EtOAc/hexane linear gradient to give 4.00 g (81%) of the title compound as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): consistent.

Step 2

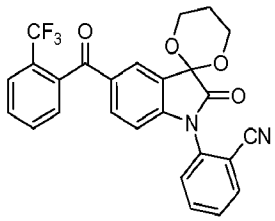
2-(5'-iodo-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'H)-yl)benzonitrile



5'-Iodospiro[[1,3]dioxane-2,3'-indolin]-2'-one (20.00g, 60.40mmol) was dissolved in DMF (100.00mL) under a N_2 atmosphere. To this solution was added NaH (60%: 2.90g, 72.48mmol) and this solution was stirred for 0.5 hour, after which the nitrile was added (19.66mL, 181.20mmol). This reaction mixture was heated to 125° C and was stirred overnight. After stirring for overnight, TLC analysis (hexane:EtOAc::1:1) indicated reaction was nearly complete, so reaction mixture was diluted with EtOAc, washed with $NaHCO_3$, followed by H_2O. Aqueous layers were re-extracted with EtOAc, and organic layers were combined, washed with brine, then dried over Na_2SO_4, concentrated and purified by flash chromatography on silica gel to afford the product as a white solid (17.0g, 65%). ^{1}H NMR (400 MHz, $CDCl_3$): consistent; MS (ES) *m/z* 432.9 (M+H).

Step 3

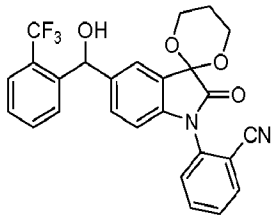
2-{2'-oxo-5'-[2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-1'(2'H)- yl}benzonitrile



2-(5'-iodo-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'H)-yl)benzonitrile (16.50g, 38.18mmol), trans-dichlorobis(triphenylphosphine)palladium(II) (0.803g, 1.15mmol), K_2CO_3 (15.82g, 114.54mmol), and boronic acid (8.43g, 45.82mmol) were added to a flask fitted with a reflux condenser, a septum inlet, and a magnetic stir bar. The flask was flushed with carbon monoxide and then charged with toluene (20 mL). The mixture was then stirred at 80° C under an atmosphere of carbon monoxide via balloon. After stirring overnight, TLC analysis (hexane:EtOAc::1:1) indicated reaction to be complete, so reaction mixture was diluted with EtOAc, washed with H_2O, followed by brine. The organic layer was dried over Na_2SO_4, concentrated and then purified by flash chromatography on silica gel to afford the product as a white solid (16.8g, 92%). ^{1}H NMR (400 MHz, $CDCl_3$): consistent; MS (ES) *m/z* 479.1 (M+H).

Step 4

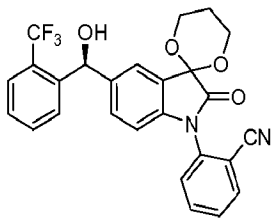
2-[5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}-2'-oxospiro[1,3-dioxane-2,3'- indol]-1'(2'H)-yl]benzonitrile



2-{2'-oxo-5'-[2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-1'(2'H)- yl}benzonitrile (6.40g, 13.37mmol) was dissolved in THF (100.00mL) and was then treated with $NaBH_4$ (1.01g, 26.73mmol). After stirring overnight, LC/MS analysis indicated reaction to be ~75% product and 25% starting material (along with other impurities), so reaction mixture was quenched with $NaHCO_3$, and was stirred for 0.5 hour. The reaction mixture was then extracted with EtOAc, washed with H_2O, followed by brine. The organic layer was dried over Na_2SO_4, concentrated and then purified by flash chromatography on silica gel to afford the product (75% product and 25% starting material) as an off-white solid as a racemate (2.50g). ^1H NMR (400 MHz, $CDCl_3$): consistent; MS (ES) *m/z* 481.2 (M+H).

Step 5

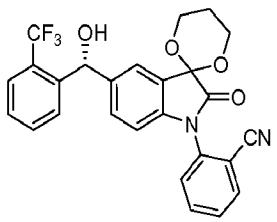
2-[5'-{(S)-hydroxy[2-(trifluoromethyl)phenyl]methyl}-2'-oxospiro[1,3-dioxane- 2,3'-indol]-1'(2'H)-yl]benzonitrile



The racemate, 2-[5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'H)-yl]benzonitrile, (6.50g) was preparatively isolated using a Luna™ CN, 5 x 25 cm column, utilizing a mobile phase of 30% EtOH in hexane. The enantiomers of the main component were then preparatively isolated using a Chiralpak AD-H, 2 x 25 cm column, utilizing a mobile phase of 15% MeOH in CO_2. The desired peak (peak 2) eluted at 6.272 minutes. ^1H NMR (400 MHz, $CDCl_3$): consistent; MS (ESI) *m/z* 503.0 (M+Na). α_D = -37.0.

Example 180

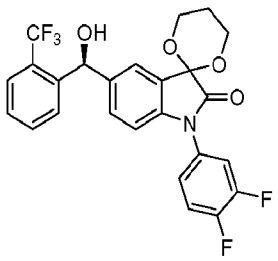
(+)2-[5'-{(R)-hydroxy[2-(trifluoromethyl)phenyl]methyl}-2'-oxospiro[1,3-dioxane- 2,3'-indol]-1'(2'H)-yl]benzonitrile



The racemate from Example 179, Step 4, 2-[5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}-2'-oxospiro[1,3-dioxane-2,3'- indol]-1'(2'H)-yl]benzonitrile, (6.50g) was preparatively isolated using a Luna™ CN, 5 x 25 cm column, utilizing a mobile phase of 30% EtOH in hexane. The enantiomers of the main component were then preparatively isolated using a Chiralpak AD-H, 2 x 25 cm column, utilizing a mobile phase of 15% MeOH in CO_2. The desired peak (peak 1) eluted at 5.727 minutes. ^{1}H NMR (400 MHz, $CDCl_3$): consistent; MS (ESI) *m/z* 503.0 (M+Na). α_D = +36.2.

Example 181

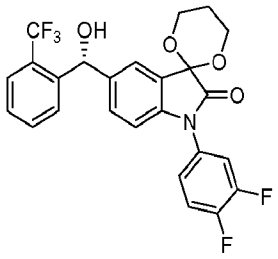
(+)-1'-(3,4-difluorophenyl)-5'-{(R)-hydroxy[2-(trifluoromethyl)phenyl]-methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



The racemate from Example 147, 1'-(3,4-difluorophenyl)-5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, was separated, and the enantiomers of the main component were then preparatively isolated using a Chiralcel™ AS, 2 x 25 cm column, utilizing a mobile phase of 10% EtOH in hexane. The desired peak (peak 1) eluted at 6.306 minutes. ^{1}H NMR (400 MHz, $CDCl_3$): consistent; MS (ESI) *m/z* 492.1 (M+H).

Example 182

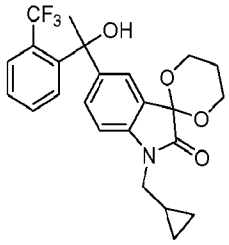
(-)-1'-(3,4-difluorophenyl)-5'-{(S)-hydroxy[2-(trifluoromethyl)phenyl]-methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



The racemate from Example 147, 1'-(3,4-difluorophenyl)-5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, was separated, and the enantiomers of the main component were then preparatively isolated using a Chiralcel AS, 2 x 25 cm column, utilizing a mobile phase of 10% EtOH in hexane. The desired peak (peak 2) eluted at 9.164 min. ^{1}H NMR (400 MHz, $CDCl_3$): consistent; MS (ESI) *m/z* 492.1 (M+H).

Example 183

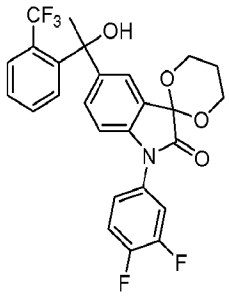
1'-(cyclopropylmethyl)-5'-{1-hydroxy-1-[2-(trifluoromethyl)phenyl]ethyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



The compound from Example 5, 1'-(cyclopropylmethyl)-5'-[2-(trifluoromethyl)-benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, (0.25g, 0.58mmol) was dissolved in THF (6.00mL) and cooled to −78° C. Once cooled, a methyl Grignard reagent (3.0M in diethyl ether; 0.21mL, 0.64mmol) was added drop wise until completion, and reaction mixture was allowed to slowly warm to room temperature. After stirring overnight, TLC analysis indicated that reaction had neared completion, so reaction mixture was quenched with sat. NH_4Cl and was stirred for 30 minutes. This mixture was then extracted with EtOAc, and organic layers were combined, washed with brine, dried over Na_2SO_4, concentrated and then purified by flash chromatography on silica gel to afford product as an off-white solid (0.19, 71%). ^{1}H NMR (400 MHz, $CDCl_3$): consistent; MS (ES) *m/z* 448.1 (M+H).

Example 184

1'-(3,4-difluorophenyl)-5'-{1-hydroxy-1-[2-(trifluoromethyl)phenyl]ethyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



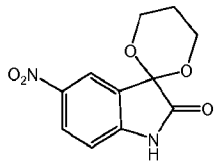
The compound from Example 126, 1'-(3,4-difluorophenyl)-5'-[2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, (0.40g, 0.82mmol) was dissolved in THF (8 mL) and cooled to −78° C. Once cooled, a methyl Grignard reagent (3.0M in diethyl ether; 0.30mL, 0.90mmol) was added drop wise until completion, and reaction mixture was allowed to slowly warm to room temperature. After stirring overnight, TLC analysis indicated that reaction had neared completion, so reaction mixture was quenched with sat. NH_4Cl and was stirred for 30 minutes. This mixture was then extracted with EtOAc, and organic layers were combined, washed with brine, dried over Na_2SO_4, concentrated and then purified by flash chromatography on silica gel to afford product as a white solid (0.16, 39%). ^{1}H NMR (400 MHz, $CDCl_3$): consistent; MS (ES) *m/z* 506.1 (M+H).

Example 185

5'-(Benzylamino)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one

Step 1

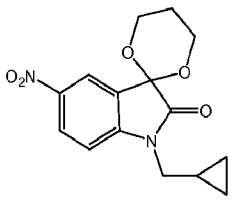
5'-nitrospiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



To a solution of 5'-nitroisatin (16.0 g, 83.27 mmol, 1 eq.) in benzene (300 mL) was added 1, 3 propanediol (20 mL, 276.7 mmol, 3.32 equivalents) and p-TsOH (3.112 g, 16.36 mmol, 0.2 equivalents). The reaction was heated to reflux temperature with a Dean-Stark trap for 3.5 hours. The reaction was cooled to room temperature, poured into H_2O and then extracted with EtOAc. The combined organic extracts were washed with brine, dried over $MgSO_4$, then filtered, concentrated *in vacuo*, and purified on silica gel eluting with a 25 to 50% EtOAc/hexane to give 20.0 (75%) of the title compound as a yellow solid.

Step 2

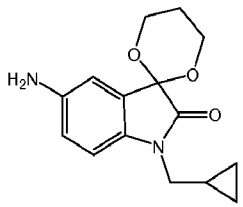
1'-(cyclopropylmethyl)-5'-nitrospiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



To a solution of 5'-nitrospiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one (3.263 g, 13.04 mmol, 1 eq.) in acetone (120 mL) was added K_2CO_3 (4.600 g, 33.28 mmol, 2.55 equivalents) and cyclopropylmethyl bromide (1.9 mL, 19.6 mmol, 1.5 equivalents). The reaction was heated at reflux 2 hours. The reaction was cooled to room temperature, diluted with H_2O and then extracted with EtOAc. The combined organic extracts were dried over $MgSO_4$, filtered, concentrated *in vacuo*, and then purified on RediSep™ silica gel eluting with a 0 to 100% EtOAc/hexane linear gradient to give 3.586 (80%) of the title compound as a light yellow solid.

Step 3

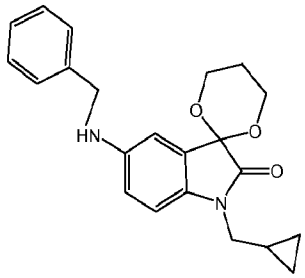
5'-amino-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



To a slurry of 10% Pd/C (0.420 g) in EtOAc was added a solution of 1'-(cyclopropylmethyl)-5'-nitrospiro[1,3-dioxane-2, 3'-indol]-2'(1'H)-one (3.586 g, 103.53 mmol, 1 equivalent) in EtOAc (80 mL) and the mixture was hydrogenated at 50 psi for 2 hours. It was filtered though a Celite and silica, concentrated *in vacuo*, and then purified on RediSep silica gel eluting with a 0 to 100% EtOAc/hexane linear gradient to give 2.700 (93%) of the title compound as a light brown solid.

Step 4

5'-(Benzylamino)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



To a of 5'-amino-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one (0.101 g, 0.37 mmol, 1 equivalent) in MeOH (3 mL) was added benzaldehyde (0.050 mL, 0.45 mmol, 1.2 equivalents), HOAc (0.020 mL, 0.36 mmol, 1 eq) and $NaCNBH_3$ (0.043 g, 0.68 mmol, 1.8 equivalents) The reaction was stirred for at room temperature for 1 hour, poured into saturated $NaHCO_3$ solution and water and then extracted with CH_2Cl_2. The combined organic extracts were concentrated and the crude product was purified on RediSep silica gel eluting with a 0 to 100% EtOAc/hexane linear gradient to give 0.108 g, (80%) of the title compound as a sticky, foamy oil. ^1H NMR (400 MHz, DMSO-d6): consistent; MS (ES^+) *m/z* 365.2 (M+H).

Examples 186-200 were prepared from 5'-amino-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one and the appropriate aldehyde according to the procedure for Example 185.

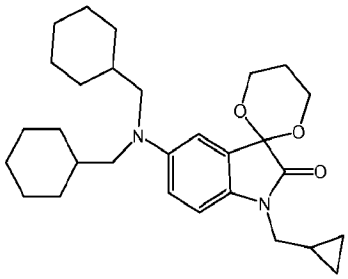
Table 7: Compounds Prepared According to the Procedure of Example 185

Example	Name	MS (ES^+) *m/z*
186	1'-(Cyclopropylmethyl)-5'-[(2-furylmethyl)amino]spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one	355.2 (M+H)
187	1'-(Cyclopropylmethyl)-5'-[(2-thienylmethyl)amino]spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one	371.2 (M+H)
188	5'-{[(5-Chloro-2-thienyl)methyl]amino}-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	405.1 (M+H)
189	5'-{[(2-Butyl-1-benzofuran-3-yl)methyl]amino}-1'-(cyclopropylmethyl)spiro[1,3- dioxane-2,3'-indol]-2'(1'H)-one	461.3 (M+H)
190	5'-[(4-Chlorobenzyl)amino]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one	399.2 (M+H)
191	1'-(Cyclopropylmethyl)-5'-[(4-methoxybenzyl)amino]spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one	395.2 (M+H)
192	1'-(Cyclopropylmethyl)-5'-[(4-methylbenzyl)amino]spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one	379.2 (M+H)
193	1'-(Cyclopropylmethyl)-5'-[(3,4-dichlorobenzyl)amino]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	433.2 (M+H)
194	5'-[(3-Chlorobenzyl)amino]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one	399.2 (M+H)
195	1'-(Cyclopropylmethyl)-5'-{[4-(trifluoromethyl)benzyl]amino}spiro[1,3-dioxane- 2,3'-indol]-2'(1'H)-one	433.2 (M+H)
196	5'-{[4-Chloro-3-(trifluoromethyl)benzyl]amino}-1'-(cyclopropylmethyl)spiro[1,3- dioxane-2,3'-indol]-2'(1'H)-one	467.2 (M+H)

197	1'-(Cyclopropylmethyl)-5'-[(1-naphthylmethyl)amino]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	415.2 (M+H)
198	1'-(Cyclopropylmethyl)-5'-[(2,3-dihydro-1,4-benzodioxin-6-ylmethyl)amino]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	423.2 (M+H)
199	1'-(Cyclopropylmethyl)-5'-[(4-fluorobenzyl)amino]spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one	383.2 (M+H)
200	5'-[(1-Benzothiophen-2-ylmethyl)amino]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	421.2 (M+H)

Example 201

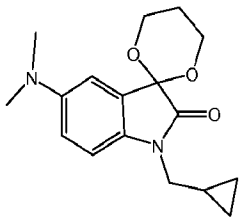
5'-[Bis(cyclohexylmethyl)amino]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one



The title compound (0.050g, 48%) was prepared from 5'-amino-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one using a procedure similar to that of Example 1, using 2 equivalents of cyclohexanecarbaldehyde in Step 4. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ES$^+$) *m/z* (M+H).

Example 202

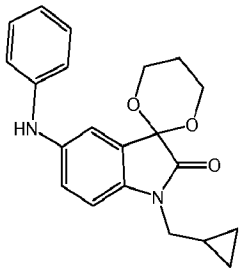
1'-(Cyclopropylmethyl)-5'-(dimethylamino)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



The title compound (0.288g, 97 %) was prepared from 5'-amino-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one using a procedure similar to that of Example 1, using 2 equivalents of formaldehyde in Step 4. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ES$^+$) *m/z* 303.2 (M+H).

Example 203

5'-Anilino-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



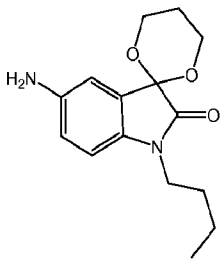
A solution consisting of 5'-amino-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one (0.091 g, 0.33 mmol), $PhB(OH)_2$ (0.120 g, 0.98 mmol, 3 equivalents), Et_3N (0.140 mL, 1.0 mmol, 3 equivalents), $Cu(OAc)_2$ (0.121 g, 0.66 mmol, 2.0 equivalents), and 4 Å molecular sieves (~0.250 g) in CH_2Cl_2 (4 mL) was stirred at room temperature for 24 hours. The reaction mixture was diluted with CH_2Cl_2 and treated with aqueous NaCl. The organic layer was separated, filtered, then concentrated and purified by RediSep silica gel eluting with a 0 to 100% EtOAc/hexane linear gradient to give 0.048 g (41%) of the title compound as a white solid. ^1H NMR (400 MHz, DMSO-d6): consistent; MS (ES^+) *m/z* 351.1 (M+H).

Example 204

1'-Butyl-5'-(methylamino)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one

Step 1

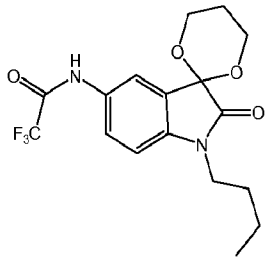
5'-Amino-1'-butyl spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



5'-Amino-1'-butyl spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one was prepared from 5-nitroisatin in a procedure similar to that of Example 1, Steps 1-3.

Step 2

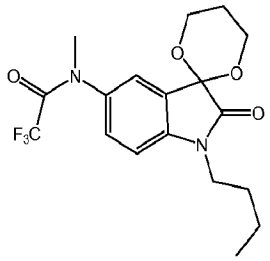
N-(1'-butyl-2'-oxo-1',2'-dihydrospiro[1,3-dioxane-2,3'-indol]-5'-yl)-2,2,2- trifluoroacetamide



To a solution of 5'-amino-1'-butyl spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one (0.164 g, 0.59 mmol, 1 equivalent) in CH_2Cl_2 (4 mL) was added Et_3N (0.160 mL, 1.95 mmol, 1.95 equivalents) and TFAA (0.110 mL, 0.78 mmol, 1.32 equivalents) and stirred at room temperature for 10 minutes. The reaction mixture was diluted with CH_2Cl_2 and treated with aqueous NaCl. The organic layer was separated, then dried over $MgSO_4$, concentrated and purified by RediSep silica gel eluting with a 0 to 100% EtOAc/hexane linear gradient to give 0.218 g, (99%) of n-(1'-butyl-2'-oxo-1',2'-dihydrospiro[1,3-dioxane-2,3'-indol]-5'-yl)-2,2,2- trifluoroacetamide (0.218 g, 99%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ES^-) *m/z* 371.1 (M-H).

Step 3

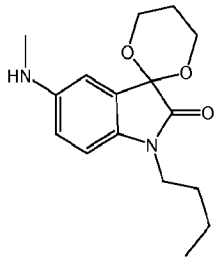
N-(1'-butyl-2'-oxo-1',2'-dihydrospiro[1,3-dioxane-2,3'-indol]-5'-yl)-2,2,2- trifluoro-N-methylacetamide



To a solution of n-(1'-butyl-2'-oxo-1',2'-dihydrospiro[1,3-dioxane-2,3'-indol]-5'-yl)-2,2,2-trifluoroacetamide) (0.190 g, 0.51 mmol, 1 equivalent) in acetone (5 mL) was added K_2CO_3 (0.160 g, 1.16 mmol, 2.27 equivalents) and MeI (0.090 mL, 1.45 mmol, 2.8 equivalents) and the reaction was heated at 50° C overnight. The reaction mixture was poured into water and then extracted with EtOAc. The organic layer was separated, dried over $MgSO_4$, concentrated and then purified by RediSep silica gel eluting with a 0 to 100% EtOAc/hexane linear gradient to give 0.187 g, (95%) of n-(1'-butyl-2'-oxo-1',2'-dihydrospiro[1,3-dioxane-2,3'-indol]-5'-yl)-2,2,2- trifluoro-N-methylacetamide (0.187 g, 95%) as a white solid. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ES^+) *m/z* 387.2 (M+H).

Step 4

1'-Butyl-5'-(methylamino)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



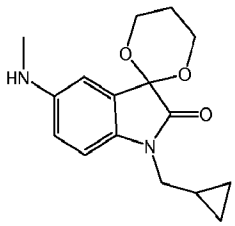
To a solution of of n-(1'-butyl-2'-oxo-1',2'-dihydrospiro[1,3-dioxane-2,3'-indol]-5'-yl)-2,2,2-trifluoro-N-methylacetamide (0.160 g, 0.4 mmol, 1 equivalent) in MeOH (8 mL) was added 1 NaOH (1.5 mL, 1.5 mmol, 3.5 equivalents) and heated at reflux temperature for 20 minutes. The reaction mixture poured into water and extracted with EtOAc. The organic layer was separated, dried over $MgSO_4$, concentrated and then purified by RediSep silica gel eluting with a 0 to 100% EtOAc/hexane linear gradient to give 0.117 g (100%) of the title compound as a sticky yellow oil. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ES^+) *m/z*

Example 205

1'-(Cyclopropylmethyl)-5'-[methyl(phenyl)amino]spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one

Step 1

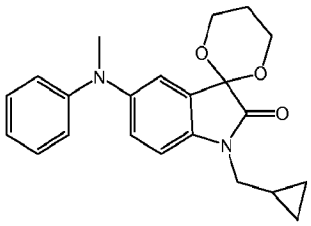
1'-(Cyclopropylmethyl)-5'-[methylamino]spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one



1'-(Cyclopropylmethyl)-5'-[methylamino]spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one was prepared from 5'-amino-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one using a procedure similar to that of Example 198.

Step 2

1'-(Cyclopropylmethyl)-5'-[methyl(phenyl)amino]spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one



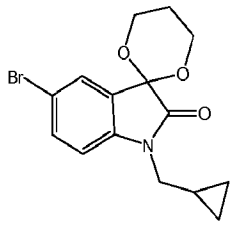
The title compound (0.097 g, 76%) was prepared from 1'-(cyclopropylmethyl)-5'-[methylamino]spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one using a procedure similar to that of Example 197. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ES^+) *m/z* 365.2 (M+H).

Example 206

1'-(Cyclopropylmethyl)-5'-piperidin-1-ylspiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one

Step 1

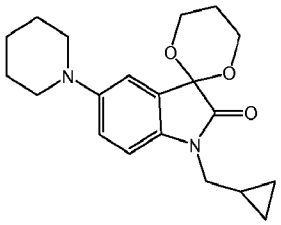
5'-Bromo-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



5'-Bromo-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one was prepared from 5-bromo-isatin using a procedure similar to that of Example 179, Steps 1 and 2.

Step 2

1'-(Cyclopropylmethyl)-5'-piperidin-1-ylspiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one

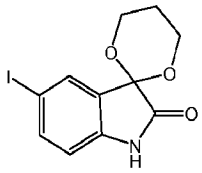


To a solution of 5'-bromo-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one (0.147 g, 0.43 mmol, 1 equivalent) in dry tetrahydrofuran (3 mL) was added piperidine (0.07 mL, 0.71 mmol, 1.6 equivalents), sodium t-butoxide (0.075 g, 0.78 mmol, 1.8 eq.) and 2-dicyclohexylphosphino-2'-(N,N-dimethylamino)biphenyl (CYMAP, 0.012 g, 0.03 mmol, 0.07 equivalent). Nitrogen was bubbled through the resulting solution for 5 minutes and then bis(dibenzylideneacetone)palladium (0) ($Pd_2(dba)_3$, 0.033 g, 0.04 mmol, 0.09 equivalent) was added. The resulting mixture was stirred at reflux temperature under nitrogen for 1 hour. It was then cooled to room temperature, diluted with diethyl ether and then filtered through a plug of celite. After concentration, the residue was purified by RediSep silica gel eluting with a 0 to 100% EtOAc/hexane linear gradient to give 0.067 g, (46%) of the title compound as a sticky yellow oil. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ES^+) *m/z* 343.2 (M+H).

Example 207

5'-(Phenylthio)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one

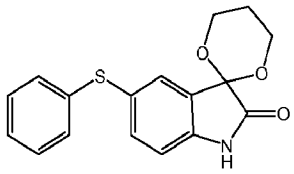
Step 1



5'-Iodospiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one was prepared from 5-iodo-isatin using a procedure similar to that of Example 185, Step 1.

Step 2

5'-(Phenylthio)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



To a solution of 5'-iodospiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one (0.334 g, 1.00 mmol, 1 eq.) in dry isopropanol (5 mL) was added thiophenol (0.110 mL, 1.07 mmol, 1.0 equivalent), ethylene glycol (0.110 ml, 1.97 mmol, 2 equivalents), potassium carbonate (0.278 g, 2.00 mmol, 2 equivalents) and copper(I) iodide (0.019 g, 0.1 mmol, 0.1 equivalent). The resulting mixture was stirred at 80° C overnight. LC/MS indicated a 2/1 mixture of product to starting material. Additional thiophenol (0.050 mL, 0.5 mmol, 0.5 equivalent) and copper (I) iodide (0.020 g, 0.1 mmol, 0.1 equivalent) was added and the reaction was heated at 80° C for 3 days. It was then cooled to room temperature, poured into water and extracted with EtOAc. After concentration, the residue was purified by RediSep silica gel eluting with a 0 to 100% EtOAc/hexane linear gradient to give 0.314 g, (100%) of the title compound as a white solid. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ES$^-$) *m/z* 312.1 (M-H).

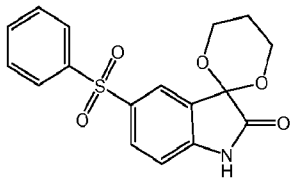
Example 208

5'-(Phenylsulfinyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one

To a solution of 5'-(phenylthio)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one (0.115 g, 0.37 mmol, 1 equivalent) in CH_2Cl_2 (5 mL) was added m-CPBA (0.0825 g, 0.37 mmol, 1 equivalent). The reaction was stirred at room temperature for 30 minutes and then partitioned between saturated $NaHCO_3$ and CH_2Cl_2. The organic layer was separated, concentrated and the residue was then purified by RediSep silica gel eluting with a 0 to 100% EtOAc/hexane linear gradient to give 0.119 g, (98%) of the title compound as a white solid. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ES$^-$) *m/z* 328.1 (M-H).

Example 209

5'-(Phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



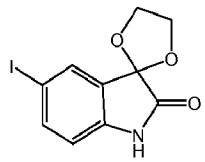
The title compound (0.047 g, 85%) was prepared from 5'-(phenylthio)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one using a procedure similar to that of Example 208, using 2 equivalents of m-CPBA. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ES$^-$) *m/z* 344.0 (M-H).

Example 210

5'-(Phenylthio)spiro[1,3-dioxolane-2,3'-indol]-2'(1'H)-one

Step 1

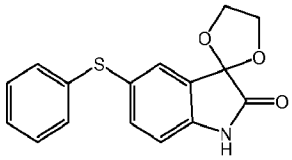
5'-Iodospiro[1,3-dioxolane-2,3'-indol]-2'(1'H)-one



5'-Iodospiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one was prepared from 5-iodo-isatin and ethylene glycol using a procedure similar to that of Example 185, Step 1.

Step 2

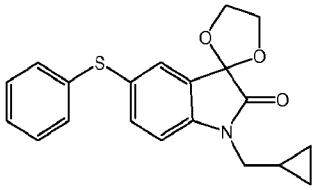
5'-(Phenylthio)spiro[1,3-dioxolane-2,3'-indol]-2'(1'H)-one



The title compound (0.327 g, 86%)was prepared from 5'-iodospiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one using a procedure similar to that of Example 207, Step 2. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ES$^-$) *m/z* 298.1 (M-H).

Example 211

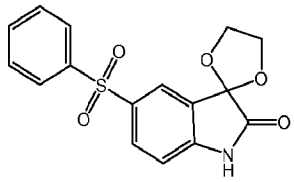
1'-(Cyclopropylmethyl)-5'-(phenylthio)spiro[1,3-dioxolane-2,3'-indol]-2'(1'H)-one



The title compound (0.067 g, 56%)was prepared from 5'-(phenylthio)spiro[1,3-dioxolane-2,3'-indol]-2'(1'H)-one, using a procedure similar to that of Example 185, Step 2. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ES^+) *m/z* 354.1 (M+H).

Example 212

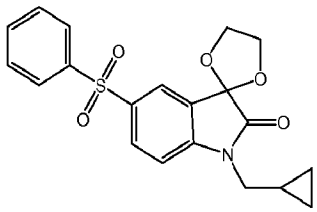
5'-(Phenylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'H)-one



The title compound (0.065 g, 58%) was prepared from 5'-(phenylthio)spiro[1,3-dioxolane-2,3'-indol]-2'(1'H)-one using a procedure similar to that of Example 209. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ES^-) *m/z* 330.0 (M-H).

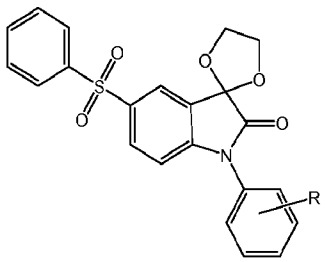
Example 213

1'-(Cyclopropylmethyl)-5'-(phenylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]- 2'(1'H)-one



The title compound (0.058 g, 100%) was prepared from 5'-(phenylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'H)-one using a procedure similar to that of Example 185, Step 2. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ES^+) *m/z* 386.0 (M+H).

Examples 214-216



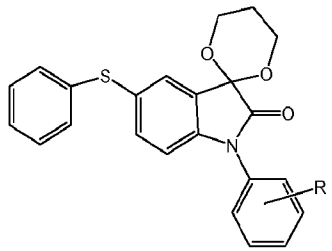
Examples 214-216 were prepared from 5'-(phenylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'H)-one and the appropriate boronic acid according to the procedure for Example 203.

Table 8: Compounds Prepared According to the Procedure of Example 203

Example	Name	MS (ES^+) *m/z*
214	1'-Phenyl-5'-(phenylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'H)-one	408.0 (M+H)
215	5'-(Phenylsulfonyl)-1'-[3-(trifluoromethyl)phenyl]spiro[1,3-dioxolane-2,3'- indol]-2'(1'H)-one	476* (M+H)
216	1'-(3,4-Difluorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]- 2'(1'H)-one	444.0 (M+H)

* MS ($APPI^+$)

Examples 217-219

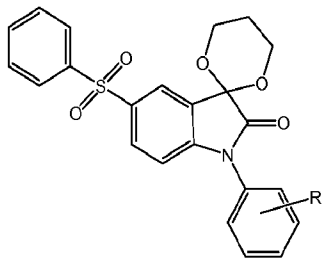


Examples 217-219 were prepared from 5'-(phenylthio)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one and the appropriate boronic acid according to the procedure for Example 203.

Table 9: Compounds Prepared According to the Procedure of Example 203

Example	Name	MS ($APPI^+$) *m/z*
217	1'-Phenyl-5'-(phenylthio)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	389 (M+)
218	5'-(Phenylthio)-1'-[3-(trifluoromethyl)phenyl]spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one	457 (M+)
219	1'-(3,4-Difluorophenyl)-5'-(phenylthio)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	425 (M+)

Example 220-249



Examples 220-249 were prepared from 5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-on and the appropriate boronic acid according to the procedure for Example 203.

Table 10: Compounds Prepared According to the Procedure of Example 203

Example	Name	MS (ES^+) *m/z*
220	1'-Phenyl-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	422.0 (M+H)
221	5'-(Phenylsulfonyl)-1'-[3-(trifluoromethyl)phenyl]spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one	507.0 [M+NH_4]
222	1'-(3,4-difluorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	458* (M+H)
223	1'-(2,5-difluorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	458.0 [M+H]
224	1'-(3-fluorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	440.0 (M+H)
225	1'-(3,5-dichlorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	489.9 [M+H]
226	1'-(3-chloro-4-fluorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	474.0 (M+H)
227	1'-(4-chlorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	456.0 (M+H)
228	5'-(phenylsulfonyl)-1'-[2-(trifluoromethyl)phenyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	490.0 [M+H]
229	1'-(2-methoxyphenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	452.0 (M+H)
230	1'-(4-fluorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	440.0 (M+H)
231	1'-(2,3-difluorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	458.0 [M+H]

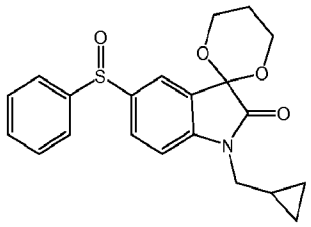
232	1'-(3,5-difluorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	458.0 (M+H)
233	1'-(2,5-dichlorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	489.9 (M+H)
234	1'-(3-methoxyphenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	452.1 [M+H]
235	5'-(phenylsulfonyl)-1'-[4-(trifluoromethoxy)phenyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	506.1 (M+H)
236	1'-(3-chlorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	456.0 (M+H)
237	1'-(3,4-dichlorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	489.9 [M+H]
238	2-[2'-oxo-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-1'(2'H)-yl]benzonitrile	447.0 (M+H)
239	1'-(2-chlorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	456.0 (M+H)
240	5'-(phenylsulfonyl)-1'-[3-(trifluoromethoxy)phenyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	506.0 [M+H]
241	1'-(4-methylphenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	436.1 (M+H)
242	1'-(2-methylphenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	436.1 (M+H)
243	1'-(4-methoxyphenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	452.1 [M+H]
244	5'-(phenylsulfonyl)-1'-[4-(trifluoromethyl)phenyl]spiro[1,3-dioxane-2,3'-	490.0 (M+H)

	indol]-2'(1'H)-one	
245	1'-(2-fluorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	440.1 (M+H)
246	5'-(phenylsulfonyl)-1'-[2-(trifluoromethoxy)phenyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	506.1 [M+H]
247	3-[2'-oxo-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-1'(2'H)-yl]benzonitrile	447.0 (M+H)
248	4-[2'-oxo-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-1'(2'H)-yl]benzonitrile	447.1 (M+H)
249	1'-(3-methylphenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	436.1 (M+H)

* MS ($APPI^+$)

Example 250

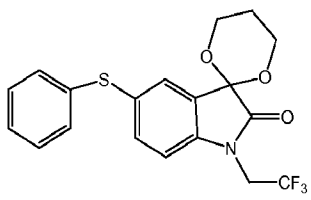
1'-(Cyclopropylmethyl)-5'-(phenylsulfinyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



The title compound (0.091 g, 91%) was prepared from 5'-(phenylsulfinyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one using a procedure similar to that of Example 185, Step 2. ^1H NMR (400 MHz, DMSO-d6): consistent; MS (ES^+) *m/z* 384.0 (M+H).

Example 251

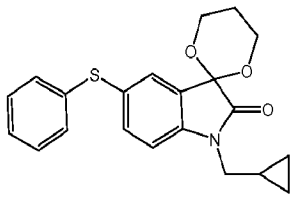
5'-(Phenylthio)-1'-(2,2,2-trifluoroethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



The title compound (0.070 g, 80%) was prepared from 5'-(phenylthio)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one and 2,2,2-trifluoroethyl trifluoromethanesulfonate using a procedure similar to that of Example 185, Step 2. ^1H NMR (400 MHz, DMSO-d6): consistent; MS ($APPI^+$) *m/z* 396 (M+H).

Example 252

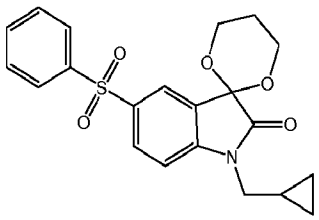
1'-(Cyclopropylmethyl)-5'-(phenylthio)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



To a solution of 1'-(cyclopropylmethyl)-5'-iodospiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one (0.1 g, 0.26 mmol, 1 equivalent) in dry acetonitrile (3 mL) was added $CoCl_2$(dppe) (0.01g, 0.18 mmol, 0.7 equivalent), Zn (0.025 g, 0.39 mmol 1.5 equivalents), pyridine (0.021 mL, 0.26 mmol 1 equivalent) and thiophenol (0.027 mL, 0.26 mmol 1 equivalent) . The reaction was heated at 110° C overnight. The reaction was cooled to room temperature, diluted with CH_2Cl_2, then filtered through celite. The filtrate was concentrated and the residue was purified on silica gel column eluting with a 10 to 30% EtOAc/hexane to give 0.071g (74%) of the title compound as clear oil. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (EI^+) *m/z* 367 (M+H).

Example 253

1'-(Cyclopropylmethyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



To a solution of 1'-(cyclopropylmethyl)-5'-(phenylthio)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one (0.051 g, 0.14 mmol, 1 equivalent) in CH_2Cl_2 (3 mL) was added potassium permanganate and Montmorillonite K10 mixture (0.11g, 0.69 mmol, 5 equivalents). The reaction was stirred at rt for 5.5 hours. The reaction was diluted with CH_2Cl_2 and then filtered through celite. The filtrate was concentrated and the residue was purified on silica gel column eluting with a 10 to 70% EtOAc/hexane to give 0.039g (71%) of the title compound as a viscous, colorless oil. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ES^+) *m/z* 400.1 (M+H).

Examples 254-260 were prepared from 1'-(cyclopropylmethyl)-5'-iodospiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one and the appropriate substituted thiopheols according to the procedure for Example 252, and oxidized to the sulfones according to the procedure for Example 253.

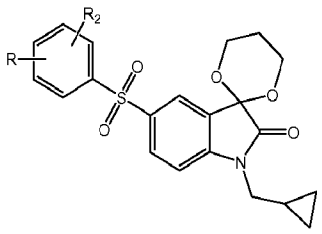
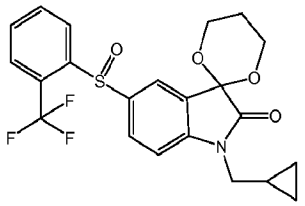


Table 11: Compounds Prepared According to the Procedure of Examples 252 and 253.

Example	Name	MS (ES^+) *m/z*
254	1'-(Cyclopropylmethyl)-5'-[(2-fluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	418.0 (M+H)
255	1'-(Cyclopropylmethyl)-5'-[(2-methoxyphenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	430.1 (M+H)
256	5'-[(2-Chlorophenyl)sulfonyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	443.0 (M+H)
257	5'-[(3-Chlorophenyl)sulfonyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	434.0 (M+H)
258	1'-(Cyclopropylmethyl)-5'-[(2-methylphenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	414.1 (M+H)
259	1'-(Cyclopropylmethyl)-5'-[(3-fluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	418.0 (M+H)
260	1'-(Cyclopropylmethyl)-5'-[(4-fluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	418.0 (M+H)

Example 261

1'-(Cyclopropylmethyl)-5'-{[2-(trifluoromethyl)phenyl]sulfinyl}spiro[1,3- dioxane-2,3'-indol]-2'(1'H)-one



The title compound (0.012g, 10%) was prepared from 1'-(cyclopropylmethyl)-5'-iodospiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one using 1 equivalent of 2-(trifluoromethyl)-benzenethiol according to the procedure for example 252, and oxidized to the sulfoxide according to the procedure for example 253. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ES^+) *m/z* 452.0 (M+H).

Examples 262-271 were prepared from 1'-(cyclopropylmethyl)-5'-iodospiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one and the appropriate substituted thiophenols according to the procedure for Step 2 of Example 207, and oxidized to the sulfones according to the procedure for Example 208.

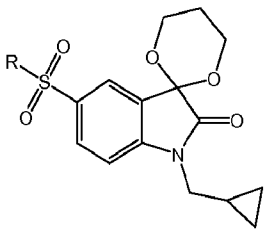
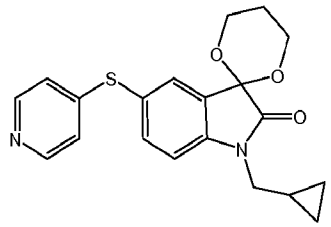


Table 12: Compounds Prepared According to the Procedure of Examples 207 and 208.

Example	Name	MS (ESI^+) *m/z*
262	1'-(Cyclopropylmethyl)-5'-[(2,5-dichlorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	468.0 (M+H)
263	5'-[(4-Chlorophenyl)sulfonyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	434.0 (M+H)
264	1'-(Cyclopropylmethyl)-5'-[(3-methoxyphenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	440.1 (M+H)
265	1'-(Cyclopropylmethyl)-5'-[(3,4-dichlorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	468.1 (M+H)
266	1'-(Cyclopropylmethyl)-5'-[(3-methylphenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	414.1 (M+H)
267	1'-(Cyclopropylmethyl)-5'-[(4-methoxyphenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	430.1 (M+H)
268	5'-(1,3-Benzothiazol-2-ylsulfonyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	457.1 (M+H)
269	1'-(Cyclopropylmethyl)-5'-[(3,4-difluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	436.1 (M+H)
270	1'-(Cyclopropylmethyl)-5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one	401.1 (M+H)
271	1'-(Cyclopropylmethyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one	401.1 (M+H)

Example 272

1'-(Cyclopropylmethyl)-5'-(pyridin-4-ylthio)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



The title compound (0.103g, 74%) light yellow solid, was prepared from 1'-(cyclopropylmethyl)-5'-iodospiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one using 1.1 eq. of 4-mercaptopyridine according to the procedure for Step 2 of Example 207. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ES^+) *m/z* 369.1 (M+H).

Examples 272-275 were prepared from 1'-(cyclopropylmethyl)-5'-iodospiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one and the appropriate substituted thiophenols according to the procedure for Step 2 of Example 207.

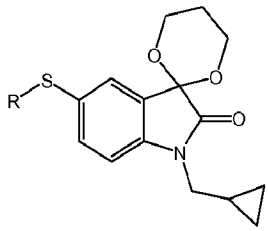
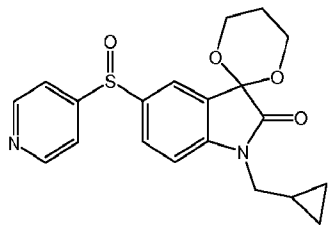


Table 13: Compounds Prepared According to the Procedure for Step 2 of Example 207.

Example	Name	MS (ESI^+) *m/z*
272	1'-(Cyclopropylmethyl)-5'-[(3,4-dichlorophenyl)thio]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	436.0 (M+H)
273	1'-(Cyclopropylmethyl)-5'-[(3,4-difluorophenyl)thio]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	404.1 (M+H)
274	1'-(Cyclopropylmethyl)-5'-{[3-(trifluoromethyl)phenyl]sulfanyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	436.1 (M+H)
275	1'-(Cyclopropylmethyl)-5'-(pyridin-2-ylsulfanyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one	369.1 (M+H)

Example 276

1'-(Cyclopropylmethyl)-5'-(pyridin-4-ylsulfinyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one



The title compound (0.097g, 51 %) light yellow solid, was prepared from Example 272 using a procedure similar to that of Example 208. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 385.1 (M+H).

Examples 277 and 278 were prepared from Example 273 and 275 respectively according to the procedure for Example 208.

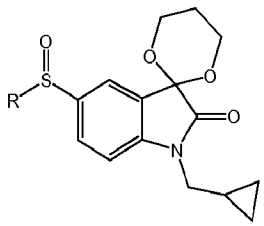


Table 14: Compounds Prepared According to the Procedure for Example 208.

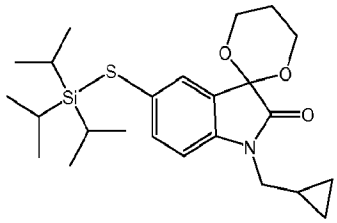
Example	Name	MS (ESI$^+$) *m/z*
277	1'-(Cyclopropylmethyl)-5'-(pyridin-2-ylsulfinyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one	385.1 (M+H)
278	1'-(Cyclopropylmethyl)-5'-[(3,4-difluorophenyl)sulfinyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	420.1 (M+H)

Example 279

1'-(Cyclopropylmethyl)-5'-(pyridin-3-ylsulfanyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one

Step 1

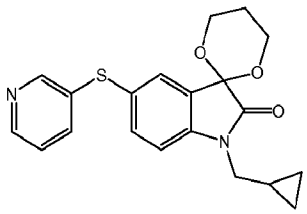
1'-(cyclopropylmethyl)-5'-[(triisopropylsilyl)sulfanyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



To a suspension of KH (0.06 g, 1.43 mmol, 1.1 equivalents) in THF (3 mL) at 5° C was added triisopropylsilanelthiol (0.27g, 1.43 mmol, 1.1 equivalents) over 15 minutes. The reaction was stirred at 5° C for 1 hour, then warmed to rt for 1 hour. The clear solution was added to a solution of 1'-(cyclopropylmethyl)-5'-iodospiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one (0.5 g, 1.3 mmol, 1 equivalent) and $(PPh_3)_4Pd$ (0.1 g, 0.86 mmol, 0.07 equivalent) in THF (4 ml) and then heated at 70 °C for 1 hour. After cooling, the reaction mixture was diluted with ether, washed with brine and then dried with $MgSO_4$. The filtrate was concentrated and the residue was purified on 40g Isco silica gel column eluting with 0 to 10% EtOAc/hexane to give 0.441g (76%) of the title compound as a viscous light yellow oil. (*J.Med Chem.* 2001, *44*, 4393). ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI^+) *m/z* 448.2 (M+H).

Step 2

1'-(Cyclopropylmethyl)-5'-(pyridin-3-ylsulfanyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one



The title compound (0.052g, 56%) clear oil, was prepared from 1'-(cyclopropylmethyl)-5'-[(triisopropylsilyl)sulfanyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one using a procedure similar to that of Step 2 of Example 207. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI^+) *m/z* 369.1 (M+H).

Examples 280-294 were prepared from 1'-(cyclopropylmethyl)-5'-[(triisopropylsilyl)sulfanyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one and the appropriate substituted aryl or heteroaryl iodides according to the procedure for Step 2 of Example 207.

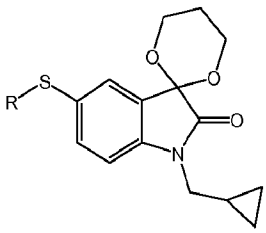


Table 15: Compounds Prepared According to the Procedure for Step 2 of Example 207.

Example	Name	MS (ESI+) *m/z*
280	1'-(Cyclopropylmethyl)-5'-[(4-methylphenyl)sulfanyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	382.1 (M+H)
281	1'-(Cyclopropylmethyl)-5'-{[4-(trifluoromethyl)phenyl]sulfanyl}spiro[1,3- dioxane-2,3'-indol]-2'(1'H)-one	436.1 (M+H)
282	5'-[(3-Chloro-4-fluorophenyl)sulfanyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane- 2,3'-indol]-2'(1'H)-one	420.0 (M+H)
283	5'-[(6-Chloropyridin-3-yl)sulfanyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane- 2,3'-indol]-2'(1'H)-one	403.0 (M+H)
284	1'-(Cyclopropylmethyl)-5'-(naphthalen-1-ylsulfanyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	418.1 (M+H)
285	1'-(Cyclopropylmethyl)-5'-(thiophen-2-ylsulfanyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one	374.0 (M+H)
286	1'-(Cyclopropylmethyl)-5'-[(5-methyl-2-thienyl)thio]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	388.0 (M+H)
287	5'-[(5-Acetyl-2-thienyl)thio]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	416.1 (M+H)
288	5'-[(2-Chloropyridin-4-yl)thio]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	403.0 (M+H)
289	1'-(Cyclopropylmethyl)-5'-[(3,5-dichlorophenyl)thio]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	435.0 (M+.) EI
290	1'-(Cyclopropylmethyl)-5'-[(3,5-dichloropyridin-4-yl)thio]spiro[1,3-dioxane- 2,3'-indol]-2'(1'H)-one	437.0 (M+H)
291	1'-(Cyclopropylmethyl)-5'-[(2,4-dichlorophenyl)thio]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	435.0 (M+.) EI
292	1'-(Cyclopropylmethyl)-5'-[(2,5-	434.9

	dichlorophenyl)thio]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	(M+.) EI
293	5'-[(4-Chloro-2-fluorophenyl)thio]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	420.0 (M+H)
294	1'-(Cyclopropylmethyl)-5'-[(2,4-difluorophenyl)thio]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	404.0 (M+H)

Examples 295-310 were prepared by oxidizing the corresponding sulfides (prepared in Examples 280-294) according to the procedure for Example 208.

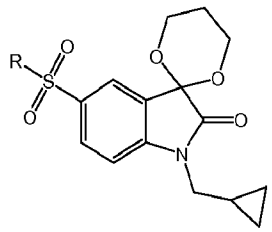


Table 16: Compounds Prepared According to the Procedure for Example 208.

Example	Name	MS (ESI^+) *m/z*
295	1'-(Cyclopropylmethyl)-5'-(pyridin-3-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one	401.1 (M+H)
296	1'-(Cyclopropylmethyl)-5'-{[3-(trifluoromethyl)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	468.1 (M+H)
297	1'-(Cyclopropylmethyl)-5'-[(4-methylphenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	414.1 (M+H)
298	1'-(Cyclopropylmethyl)-5'-{[4-(trifluoromethyl)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	468.1 (M+H)
299	5'-[(3-Chloro-4-fluorophenyl)sulfonyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	452.0 (M+H)
300	5'-[(6-Chloropyridin-3-yl)sulfonyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	435.0 (M+H)
301	1'-(Cyclopropylmethyl)-5'-(naphthalen-1-ylsulfonyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	450.1 (M+H)
302	1'-(Cyclopropylmethyl)-5'-(thiophen-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one	406.0 (M+H)
303	1'-(Cyclopropylmethyl)-5'-[(5-methyl-2-thienyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	420.0 (M+H)
304	5'-[(5-Acetyl-2-thienyl)sulfonyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	448.0 (M+H)
305	5'-[(2-Chloropyridin-4-yl)sulfonyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	435.0 (M+H)

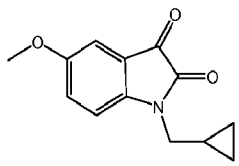
306	1'-(Cyclopropylmethyl)-5'-[(3,5-dichlorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	468.0 (M+H)
307	1'-(Cyclopropylmethyl)-5'-[(3,5-dichloropyridin-4-yl)sulfonyl]spiro[1,3-dioxane- 2,3'-indol]-2'(1'H)-one	468.9 (M+H)
308	1'-(Cyclopropylmethyl)-5'-[(2,4-dichlorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	490.0 (M+Na)
309	5'-[(4-Chloro-2-fluorophenyl)sulfonyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	451.9 (M+H)
310	1'-(Cyclopropylmethyl)-5'-[(2,4-difluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one	436.1 (M+H)

Example 311

1'-(Cyclopropylmethyl)-5'-(4-methoxyphenoxy)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one

Step 1

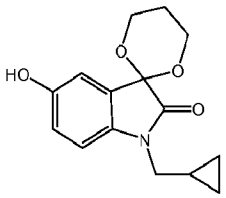
N-cyclopropylmethyl-5-methoxyisatin



5-Methoxyisatin (3.6 g, 15.6 mmol, 1 equivalent) was dissolved in DMF (50 mL) and treated with cesium carbonate (8.0 g, 24.6mmol, 1.6 equivalents) and cyclopropylmethyl bromide (2.8 g, 20.7 mmol, 1.33 equivalents). The mixture was stirred at ambient temperature for 3 days. The reaction mixture was diluted with ethyl acetate (50 mL), extracted and washed with brine (100 mL x 3), then dried over sodium sulfate and concentrated under reduced pressure. Chromatography with ethyl acetate/hexanes (0-70% gradient elution) afforded n-cyclopropylmethyl-5-methoxyisatin. The product was used in the following reaction.

Step 2

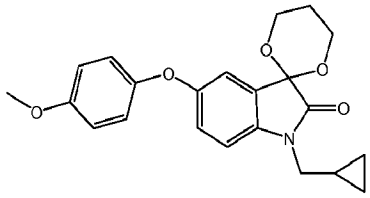
1'-(cyclopropylmethyl)-5'-hydroxyspiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



N-cyclopropylmethyl-5-methoxyisatin was dissolved in dichloromethane (60 mL), treated with neat boron tribromide (3.0 mL, 31.7 mmol) and stirred at ambient temperature for 1 hour. The reaction mixture was diluted with dichloromethane (100 mL) and extracted from 1.0 N HCl. The organic layer was dried over sodium sulfate and then concentrated to dryness. The residue was dissolved in toluene (200 mL), treated with 1,3-propanediol (6.0 mL, 83.0 mmol) and toluenesulfonic acid (1.0 g, 5.25 mmol). The mixture was stirred at reflux temperature under a Dean-Stark apparatus for 20 hours. The reaction mixture was then concentrated under reduced pressure and purified by chromatography with ethyl acetate/hexanes (0-70% gradient elution) to afford 1'-(cyclopropylmethyl)-5'-hydroxyspiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one (1.0 g) as a dark solid.

Step 3

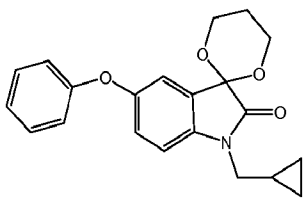
1'-(Cyclopropylmethyl)-5'-hydroxyspiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



1'-(Cyclopropylmethyl)-5'-hydroxyspiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one (0.1 g, 0.36 mmol, 1 equivalent) and 4-anisoliodonium tetrafluoroborate (0.230 g, 0.71 mmol, 1.97 equivalents) were dissolved in dichloromethane (5.0 mL), treated with copper powder (0.110 g, 1.17 mmol, 3.25 equivalents) and triethylamine (0.1 mL, 0.72 mmol, 2 equivalents). The mixture was stirred at ambient temperature in dark for 24 hours. The reaction mixture was loaded directly to a flash chromatography column and purified with ethyl acetate/hexanes (0-50% gradient elution) to provide 1'-(cyclopropylmethyl)-5'-(4-methoxyphenoxy) spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one (0.025 g, 18%) as a dark oil. MS (ES), m/z: 382.2.

Example 312

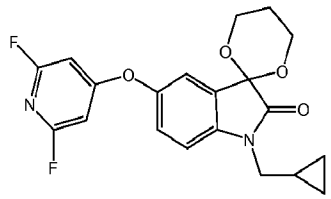
1'-(Cyclopropylmethyl)-5'-(4-methoxyphenoxy)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



1'-(cyclopropylmethyl)-5'-hydroxyspiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one (0.200 g, 0.73 mmol, 1 equivalent) and diphenyliodonium tetrafluoroborate (0.500 g, 1.36 mmol, 1.86 equivalent) were dissolved in dichloromethane (5.0 mL), treated with copper powder (0.200 g, 2.13 mmol, 2.91 equivalents) and triethylamine (0.1 mL, 0.72 mmol, 1 equivalents). The mixture was stirred at ambient temperature in dark for 20 hours. The reaction mixture was loaded directly to a flash chromatography column and then purified with ethyl acetate/hexanes (0-50% gradient elution) to provide 1'-(cyclopropylmethyl)-5'-(phenoxy)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one (107.0 mg, 42 %, dark oil). MS (ES), m/z: 352.1.

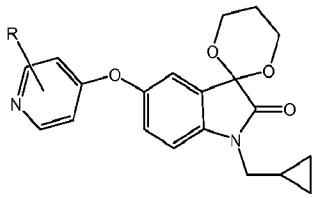
Example 313

1'-(Cyclopropylmethyl)-5'-[(2,6-difluoropyridin-4-yl)oxy]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



1'-(Cyclopropylmethyl)-5'-hydroxyspiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one (0.040 g, 0.14 mmol, 1 equivalent) and 2,4,6-trifluoropyridine (0.038 g, 0.028 mmol, 2 equivalents) were dissolved in DMF (2.0 mL), treated with potassium carbonate (0.100 g, 0.72 mmol, 5.1 equivalents) and stirred at ambient temperature for 5 hours. The reaction mixture was extracted with ethyl acetate (100 mL) from brine (100 mL) and followed by washing with brine (50 mL x 2). The organic layers were combined and then dried with sodium sulfate. Flash chromatography with ethyl acetate/hexanes (0-50% gradient elution) provided 1'-(cyclopropylmethyl)-5'-[(2,6-difluoropyridin-4-yl)oxy]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one (0.037 g, 69%) as a dark solid. MS (ES), m/z: 389.1.

Example 314-318



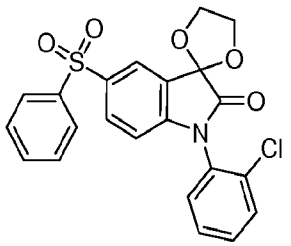
Examples 314-318 were prepared from 1'-(cyclopropylmethyl)-5'-hydroxyspiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one and the appropriately substituted 4-fluoropyridines according to the procedure for Example 313.

Table 17: Compounds Prepared According to the Procedure of Example 313

Example	Name	MS (ES^+) *m/z*
314	1'-(Cyclopropylmethyl)-5'-[(2,3,5,6-tetrafluoropyridin-4-yl)oxy]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	425* (M+H)
315	5'-[(3-Chloro-2,5,6-trifluoropyridin-4-yl)oxy]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	441* (M+H)
316	1'-(Cyclopropylmethyl)-5'-[(3,5-difluoro-2,6-dimethoxypyridin-4-yl)oxy]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	449.1 (M+H)
317	5'-[(3-Chloro-5-fluoro-2,6-dimethoxypyridin-4-yl)oxy]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	465.2 (M+H)
318	1'-(Cyclopropylmethyl)-5'-[(2,3,5-trifluoro-6-methoxypyridin-4-yl)oxy]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	437.1 (M+H)

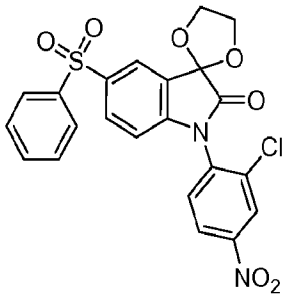
Example 319

1'-(2-Chlorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one



Step 1

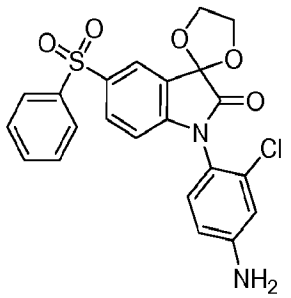
1'-(2-Chloro-4-nitrophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one



To a solution of 5'-(phenylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one (0.106 g, 0.32 mmol) in acetone (10 ml) was added cesium carbonate (0.266 g, 0.82 mmol) and 2-chloro-1-fluoro-4-nitrobenzene (0.108 g, 0.614 mmol). The reaction was heated at 65° C for 3 hours (until starting material was consumed, as determined by TLC). The reaction was cooled, then poured into water and extracted with EtOAc. The combined organic extracts were dried over $MgSO_4$, filtered, concentrated *in vacuo*, and purified on RediSep™ silica gel eluting with a 0 to 100% EtOAc/hexane linear gradient to give 0.069g (44%) of the title compound as a light yellow solid. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 487.0 (M+H).

Step 2

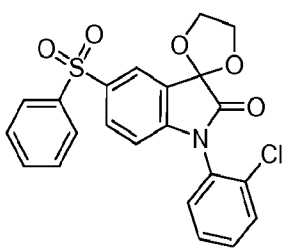
1'-(4-Amino-2-chlorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one



To a solution of 1'-(2-chloro-4-nitrophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one (0.063 g, 0.13 mmol) in EtOAc (2 ml) and EtOH (3 ml) was added tin chloride -dihydrate (0.106 g, 0.47 mmol) and the reaction was heated at 70° C over night. After cooling, 2 mL saturated $NaHCO_3$ solution and celite was added and the reaction was stirred for 5 minutes. The solids were then filtered and washed with EtOAc. The organics were washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude material was purified on RediSep silica gel eluting with a 0 to 100% EtOAc/hexane linear gradient to give 0.050g (85%) of the title compound as an off-white solid. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 457.0 (M+H).

Step 3

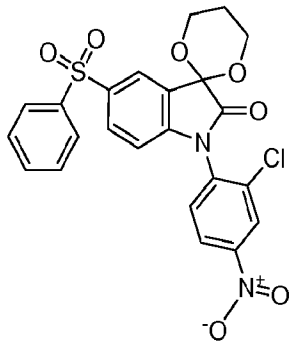
1'-(2-Chlorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one



To a slurry of 1'-(4-amino-2-chlorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one (0.043 g, 0.09 mmol) in water (2 ml) and conc. HCl (1 ml) was added ethanol (2 ml) and TFA (2 ml). Sodium nitrite (0.010 g, 0.15 mmol) in water (0.5 ml) was added. The reaction was heated briefly (5 min) to 50° C and then stirred at room temperature for 90 minutes. Water was then added and the reaction was extracted with EtOAc. The organics were concentrated to a small volume and neutralized with saturated $NaHCO_3$ solution and solid $NaHCO_3$. This solution was extracted with EtOAc, dried over $MgSO_4$ and concentrated. The crude material was purified on RediSep silica gel eluting with a 0 to 100% EtOAc/hexane linear gradient to give 0.020g (50%) of the title compound as a light yellow solid. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI^+) *m/z* 442.0 (M+H).

Example 320

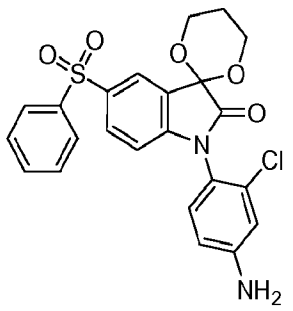
1'-(2-Chloro-4-nitrophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



The title compound (0.422 g, 73%) was prepared from 5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one using a procedure similar to that of step 1 of Example 319. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI^+) *m/z* 523.0 (M+Na).

Example 321

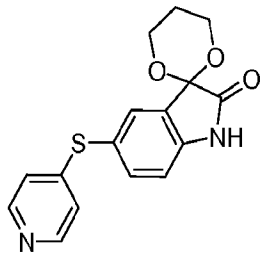
1'-(4-Amino-2-chlorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



The title compound (0.355 g, 91%) was prepared from 1'-(2-chloro-4-nitrophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one using a procedure similar to that of step 2 of example 319. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 471.0 (M+H).

Example 322

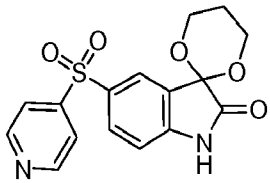
5'-(Pyridin-4-ylthio)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



The title compound (0.940 g, 96%) was prepared from 5'-iodospiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one and 4-mercaptopyridine using a procedure similar to that of Example 201, step 2. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 315.0 (M+H).

Example 323

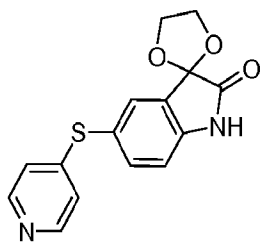
5'-(Pyridin-4-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



The title compound (0.040 g, 18%) was prepared from 5'-(pyridin-4-ylthio)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one using a procedure similar to that of Example 203. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 347.0 (M+H).

Example 324

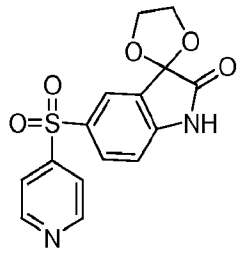
5'-(Pyridin-4-ylthio)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one



The title compound (2.154 g, 76%) was prepared from 5'-iodospiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one and 4-mercaptopyridine using a procedure similar to that of Example 201, step 2. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 301.0 (M+H).

Example 325

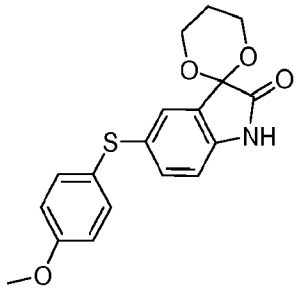
5'-(Pyridin-4-ylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one



The title compound (0.069 g, 61%) was prepared from 5'-(pyridin-4-ylthio)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one using a procedure similar to that of Example 203. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 333.0 (M+H).

Example 326

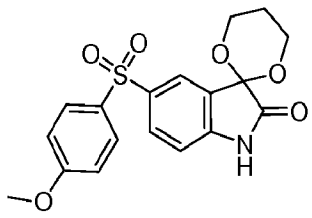
5'-[(4-Methoxyphenyl)thio]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



The title compound (4.085 g, 98%) was prepared from 5'-iodospiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one and 4-methoxybenzenethiol using a procedure similar to that of Example 201, step 2. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 344.1 (M+H).

Example 327

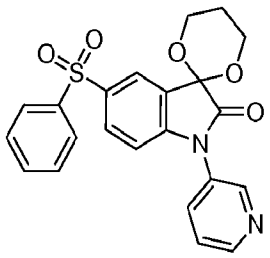
5'-[(4-Methoxyphenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



The title compound (2.612 g, 96%) was prepared from 5'-[(4-methoxyphenyl)thio]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one using a procedure similar to that of Example 203. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 376.0 (M+H).

Example 328

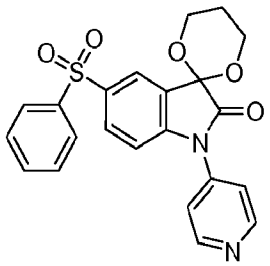
5'-(phenylsulfonyl)-1'-pyridin-3-ylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



The title compound (0.035 g, 59%) was prepared from 5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one and 3-pyridine boronic acid using a procedure similar to that of Example 197. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 423.0 (M+H).

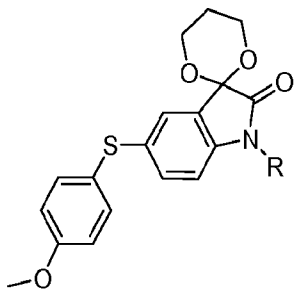
Example 329

5'-(Phenylsulfonyl)-1'-pyridin-4-ylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



The title compound (0.017 g, 29%) was prepared from 5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one and 4-pyridine boronic acid using a procedure similar to that of Example 197. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 423.0 (M+H).

Examples 330-335

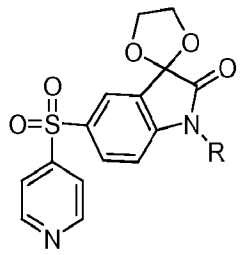


Examples 330-335 were prepared from 5'-[(4-methoxyphenyl)thio]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one and the appropriate alkylating agent using a procedure similar to that of Example 179, step 2 and summarized in Table 12.

Table 18: Compounds Prepared According to the Procedure of Example 179, step 2.

Example	Name	Mass (g)	MS (ESI^+) *m/z*
330	1'-(Cyclopropylmethyl)-5'-[(4-methoxyphenyl)thio]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.057	398.1 (M+H)
331	1'-Butyl-5'-[(4-methoxyphenyl)thio]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.056	400.2 (M+H)
332	5'-[(4-Methoxyphenyl)thio]-1'-pent-4-yn-1-ylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.061	410.0 (M+H)
333	5'-[(4-Methoxyphenyl)thio]-1'-propylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.060	386.1 (M+H)
334	5'-[(4-Methoxyphenyl)thio]-1'-(2,2,2-trifluoroethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.064	426.1 (M+H)
335	5'-[(4-Methoxyphenyl)thio]-1'-methylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.054	358.1 (M+H)

Examples 336-341

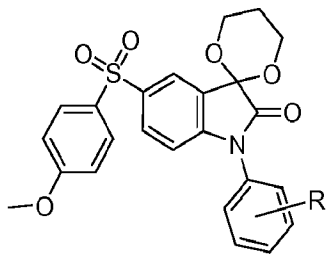


Examples 336-341 were prepared from 5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one and the appropriate alkylating agent using a procedure similar to that of Example 179, step 2 and summarized in Table 13.

Table 19: Compounds Prepared According to the Procedure of Example 179, step 2.

Example	Name	Mass (g)	MS (ESI^+) *m/z*
336	1'-(Cyclopropylmethyl)-5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one	0.041	387.1 (M+H)
337	1'-Butyl-5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one	0.046	389.1 (M+H)
338	1'-Pent-4-yn-1-yl-5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one	0.035	399.1 (M+H)
339	1'-Propyl-5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one	0.057	375.1 (M+H)
340	5'-(Pyridin-4-ylsulfonyl)-1'-(2,2,2-trifluoroethyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one	0.056	415.0 (M+H)
341	1'-Methyl-5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one	0.023	347.0 (M+H)

Examples 342-357



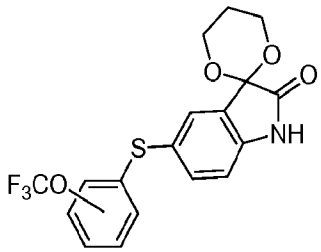
Examples 342-357 were prepared from 5'-[(4-methoxyphenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one and the appropriate boronic acid using a procedure similar to that of Example 197 and summarized in Table 20.

Table 20: Compounds Prepared According to the Procedure of Example 197.

Example	Chemical Name	Mass (g)	MS (ESI^+) *m/z*
342	5'-[(4-Methoxyphenyl)sulfonyl]-1'-phenylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.021	452.0 (M+H)
343	1'-(3-Fluorophenyl)-5'-[(4-methoxyphenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.034	470.0 (M+H)
344	1'-(4-Fluorophenyl)-5'-[(4-methoxyphenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.060	470.1 (M+H)
345	1'-(3-Chlorophenyl)-5'-[(4-methoxyphenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.052	486.0 (M+H)
346	1'-(4-Chlorophenyl)-5'-[(4-methoxyphenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.047	486.0 (M+H)
347	5'-[(4-Methoxyphenyl)sulfonyl]-1'-[3-(trifluoromethyl)phenyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.036	520.1 (M+H)
348	5'-[(4-Methoxyphenyl)sulfonyl]-1'-[4-(trifluoromethyl)phenyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.056	520.1 (M+H)
349	3-{5'-[(4-Methoxyphenyl)sulfonyl]-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl}benzonitrile	0.023	477.0 (M+H)
350	4-{5'-[(4-Methoxyphenyl)sulfonyl]-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl}benzonitrile	0.039	477.0 (M+H)
351	1'-(3,4-Difluorophenyl)-5'-[(4-methoxyphenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.044	488.0 (M+H)
352	1'-(3,4-Dichlorophenyl)-5'-[(4-methoxyphenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.056	520.0 (M+H)
353	1'-(3-Chloro-4-fluorophenyl)-5'-[(4-methoxyphenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.062	504.0 (M+H)

354	5'-[(4-Methoxyphenyl)sulfonyl]-1'-[2-(trifluoromethyl)phenyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.055	520.1 (M+H)
355	2-{5'-[(4-Methoxyphenyl)sulfonyl]-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl}benzonitrile	0.041	477.0 (M+H)
356	1'-(2-Fluorophenyl)-5'-[(4-methoxyphenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.026	470.0 (M+H)
357	1'-(2-Chlorophenyl)-5'-[(4-methoxyphenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.009	486.0 (M+H)

Example 358-360

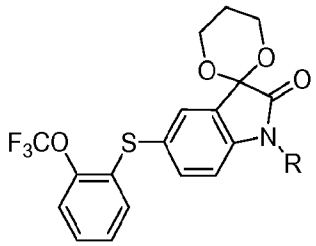


Examples 358-360 were prepared from 5'-iodospiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one and the appropriate trifluoromethoxy thiophenol using a procedure similar to that of Example 201, step 2 and summarized in Table 21.

Table 21: Compounds Prepared According to the Procedure of Example 201, step 2.

Example	**Chemical Name**	**Mass (g)**	**MS (ESI-) m/z**
358	5'-{[2-(Trifluoromethoxy)phenyl]sulfanyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)- one	0.581	396.0 (M-H)
359	5'-{[3-(Trifluoromethoxy)phenyl]sulfanyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)- one	0.549	396.0 (M-H)
360	5'-{[4-(Trifluoromethoxy)phenyl]sulfanyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)- one	0.548	396.0 (M-H)

Examples 361-363

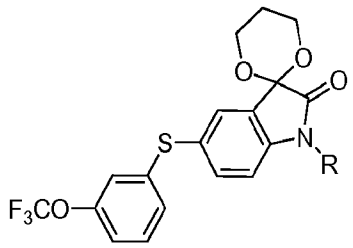


Examples 361-363 were prepared from 5'-{[2-(trifluoromethoxy)phenyl]sulfanyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)- one and the appropriate alkylating agent using a procedure similar to that of Example 179, step 2 and summarized in Table 22.

Table 22: Compounds Prepared According to the Procedure of Example 179, step 2.

Example	Name	Mass (g)	MS (ESI^+) *m/z*
361	1'-(Cyclopropylmethyl)-5'-{[2-(trifluoromethoxy)phenyl]sulfanyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.046	452.0 (M+H)
362	1'-Butyl-5'-{[2-(trifluoromethoxy)phenyl]sulfanyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.048	454.0 (M+H)
363	1'-(2,2,2-Trifluoroethyl)-5'-{[2-(trifluoromethoxy)phenyl]sulfanyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.057	480.0 (M+H)

Examples 364-366

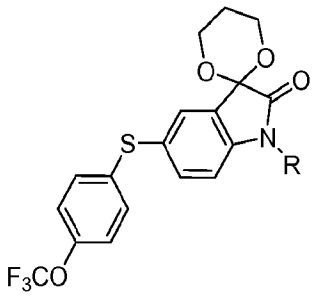


Examples 364-366 were prepared from 5'-{[3-(trifluoromethoxy)phenyl]sulfanyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)- one and the appropriate alkylating agent using a procedure similar to that of Example 179, step 2 and summarized in Table 23.

Table 23: Compounds Prepared According to the Procedure of Example 179, step 2.

Example	Name	Mass (g)	MS (ESI^+) *m/z*
364	1'-(Cyclopropylmethyl)-5'-{[3-(trifluoromethoxy)phenyl]sulfanyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.051	452.0 (M+H)
365	1'-Butyl-5'-{[3-(trifluoromethoxy)phenyl]sulfanyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.055	454.1 (M+H)
366	1'-(2,2,2-Trifluoroethyl)-5'-{[3-(trifluoromethoxy)phenyl]sulfanyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.054	480.0 (M+H)

Examples 367-369

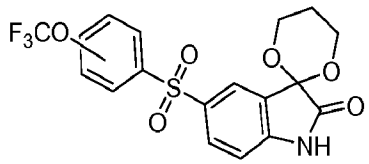


Examples 367-369 were prepared from 5'-{[4-(trifluoromethoxy)phenyl]sulfanyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)- one and the appropriate alkylating agent using a procedure similar to that of Example 179, step 2 and summarized in Table 24.

Table 24: Compounds Prepared According to the Procedure of Example 179, step 2.

Example	Name	Mass (g)	MS (ESI) *m/z*
367	1'-(Cyclopropylmethyl)-5'-{[4-(trifluoromethoxy)phenyl]sulfanyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.056	452.0 (M+H)
368	1'-Butyl-5'-{[4-(trifluoromethoxy)phenyl]sulfanyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.040	454.0 (M+H)
369	1'-(2,2,2-Trifluoroethyl)-5'-{[4-(trifluoromethoxy)phenyl]sulfanyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.044	478.1 (M-H)

Example 370-372

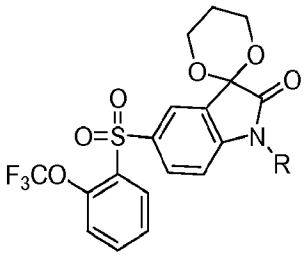


Examples 370-372 were prepared from the appropriate 5'-{[(Trifluoromethoxy)phenyl]sulfanyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one using a using a procedure similar to that of Example 203 and summarized in Table 25.

Table 25: Compounds Prepared According to the Procedure of Example 203.

Example	Chemical Name	Mass (g)	MS (ESI^+) m/z
370	5'-{[2-(Trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.346	430.0 (M+H)
371	5'-{[3-(Trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.171	429.9 (M+H)
372	5'-{[4-(Trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.323	430.0 (M+H)

Examples 373-378

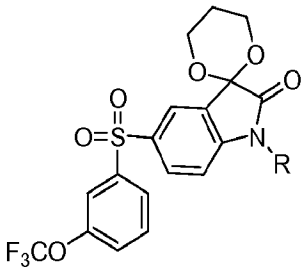


Examples 373-378 were prepared from 5'-{[2-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one and the appropriate alkylating agent using a procedure similar to that of Example 179, step 2 and summarized in Table 26.

Table 26: Compounds Prepared According to the Procedure of Example 179, step 2.

Example	Name	Mass (g)	MS (ESI^+) *m/z*
373	1'-(Cyclopropylmethyl)-5'-{[2-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.041	484.0 (M+H)
374	1'-Butyl-5'-{[2-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.043	486.0 (M+H)
375	1'-Pent-4-yn-1-yl-5'-{[2-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.043	496.0 (M+H)
376	1'-Propyl-5'-{[2-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.043	472.0 (M+H)
377	1'-(2,2,2-Trifluoroethyl)-5'-{[2-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.048	512.0 (M+H)
378	1'-Methyl-5'-{[2-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.038	444.0 (M+H)

Examples 379-384

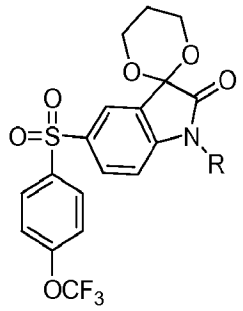


Examples 379-384 were prepared from 5'-{[3-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one and the appropriate alkylating agent using a procedure similar to that of Example 179, step 2 and summarized in Table 27.

Table 27: Compounds Prepared According to the Procedure of Example 179, step 2.

Example	Name	Mass (g)	MS (ESI) *m/z*
379	1'-(Cyclopropylmethyl)-5'-{[3-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.040	484.1 (M+H)
380	1'-Butyl-5'-{[3-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.038	486.1 (M+H)
381	1'-Pent-4-yn-1-yl-5'-{[3-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.045	496.1 (M+H)
382	1'-Propyl-5'-{[3-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.040	472.1 (M+H)
383	1'-(2,2,2-Trifluoroethyl)-5'-{[3-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.048	510.0 (M-H)
384	1'-Methyl-5'-{[3-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.038	444.0 (M+H)

Examples 385-390



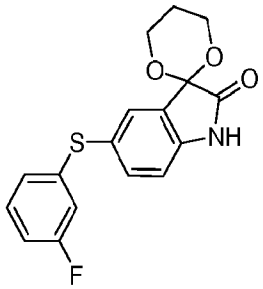
Examples 385-390 were prepared from 5'-{[4-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one and the appropriate alkylating agent using a procedure similar to that of Example 179, step 2 and summarized in Table 28.

Table 28: Compounds Prepared According to the Procedure of Example 179, step 2.

Example	Name	Mass (g)	MS (ESI^+) *m/z*
385	1'-(Cyclopropylmethyl)-5'-{[4-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.043	484.0 (M+H)
386	1'-Butyl-5'-{[4-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.042	486.0 (M+H)
387	1'-Pent-4-yn-1-yl-5'-{[4-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.041	496.0 (M+H)
388	1'-Propyl-5'-{[4-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.041	472.0 (M+H)
389	1'-(2,2,2-Trifluoroethyl)-5'-{[4-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.048	512.0 (M+H)
390	1'-Methyl-5'-{[4-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.036	444.0 (M+H)

Example 391

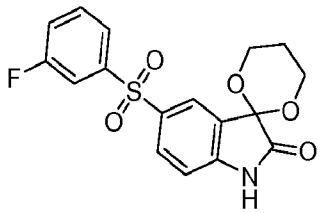
5'-[(3-Fluorophenyl)sulfanyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



The title compound (4.039 g, 100%) was prepared from 5'-iodospiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one and 3-fluorothiophenol using a procedure similar to that of Example 201, step 2. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^-$) *m/z* 330.0 (M-H).

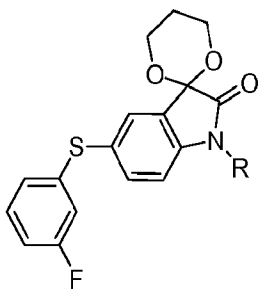
Example 392

5'-[(3-Fluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



The title compound (2.251 g, 81%)was prepared from 5'-[(3-fluorophenyl)sulfanyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one using a procedure similar to that of Example 203. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^-$) *m/z* 362.0 (M-H).

Examples 393-398

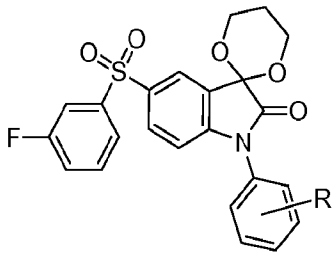


Examples 393-398 were prepared from 5'-[(3-fluorophenyl)sulfanyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one and the appropriate alkylating agent using a procedure similar to that of Example 179, step 2 and summarized in Table 29.

Table 29: Compounds Prepared According to the Procedure of Example 179, step 2.

Example	Name	Mass (g)	MS (ESI^+) *m/z*
393	1'-(Cyclopropylmethyl)-5'-[(3-fluorophenyl)sulfanyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.047	386.1 (M+H)
394	1'-Butyl-5'-[(3-fluorophenyl)sulfanyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.049	388.1 (M+H)
395	5'-[(3-Fluorophenyl)sulfanyl]-1'-pent-4-yn-1-ylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.046	398.1 (M+H)
396	5'-[(3-Fluorophenyl)sulfanyl]-1'-propylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.046	374.1 (M+H)
397	5'-[(3-Fluorophenyl)sulfanyl]-1'-(2,2,2-trifluoroethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.050	414.0 (M+H)
398	5'-[(3-Fluorophenyl)sulfanyl]-1'-methylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.044	346.0 (M+H)

Examples 399-428



Examples 399-428 were prepared from 5'-[(3-fluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one and the appropriate boronic acid using a procedure similar to that of Example 197 and summarized in Table 30.

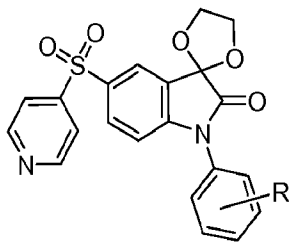
Table 30: Compounds Prepared According to the Procedure of Example 197.

Example	Chemical Name	Mass (g)	MS (ESI^+) *m/z*
399	5'-[(3-Fluorophenyl)sulfonyl]-1'-phenylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.038	440.0 (M+H)
400	1'-(2-Fluorophenyl)-5'-[(3-fluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.012	458.0 (M+H)
401	1'-(3-Fluorophenyl)-5'-[(3-fluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.039	458.0 (M+H)
402	1'-(4-Fluorophenyl)-5'-[(3-fluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.045	458.0 (M+H)
403	1'-(3-Chlorophenyl)-5'-[(3-fluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.045	474.0 (M+H)
404	1'-(4-Chlorophenyl)-5'-[(3-fluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.045	474.0 (M+H)
405	5'-[(3-Fluorophenyl)sulfonyl]-1'-[2-(trifluoromethyl)phenyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.029	508.0 (M+H)
406	5'-[(3-Fluorophenyl)sulfonyl]-1'-[3-(trifluoromethyl)phenyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.051	508.0 (M+H)
407	5'-[(3-Fluorophenyl)sulfonyl]-1'-[4-(trifluoromethyl)phenyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.048	508.1 (M+H)
408	3-{5'-[(3-Fluorophenyl)sulfonyl]-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl}benzonitrile	0.041	465.0 (M+H)
409	4-{5'-[(3-Fluorophenyl)sulfonyl]-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl}benzonitrile	0.040	465.0 (M+H)
410	1'-(3,4-Difluorophenyl)-5'-[(3-fluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.045	476.0 (M+H)

411	1'-(3,4-Dichlorophenyl)-5'-[(3-fluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.049	507.9 (M+H)
412	1'-(3-Chloro-4-fluorophenyl)-5'-[(3-fluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.053	492.0 (M+H)
413	1'-(2-Chlorophenyl)-5'-[(3-fluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.010	474.0 (M+H)
414	5'-[(3-Fluorophenyl)sulfonyl]-1'-(2-methylphenyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.034	454.1 (M+H)
415	5'-[(3-Fluorophenyl)sulfonyl]-1'-(3-methylphenyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.042	454.1 (M+H)
416	5'-[(3-Fluorophenyl)sulfonyl]-1'-(4-methylphenyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.045	454.1 (M+H)
417	5'-[(3-Fluorophenyl)sulfonyl]-1'-(3-methoxyphenyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.046	470.0 (M+H)
418	5'-[(3-Fluorophenyl)sulfonyl]-1'-(4-methoxyphenyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.048	470.1 (M+H)
419	5'-[(3-Fluorophenyl)sulfonyl]-1'-[3-(trifluoromethoxy)phenyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.053	524.0 (M+H)
420	5'-[(3-Fluorophenyl)sulfonyl]-1'-[4-(trifluoromethoxy)phenyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.058	524.0 (M+H)
421	1'-(3,5-Difluorophenyl)-5'-[(3-fluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.046	476.0 (M+H)
422	1'-(3,5-Dichlorophenyl)-5'-[(3-fluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.048	508.0 (M+H)
423	1'-[4-Chloro-3-(trifluoromethyl)phenyl]-5'-	0.052	542.0

	[(3-fluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one		(M+H)
424	1'-(3-Fluoro-4-methoxyphenyl)-5'-[(3-fluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.047	488.0 (M+H)
425	5'-[(3-Fluorophenyl)sulfonyl]-1'-(2-methoxyphenyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.023	470.1 (M+H)
426	5'-[(3-Fluorophenyl)sulfonyl]-1'-[2-(trifluoromethoxy)phenyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.007	524.0 (M+H)
427	1'-(2,3-Difluorophenyl)-5'-[(3-fluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.004	476.1 (M+H)
428	1'-(2,5-Difluorophenyl)-5'-[(3-fluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.004	476.0 (M+H)

Examples 429-440



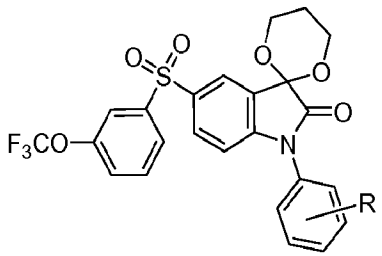
Examples 429-440 were prepared from 5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one and the appropriate boronic acid using a procedure similar to that of Example 197 and summarized in Table 31.

Table 31: Compounds Prepared According to the Procedure of Example 197.

Example	Chemical Name	Mass (g)	MS (ESI^+) *m/z*
429	1'-Phenyl-5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one	0.031	409.0 (M+H)
430	1'-(3-Fluorophenyl)-5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one	0.032	427.0 (M+H)
431	1'-(4-Fluorophenyl)-5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one	0.041	427.1 (M+H)
432	1'-(3-Chlorophenyl)-5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one	0.043	443.0 (M+H)
433	1'-(4-Chlorophenyl)-5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one	0.043	443.0 (M+H)
434	5'-(Pyridin-4-ylsulfonyl)-1'-[3-(trifluoromethyl)phenyl]spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one	0.041	477.0 (M+H)
435	5'-(Pyridin-4-ylsulfonyl)-1'-[4-(trifluoromethyl)phenyl]spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one	0.036	477.0 (M+H)
436	3-[2'-Oxo-5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-1'(2'*H*)-yl]benzonitrile	0.033	434.0 (M+H)
437	4-[2'-Oxo-5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-1'(2'*H*)-yl]benzonitrile	0.026	434.0 (M+H)
438	1'-(3,4-Difluorophenyl)-5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one	0.041	445.0 (M+H)
439	1'-(3,4-Dichlorophenyl)-5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one	0.045	476.9 (M+H)
440	1'-(3-Chloro-4-fluorophenyl)-5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-	0.041	461.0 (M+H)

	one		

Examples 441-451

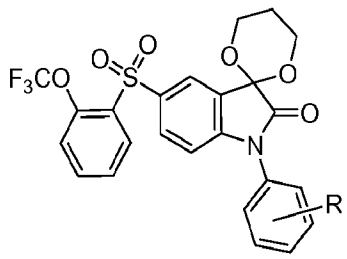


Examples 441-451 were prepared from 5'-{[3-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one one and the appropriate boronic acid using a procedure similar to that of Example 197 and summarized in Table 32.

Table 32: Compounds Prepared According to the Procedure of Example 197.

Example	Chemical Name	Mass (g)	MS (ESI^+) *m/z*
441	1'-Phenyl-5'-{[3-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.022	506.0 (M+H)
442	1'-(3-Fluorophenyl)-5'-{[3-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.023	524.0 (M+H)
443	1'-(4-Fluorophenyl)-5'-{[3-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.021	524.0 (M+H)
444	1'-(3-Chlorophenyl)-5'-{[3-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.026	540.0 (M+H)
445	1'-(4-Chlorophenyl)-5'-{[3-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.026	540.0 (M+H)
446	5'-{[3-(Trifluoromethoxy)phenyl]sulfonyl}-1'-[3-(trifluoromethyl)phenyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.028	574.0 (M+H)
447	5'-{[3-(Trifluoromethoxy)phenyl]sulfonyl}-1'-[4-(trifluoromethyl)phenyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.027	574.0 (M+H)
448	3-[2'-Oxo-5'-{[3-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl]benzonitrile	0.021	531.1 (M+H)
449	1'-(3,4-Difluorophenyl)-5'-{[3-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.023	542.0 (M+H)
450	1'-(3,4-Dichlorophenyl)-5'-{[3-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.027	574.0 (M+H)
451	1'-(3-Chloro-4-fluorophenyl)-5'-{[3-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.031	558.0 (M+H)

Examples 452-455

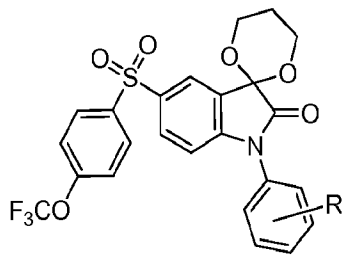


Examples 452-455 were prepared from 5'-{[2-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one one and the appropriate boronic acid using a procedure similar to that of Example 197 and summarized in Table 33.

Table 33: Compounds Prepared According to the Procedure of Example 197.

Example	Chemical Name	Mass (g)	MS (ESI^+) *m/z*
452	1'-(3-Fluorophenyl)-5'-{[2-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.020	524.1 (M+H)
453	1'-(4-Fluorophenyl)-5'-{[2-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.020	524.0 (M+H)
454	1'-(3,4-Difluorophenyl)-5'-{[2-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.020	542.0 (M+H)
455	1'-(3-Chloro-4-fluorophenyl)-5'-{[2-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.024	558.0 (M+H)

Examples 456-458

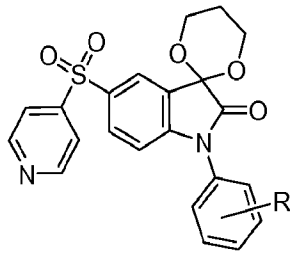


Examples 456-458 were prepared from 5'-{[4-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one one and the appropriate boronic acid using a procedure similar to that of Example 197 and summarized in Table 34.

Table 34: Compounds Prepared According to the Procedure of Example 197.

Example	Chemical Name	Mass (g)	MS (ESI^+) *m/z*
456	1'-(3-Fluorophenyl)-5'-{[4-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.021	524.0 (M+H)
457	1'-(4-Fluorophenyl)-5'-{[4-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.022	524.0 (M+H)
458	1'-(3,4-Difluorophenyl)-5'-{[4-(trifluoromethoxy)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.020	542.0 (M+H)

Examples 459-472

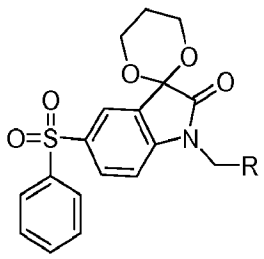


Examples 459-472 were prepared from 5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one and the appropriate boronic acid using a procedure similar to that of Example 197, step 2 and summarized in Table 35.

Table 35: Compounds Prepared According to the Procedure of Example 179, step 2.

Example	Chemical Name	Mass (g)	MS (ESI^+) *m/z*
459	1'-Phenyl-5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.027	423.0 (M+H)
460	1'-(3-Fluorophenyl)-5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.036	441.0 (M+H)
461	1'-(4-Fluorophenyl)-5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.040	441.0 (M+H)
462	1'-(3-Chlorophenyl)-5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.008	457.0 (M+H)
463	1'-(4-Chlorophenyl)-5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.051	457.0 (M+H)
464	5'-(Pyridin-4-ylsulfonyl)-1'-[3-(trifluoromethyl)phenyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.053	491.0 (M+H)
465	5'-(Pyridin-4-ylsulfonyl)-1'-[4-(trifluoromethyl)phenyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.056	491.0 (M+H)
466	3-[2'-Oxo-5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl]benzonitrile	0.047	448.0 (M+H)
467	4-[2'-Oxo-5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl]benzonitrile	0.049	448.1 (M+H)
468	1'-(3,4-Difluorophenyl)-5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.045	459.0 (M+H)
469	1'-(3,4-Dichlorophenyl)-5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.051	491.0 (M+H)
470	1'-(3-Chloro-4-fluorophenyl)-5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.050	475.0 (M+H)
471	1'-(2-Fluorophenyl)-5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.010	441.1 (M+H)
472	5'-(Pyridin-4-ylsulfonyl)-1'-[2-(trifluoromethyl)phenyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.019	491.1 (M+H)

Examples 473-500



Examples 473-500 were prepared from 5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one and the appropriate alkylating agent using a procedure similar to that of Example 179, step 2 and summarized in Table 36.

Table 36: Compounds Prepared According to the Procedure of Example 179, step 2.

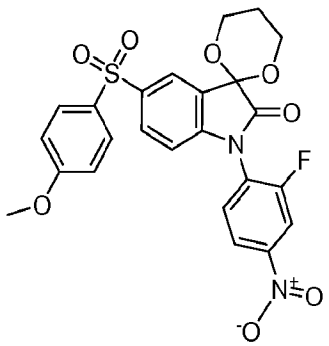
Example	Chemical Name	Mass (g)	MS (ESI^+) *m/z*
473	1'-Benzyl-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.037	436.1 (M+H)
474	1'-(2-Fluorobenzyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.040	454.1 (M+H)
475	1'-(3-Fluorobenzyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.039	454.1 (M+H)
476	1'-(4-Fluorobenzyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.041	454.1 (M+H)
477	1'-(2-Chlorobenzyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.039	470.1 (M+H)
478	1'-(3-Chlorobenzyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.040	470.0 (M+H)
479	1'-(4-Chlorobenzyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.047	470.0 (M+H)
480	5'-(Phenylsulfonyl)-1'-[2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.049	504.0 (M+H)
481	5'-(Phenylsulfonyl)-1'-[3-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.048	504.1 (M+H)
482	5'-(Phenylsulfonyl)-1'-[4-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.043	504.1 (M+H)
483	2-{[2'-Oxo-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl]methyl}benzonitrile	0.039	461.1 (M+H)
484	3-{[2'-Oxo-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl]methyl}benzonitrile	0.038	461.1 (M+H)
485	4-{[2'-Oxo-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl]methyl}benzonitrile	0.041	461.1 (M+H)

486	1'-(2-Methylbenzyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.040	450.1 (M+H)
487	1'-(3-Methylbenzyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.038	450.1 (M+H)
488	1'-(4-Methylbenzyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.040	450.1 (M+H)
489	5'-(Phenylsulfonyl)-1'-[2-(trifluoromethoxy)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.046	520.1 (M+H)
490	5'-(Phenylsulfonyl)-1'-[3-(trifluoromethoxy)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.046	520.1 (M+H)
491	5'-(Phenylsulfonyl)-1'-[4-(trifluoromethoxy)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.044	520.1 (M+H)
492	1'-(2-Methoxybenzyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.037	466.1 (M+H)
493	1'-(3-Methoxybenzyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.041	466.1 (M+H)
494	1'-(4-Methoxybenzyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.040	466.1 (M+H)
495	5'-(Phenylsulfonyl)-1'-(pyridin-2-ylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.037	437.1 (M+H)
496	5'-(Phenylsulfonyl)-1'-(pyridin-3-ylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.021	437.1 (M+H)
497	5'-(Phenylsulfonyl)-1'-(pyridin-4-ylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.027	437.1 (M+H)
498	1'-[2-(Difluoromethoxy)benzyl]-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.036	502.1 (M+H)
499	1'-[3-(Difluoromethoxy)benzyl]-5'-	0.036	502.0

	(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one		(M+H)
500	1'-[4-(Difluoromethoxy)benzyl]-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.037	520.1 (M+H)

Example 501

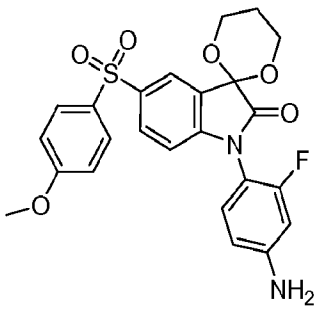
1'-(2-Fluoro-4-nitrophenyl)-5'-[(4-methoxyphenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



The title compound (0.056g, 34%) was prepared from 5'-[(4-methoxyphenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one and 3,4 difluoronitrobenzene using a procedure similar to that of step 1 of example 319. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 515.0 (M+H).

Example 502

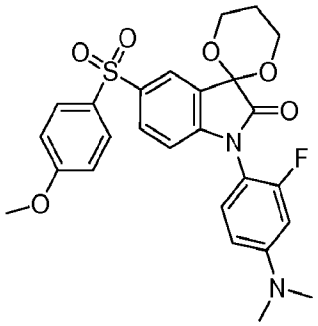
1'-(2-Fluoro-4-nitrophenyl)-5'-[(4-methoxyphenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



The title compound (0.045g, 92%) was prepared from 1'-(2-fluoro-4-nitrophenyl)-5'-[(4-methoxyphenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one using a procedure similar to that of step 2 of example 319. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^-$) *m/z* 485.1 (M+H).

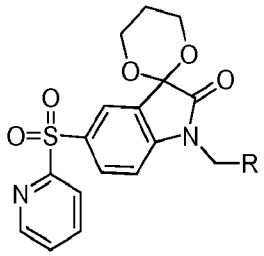
Example 503

1'-[4-(Dimethylamino)-2-fluorophenyl]-5'-[(4-methoxyphenyl)sulfonyl]spiro[1,3- dioxane-2,3'-indol]-2'(1'*H*)-one



The title compound (0.005g, 12%) was prepared from 1'-(4-amino-2-fluorophenyl)-5'-[(4-methoxyphenyl)sulfonyl]spiro[1,3-dioxane- 2,3'-indol]-2'(1'*H*)-one and methyl iodide (5 eq.) using a procedure similar to that of Example 179, step 2. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 513.1 (M+H).

Examples 504-531



Examples 504-531 were prepared from 5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one and the appropriate alkylating agent using a procedure similar to that of Example 179, step 2 and summarized in Table 37.

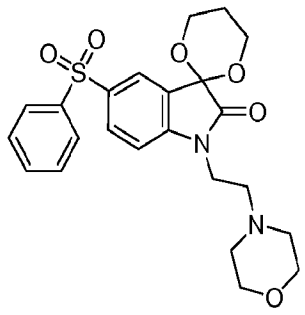
Table 37: Compounds Prepared According to the Procedure of Example 179, step 2.

Example	Chemical Name	Mass (g)	MS (ESI^+) *m/z*
504	1'-Benzyl-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.028	437.1 (M+H)
505	1'-(2-Fluorobenzyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.031	455.0 (M+H)
506	1'-(3-Fluorobenzyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.032	455.1 (M+H)
507	1'-(4-Fluorobenzyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.031	455.1 (M+H)
508	1'-(2-Chlorobenzyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.033	471.0 (M+H)
509	1'-(3-Chlorobenzyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.033	471.0 (M+H)
510	1'-(4-Chlorobenzyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.034	471.0 (M+H)
511	5'-(Pyridin-2-ylsulfonyl)-1'-[2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.035	505.1 (M+H)
512	5'-(Pyridin-2-ylsulfonyl)-1'-[3-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.036	505.1 (M+H)
513	5'-(Pyridin-2-ylsulfonyl)-1'-[4-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.036	505.0 (M+H)
514	2-{[2'-Oxo-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl]methyl}benzonitrile	0.031	462.1 (M+H)
515	3-{[2'-Oxo-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl]methyl}benzonitrile	0.036	462.0 (M+H)
516	4-{[2'-Oxo-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl]methyl}benzonitrile	0.031	462.1 (M+H)
517	1'-(Pyridin-2-ylmethyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.025	438.1 (M+H)
518	1'-(2-Methylbenzyl)-5'-(pyridin-2-	0.027	451.0

	ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one		(M+H)
519	1'-(3-Methylbenzyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.028	451.0 (M+H)
520	1'-(4-Methylbenzyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.028	451.1 (M+H)
521	5'-(Pyridin-2-ylsulfonyl)-1'-[2-(trifluoromethoxy)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.037	521.1 (M+H)
522	5'-(Pyridin-2-ylsulfonyl)-1'-[3-(trifluoromethoxy)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.038	521.1 (M+H)
523	5'-(Pyridin-2-ylsulfonyl)-1'-[4-(trifluoromethoxy)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.034	521.1 (M+H)
524	1'-(2-Methoxybenzyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.030	467.1 (M+H)
525	1'-(3-Methoxybenzyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.030	467.1 (M+H)
526	1'-(4-Methoxybenzyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.026	467.1 (M+H)
527	1'-[2-(Difluoromethoxy)benzyl]-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.035	503.1 (M+H)
528	1'-[3-(Difluoromethoxy)benzyl]-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.037	503.1 (M+H)
529	1'-[4-(Difluoromethoxy)benzyl]-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.035	503.1 (M+H)
530	1'-(Pyridin-3-ylmethyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.043	438.1 (M+H)
531	1'-(Pyridin-4-ylmethyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.036	438.1 (M+H)

Example 532

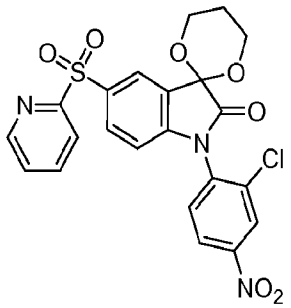
1'-(2-Morpholin-4-ylethyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



The title compound (0.055g, 83%) was prepared from 5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one and 4-(2-chloroethyl)morpholine hydrochloride using a procedure similar to that of Example 179, step 2. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 459.1 (M+H).

Example 533

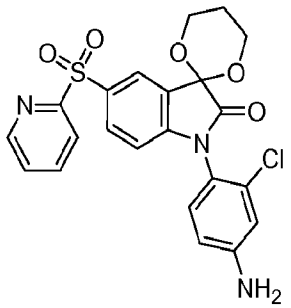
1'-(2-Chloro-4-nitrophenyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



The title compound (0.132, 60%) was prepared from 5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one using a procedure similar to that of step 1 of example 319. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 502.0 (M+H).

Example 534

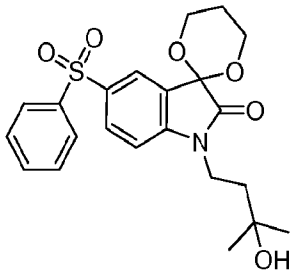
1'-(4-Amino-2-chlorophenyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



The title compound (0.101, 90%) was prepared from 1'-(2-chloro-4-nitrophenyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one using a procedure similar to that of step 2 of example 319. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 472.0 (M+H).

Example 535

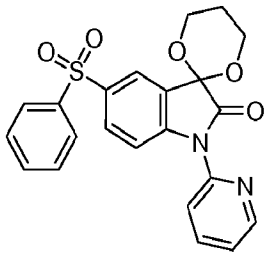
1'-(3-Hydroxy-3-methylbutyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



The title compound (0.058g, 86%) was prepared from 5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one and 4-bromo-2-methylbutan-2-ol (EP78704) using a procedure similar to that of Example 179, step 2. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 432.1 (M+H).

Example 536

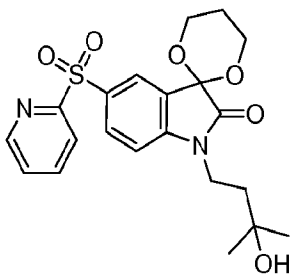
5'-(Phenylsulfonyl)-1'-(pyridin-2-yl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



To a solution of 25% sodium methoxide (0.079 ml, 0.347 mmol) in DMSO (2 ml) was added oxazolidin-2-one (0.010 g, 0.115 mmol) and copper(I) iodide (0.010 g, 0.053 mmol) and the reaction was stirred at room temperature for 1 hour. 5'-(Phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one (0.080 g, 0.232 mmol) and 2-bromopyridine (0.029 ml, 0.301 mmol) were added and the reaction was heated at 120° C over night. The reaction was then cooled, poured into water with a small amount of brine and extracted w/ EtOAc. The combined organics were dried over $MgSO_4$ and concentrated. The crude mixture was purified on RediSep™ silica gel eluting with a 0 to 100% EtOAc/hexane linear gradient to give 0.045g (46%) of the title compound as a white solid. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 423.1 (M+H).

Example 537

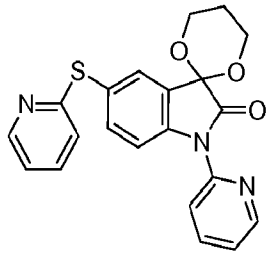
1'-(3-Hydroxy-3-methylbutyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



The title compound (0.043g, 96%) was prepared from 5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one and 4-bromo-2-methylbutan-2-ol (EP78704) using a procedure similar to that of Example 179, step 2. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 433.1 (M+H).

Example 538

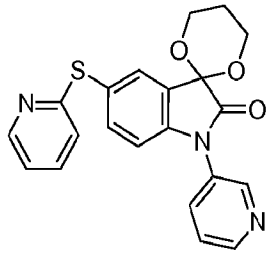
1'-(Pyridin-2-yl)-5'-(pyridin-2-ylsulfanyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



The title compound (0.071g, 71%) was prepared from 5'-(pyridin-2-ylsulfanyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one using a procedure similar to that of Example 536. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 392.1 (M+H).

Example 539

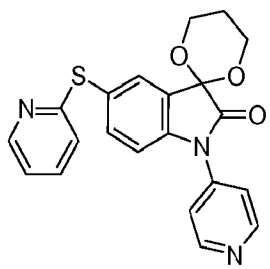
1'-(Pyridin-3-yl)-5'-(pyridin-2-ylsulfanyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



The title compound (0.035g, 35%) was prepared from 5'-(pyridin-2-ylsulfanyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one and 3-iodopyridine using a procedure similar to that of Example 536. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 392.1 (M+H).

Example 540

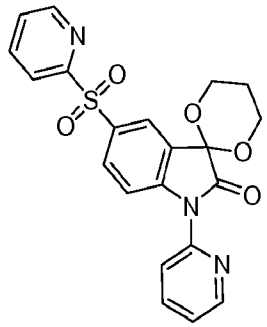
1'-(Pyridin-4-yl)-5'-(pyridin-2-ylsulfanyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



To a solution of 5'-(pyridin-2-ylsulfanyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one (0.080 g, 0.254 mmol) in dioxane (2 ml) was added potassium phosphate (0.108 g, 0.509 mmol) *N,N*-dimethylethane-1,2-diamine (9.14 µl, 0.102 mmol), 4-iodopyridine (0.104 g, 0.509 mmol) and copper(I) iodide (0.019 g, 0.102 mmol). The reaction mixture was purged with N_2 for 15 minutes and then heated at 110° C over night. After cooling, the solids were filtered off and washed with EtOAc. The filtrate was concentrated and the crude mixture was purified on RediSep™ silica gel eluting with a 0 to 100% EtOAc/hexane + 1% Et_3N linear gradient to give 0.053g (53%) of the title compound as a off-white solid. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI^+) *m/z* 392.1 (M+H).

Example 541

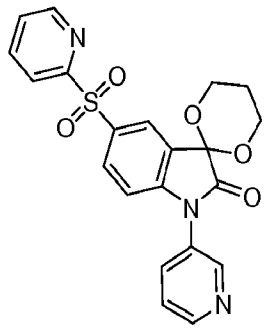
1'-(Pyridin-2-yl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



The title compound (0.029g, 100%) was prepared from 1'-(pyridin-2-yl)-5'-(pyridin-2-ylsulfanyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one using a procedure similar to that of Example 203. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI^+) *m/z* 424.1 (M+H).

Example 542

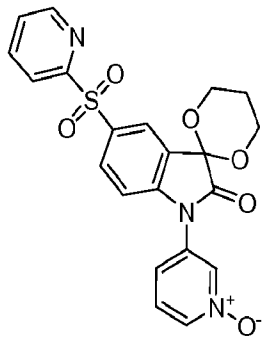
1'-(Pyridin-3-yl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



The title compound (0.007g, 31%) was prepared from 1'-(pyridin-3-yl)-5'-(pyridin-2-ylsulfanyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one using a procedure similar to that of Example 203. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI^+) *m/z* 424.1 (M+H).

Example 543

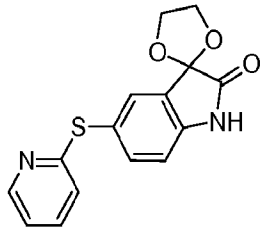
1'-(1-Oxidopyridin-3-yl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



The title compound (0.006g, 26%) was also isolated from the reaction described in Example 542. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 440.1 (M+H).

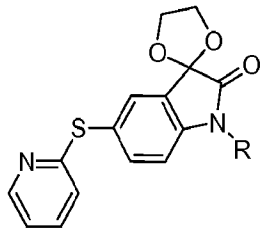
Example 544

5'-(Pyridin-2-ylsulfanyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one



The title compound (0.673g, 59%) was prepared from 5'-iodospiro[1,3-dioxolane-2,3'-indol]-2'(1'H)-one and 2-mercaptopyridine using a procedure similar to that of Example 201, step 2. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 301.0 (M+H).

Examples 545-548



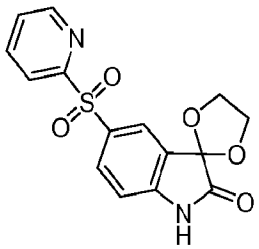
Examples 545-548 were prepared from prepared from 5'-(pyridin-2-ylsulfanyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one and the appropriate alkylating agent using a procedure similar to that of Example 179, step 2 and are summarized in Table 38.

Table 38: Compounds Prepared According to the Procedure of Example 179, step 2.

Example	Name	Mass (g)	MS (ESI^+) *m/z*
545	1'-Propyl-5'-(pyridin-4-ylsulfanyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one	0.125	343.1 (M+H)
546	1'-(Cyclopropylmethyl)-5'-(pyridin-4-ylsulfanyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one	0.016	355.1 (M+H)
547	1'-(3-Hydroxy-3-methylbutyl)-5'-(pyridin-4-ylsulfanyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one	0.023	387.1 (M+H)
548	5'-(Pyridin-4-ylsulfanyl)-1'-(2,2,2-trifluoroethyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one	0.019	383.1 (M+H)

Example 549

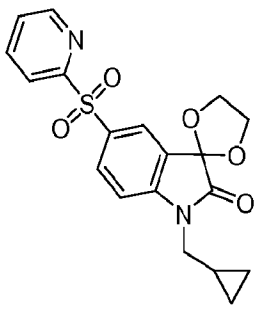
5'-(Pyridin-2-ylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one



The title compound (0.631g, 86 %) was prepared from 5'-(pyridin-2-ylsulfanyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one using a procedure similar to that of Example 203. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI^+) *m/z* 333.1 (M+H).

Example 550

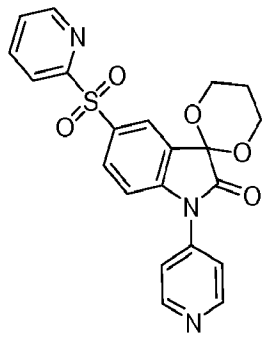
1'-(Cyclopropylmethyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one



The title compound (0.029g, 100 %) was prepared from 5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one using a procedure similar to that of Example 179, step 2. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 387.1 (M+H).

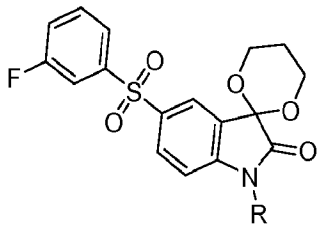
Example 551

1'-(Pyridin-4-yl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



To a solution of 1'-(pyridin-4-yl)-5'-(pyridin-2-ylsulfanyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one (0.044 g, 0.112 mmol) in DCM (5 ml) was added TFA (0.200 ml) and 30% hydrogen peroxide (0.035 ml, 0.309 mmol) and the reaction was stirred at rt for 4h. Saturated sodium bisulfite solution was then added, the mixture was stirred 15min. and then extracted w/ EtOAc. The organic extracts were stirred with saturated $NaHCO_3$ to neutralize. The organics were separated, dried over $MgSO_4$ and concentrated. The crude mixture was purified on RediSep silica gel eluting with a 0 to 100% EtOAc/hexane + 1% Et_3N linear gradient to give 0.014g (29%) of the title compound as a white solid. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 424.1 (M+H).

Examples 552-554

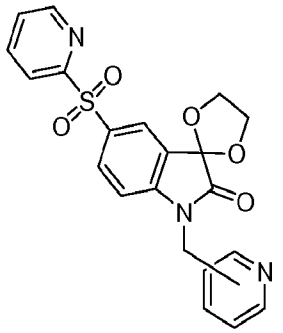


Examples 552-554 were prepared from 5'-[(3-fluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one and the appropriate iodo-pyridine using a procedure similar to that of Example 540 and are summarized in Table 39.

Table 39: Compounds Prepared According to the Procedure of Example 540.

Example	Name	Mass (g)	MS (ESI^+) *m/z*
552	5'-[(3-Fluorophenyl)sulfonyl]-1'-(pyridin-2-yl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.037	441.1 (M+H)
553	5'-[(3-Fluorophenyl)sulfonyl]-1'-(pyridin-3-yl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.010	441.1 (M+H)
554	5'-[(3-Fluorophenyl)sulfonyl]-1'-(pyridin-4-yl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.042	441.1 (M+H)

Examples 555-557



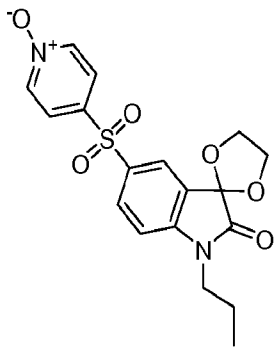
Examples 555-557 were prepared from 5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one and the appropriate bromomethyl pyridine using a procedure similar to that of Example 179, step 2 and are summarized in Table 40.

Table 40: Compounds Prepared According to the Procedure of Example 179, step 2.

Example	Name	Mass (g)	MS (ESI^+) *m/z*
555	1'-(Pyridin-2-ylmethyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one	0.058	424.1 (M+H)
556	1'-(Pyridin-3-ylmethyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one	0.033	424.1 (M+H)
557	1'-(Pyridin-4-ylmethyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one	0.035	424.1 (M+H)

Examples 558

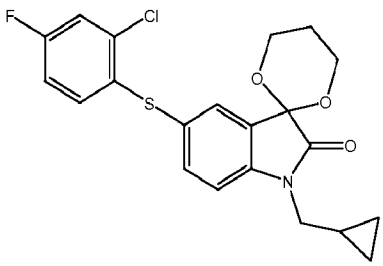
5'-[(1-Oxidopyridin-4-yl)sulfonyl]-1'-propylspiro[1,3-dioxolane-2,3'-indol]- 2'(1'*H*)-one



The title compound (0.022g, 16 %) and 1'-propyl-5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one (0.108g, 83%) (Example 339) were prepared from 1'-propyl-5'-(pyridin-4-ylsulfanyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'*H*)-one using a procedure similar to that of Example 551. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI^+) *m/z* 391.1 (M+H).

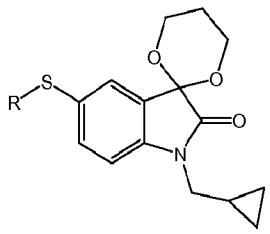
Example 559

5'-[(2-Chloro-4-fluorophenyl)sulfanyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



The title compound (0.012g, 64%) was prepared as a clear oil from 1'-(cyclopropylmethyl)-5'-[(triisopropylsilyl)sulfanyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one using a procedure similar to that of Step 2 of Example 201. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 420.1 (M+H).

Examples 560-565



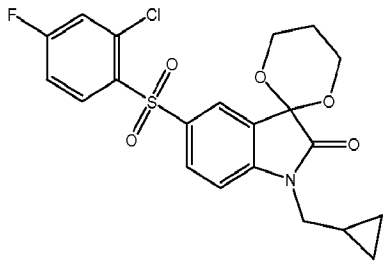
Examples 560-565 were prepared from 1'-(cyclopropylmethyl)-5'-[(triisopropylsilyl)sulfanyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one and the appropriate commercially available or synthesized, according to procedures described in *Tetrahedron*. **2005**, 61, 4779-4784 or WO 2006/004533, substituted aryl or heteroaryl iodides and according to the procedure for Step 2 of Example 201 and are summarized in Table 41.

Table 41: Compounds Prepared According to the Procedure of Example 201, step 2.

Example	Name	Mass (g)	MS (ESI$^+$) *m/z*
560	1'-(Cyclopropylmethyl)-5'-[(4-fluoro-3-methylphenyl)sulfanyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.120	400.1 (M+H)
561	1'-(Cyclopropylmethyl)-5'-{[2-(trifluoromethyl)phenyl]sulfanyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.093	436.1 (M+H)
562	1'-(Cyclopropylmethyl)-5'-[(2,3-dichlorophenyl)sulfanyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.137	436.0 (M+H)
563	5'-[(5-Chloro-2-thienyl)sulfanyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.010	408.0 (M+H)
564	1'-(Cyclopropylmethyl)-5'-{[4-fluoro-2-(trifluoromethyl)phenyl]sulfanyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.079	454.0 (M+H)
565	1'-(Cyclopropylmethyl)-5'-{[6-(trifluoromethyl)pyridin-3-yl]sulfanyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.043	437.1 (M+H)

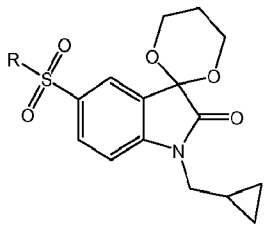
Examples 566

5'-[(2-Chloro-4-fluorophenyl)sulfonyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



The title compound (0.089g, 69%) was prepared as a white solid from 5'-[(2-chloro-4-fluorophenyl)sulfanyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one using a procedure similar to that of Example 202. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 452.0 (M+H).

Examples 567-573



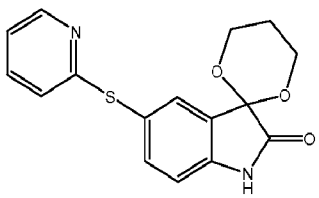
Examples 567-573 were oxidized to the sulfones according to the procedure for Example 202 and are summarized in Table 42.

Table 42: Compounds Prepared According to the Procedure of Example 202.

Example	Name	Mass (g)	MS (ESI^+) *m/z*
567	1'-(Cyclopropylmethyl)-5'-[(4-fluoro-3-methylphenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.053	432.1 (M+H)
568	1'-(Cyclopropylmethyl)-5'-{[2-(trifluoromethyl)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.062	468.1 (M+H)
569	1'-(Cyclopropylmethyl)-5'-[(2,3-dichlorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.106	468.0 (M+H)
570	5'-[(5-Chloro-2-thienyl)sulfonyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.071	440.0 (M+H)
571	1'-(Cyclopropylmethyl)-5'-{[4-fluoro-2-(trifluoromethyl)phenyl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.050	486.1 (M+H)
572	1'-(Cyclopropylmethyl)-5'-{[5-(trifluoromethyl)pyridin-2-yl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.133	469.0 (M+H)
573	1'-(Cyclopropylmethyl)-5'-{[6-(trifluoromethyl)pyridin-3-yl]sulfonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.034	468.9 (M+H)

Example 574

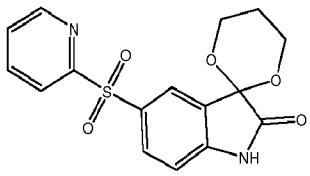
5'-(Pyridin-2-ylsulfanyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



The title compound (0.377g, 80%) was prepared from 5'-(phenylthio)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one using a procedure similar to that of Example 201, step 2. ^1H NMR (400 MHz, DMSO-d6): consistent; MS (ESI^+) *m/z* 313.0 (M+H).

Example 575

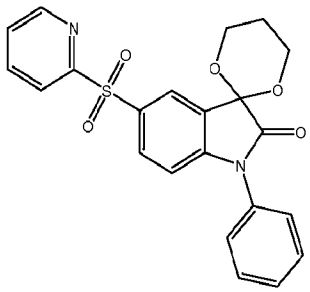
5'-(Pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



The title compound (0.404g, 73%) was prepared from 5'-(pyridin-2-ylsulfanyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one using a procedure similar to that of Example 202. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 347.1 (M+H).

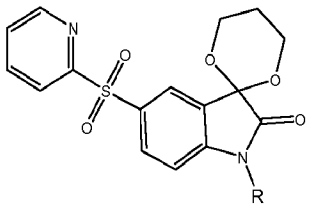
Example 576

1'-Phenyl-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



The title compound (0.089g, 72%) was prepared from 5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one and phenyl boronic acid using a procedure similar to that of Example 197. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 423.0 (M+H).

Examples 577-604



Examples 577-604 were prepared from 5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one and the appropriate substituted boronic acids using a procedure similar to that of Example 197 and are summarized in Table 43.

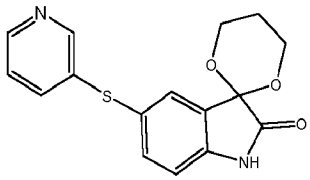
Table 43: Compounds Prepared According to the Procedure of Example 197.

Example	Name	Mass (g)	MS (ESI^+) *m/z*
577	1'-(2-Methoxyphenyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.036	453.1 (M+H)
578	1'-(3-Methoxyphenyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.084	453.0 (M+H)
579	1'-(4-Methoxyphenyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.069	453.0 (M+H)
580	1'-(3-Methylphenyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.074	437.0 (M+H)
581	1'-(2,4-Dichlorophenyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.007	491.0 (M+H)
582	1'-(3-Chlorophenyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.098	457.0 (M+H)
583	5'-(Pyridin-2-ylsulfonyl)-1'-[3-(trifluoromethyl)phenyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.122	491.0 (M+H)
584	5'-(Pyridin-2-ylsulfonyl)-1'-[4-(trifluoromethyl)phenyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.066	491.0 (M+H)
585	1'-(3,4-Difluorophenyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.137	459.0 (M+H)
586	1'-(3,4-Dichlorophenyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.126	491.0 (M+H)
587	1'-(4-Fluorophenyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.116	441.1 (M+H)
588	5'-(Pyridin-2-ylsulfonyl)-1'-[3-(trifluoromethoxy)phenyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.051	507.0 (M+H)
589	5'-(Pyridin-2-ylsulfonyl)-1'-[4-(trifluoromethoxy)phenyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.101	507.0 (M+H)
590	4-[2'-Oxo-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-1'(2'H)-yl]benzonitrile	0.034	448.0 (M+H)
591	5'-(Pyridin-2-ylsulfonyl)-1'-[2-(trifluoromethyl)phenyl]spiro[1,3-dioxane-2,3'-	0.052	491.0 (M+H)

	indol]-2'(1'H)-one		
592	1'-(3,5-Difluorophenyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.081	459.0 (M+H)
593	1'-(3,5-Dichlorophenyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.054	491.0 (M+H)
594	1'-(2-Fluorophenyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.015	441.0 (M+H)
595	1'-(2,3-Difluorophenyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.002	459.0 (M+H)
596	1'-(2,5-Difluorophenyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.004	459.0 (M+H)
597	1'-(2-Chlorophenyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.001	457.0 (M+H)
598	2-[2'-Oxo-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-1'(2'H)-yl]benzamide	0.024	466.1 (M+H)
599	3-[2'-Oxo-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-1'(2'H)-yl]benzonitrile	0.036	448.1 (M+H)
600	1'-(3-Fluorophenyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.039	441.0 (M+H)
601	1'-(4-Chlorophenyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.043	457.0 (M+H)
602	1'-(3-Chloro-4-fluorophenyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.043	475.0 (M+H)
603	1'-[4-Chloro-3-(trifluoromethyl)phenyl]-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.038	525.0 (M+H)
604	1'-(3-Fluoro-4-methoxyphenyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one	0.037	471.1 (M+H)

Example 605

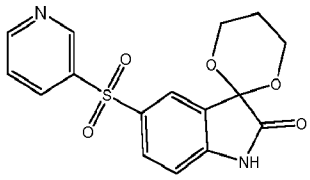
5'-(Pyridin-3-ylsulfanyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



The title compound (0.974g, 71%) was prepared as a white solid from 5'-[(triisopropylsilyl)sulfanyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one using a procedure similar to that of Example 201 step 2. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 315.0 (M+H).

Example 606

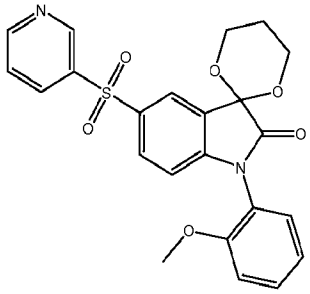
5'-(Pyridin-3-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



The title compound (0.17g, 20%) was prepared from 5'-(pyridin-3-ylsulfanyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one using a procedure similar to that of Example 202. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 347.0 (M+H).

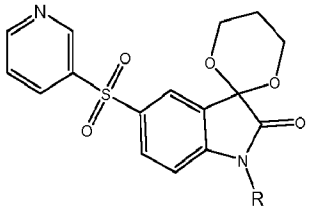
Example 607

1'-(2-Methoxyphenyl)-5'-(pyridin-3-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



The title compound (0.030g, 23%) was prepared from 5'-(pyridin-3-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one and 2-methoxy-phenyl boronic acid using a procedure similar to that of Example 197. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 453.1 (M+H).

Examples 608-632



Examples 608-632 were prepared from 5'-(pyridin-3-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one and the appropriate substituted boronic acids using a procedure similar to that of Example 197 and summarized in Table 44.

Table 44: Compounds Prepared According to the Procedure of Example 197.

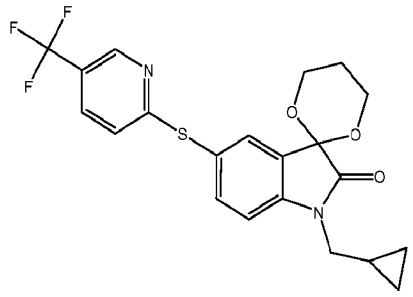
Example	Name	Mass (g)	MS (ESI+) m/z
608	1'-(3-Methoxyphenyl)-5'-(pyridin-3-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.023	453.0 (M+H)
609	1'-(4-Methoxyphenyl)-5'-(pyridin-3-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.028	453.0 (M+H)
610	1'-(3-Methylphenyl)-5'-(pyridin-3-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.022	437.0 (M+H)
611	1'-(2,4-Dichlorophenyl)-5'-(pyridin-3-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.003	491.0 (M+H)
612	1'-(3-Chloro-4-fluorophenyl)-5'-(pyridin-3-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.094	475.0 (M+H)
613	1'-Phenyl-5'-(pyridin-3-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.100	423.0 (M+H)
614	1'-(3-Fluorophenyl)-5'-(pyridin-3-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.045	441.0 (M+H)
615	1'-(3-Chlorophenyl)-5'-(pyridin-3-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.109	457.0 (M+H)
616	5'-(Pyridin-3-ylsulfonyl)-1'-[3-(trifluoromethyl)phenyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.013	491.0 (M+H)
617	5'-(Pyridin-3-ylsulfonyl)-1'-[4-(trifluoromethyl)phenyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.061	491.0 (M+H)
618	1'-(3,4-Difluorophenyl)-5'-(pyridin-3-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.009	459.1 (M+H)
619	1'-(3,4-Dichlorophenyl)-5'-(pyridin-3-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.127	491.0 (M+H)

620	1'-(4-Fluorophenyl)-5'-(pyridin-3-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.007	441.0 (M+H)
621	5'-(Pyridin-3-ylsulfonyl)-1'-[3-(trifluoromethoxy)phenyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.033	507.0 (M+H)
622	5'-(Pyridin-3-ylsulfonyl)-1'-[4-(trifluoromethoxy)phenyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.072	507.0 (M+H)
623	3-[2'-Oxo-5'-(pyridin-3-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-1'(2'H)-yl]benzonitrile	0.033	448.0 (M+H)
624	4-[2'-Oxo-5'-(pyridin-3-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-1'(2'H)-yl]benzonitrile	0.025	448.0 (M+H)
625	5'-(Pyridin-3-ylsulfonyl)-1'-[2-(trifluoromethyl)phenyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.056	491.0 (M+H)
626	1'-(2-Methylphenyl)-5'-(pyridin-3-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.035	437.0 (M+H)
627	1'-(3,5-Difluorophenyl)-5'-(pyridin-3-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.077	459.0 (M+H)
628	1'-(3,5-Dichlorophenyl)-5'-(pyridin-3-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.060	491.0 (M+H)
629	1'-(2,3-Difluorophenyl)-5'-(pyridin-3-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.006	459.0 (M+H)
630	1'-(2,5-Difluorophenyl)-5'-(pyridin-3-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.003	459.0 (M+H)
631	1'-(2-Chlorophenyl)-5'-(pyridin-3-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.003	457.0 (M+H)
632	1'-(4-Chlorophenyl)-5'-(pyridin-3-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	0.100	457.1 (M+H)

Example 633

1'-(Cyclopropylmethyl)-5'-{[5-(trifluoromethyl)pyridin-2-yl]sulfanyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one

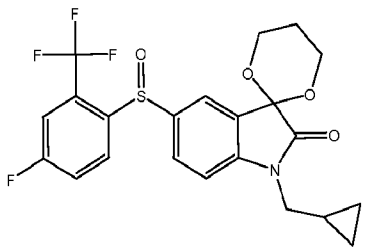
5



The title compound (0.193g, 74 %) was prepared as a clear oil from 1'-(cyclopropylmethyl)-5'-iodospiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one and 5-(trifluoromethyl)pyridine-2-thiol using a procedure similar to that of Example 201 step 2. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 437.1 (M+H).

Example 634

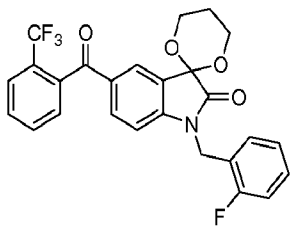
1'-(Cyclopropylmethyl)-5'-{[4-fluoro-2-(trifluoromethyl)phenyl]sulfinyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



The title compound (0.012g, 10%) was prepared as a white solid from 1'-(cyclopropylmethyl)-5'-{[4-fluoro-2-(trifluoromethyl)phenyl]sulfanyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one using a procedure similar to that of Example 202. ^{1}H NMR (400 MHz, DMSO-d6): consistent; MS (ESI$^+$) *m/z* 470.0 (M+H).

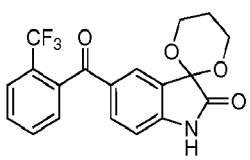
Example 635

1'-(2-fluorobenzyl)-5'-{[2-(trifluoromethyl)phenyl]carbonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



Step 1

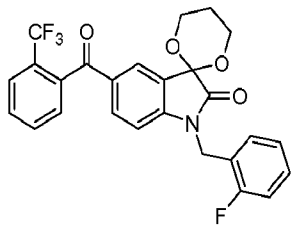
5'-[2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one



5'-Iodospiro[[1,3]dioxane-2,3'-indolin]-2'-one (4.00g, 12.08mmol), trans-dichlorobis(triphenylphosphine)palladium(II) (0.25g, 0.36mmol), K_2CO_3 (5.00g, 36.21mmol), and 2-(trifluoromethyl)-phenylboronic acid (2.66g, 14.50mmol) were added to a flask fitted with a reflux condenser, a septum inlet, and a magnetic stir bar. The flask was flushed with carbon monoxide and then charged with toluene (1200.00mL). The mixture was then stirred at 80° C under a balloon of carbon monoxide. After stirring overnight, TLC analysis indicated reaction to be complete, so reaction mixture was diluted with EtOAc, washed with H_2O, followed by brine. Organic layer was dried over Na_2SO_4, concentrated and purified by flash chromatography on silica gel to afford product as a white solid (1.94g, 43%). ^{1}H NMR (400 MHz, $CDCl_3$): consistent; MS (ES) *m/z* 376.0 (M-H).

Step 2

1'-(2-fluorobenzyl)-5'-{[2-(trifluoromethyl)phenyl]carbonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



The compound 5'-[2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one (0.30g, 0.80mmol) was dissolved in DMF (5.00mL) under a N_2 atmosphere. To this solution was added Cs_2CO_3(0.79g, 2.41mmol) and 2-flurobenzyl bromide (0.29mL, 2.41mmol), and this mixture was stirred at room temperature. After stirring for 1 hour, TLC indicated reaction was complete. Reaction mixture was diluted with EtOAc, washed with H_2O, followed by brine. Organic layer was dried over Na_2SO_4, concentrated and purified by flash chromatography on silica gel to afford product as a white solid (0.28g, 72%). ^{1}H NMR (400 MHz, $CDCl_3$): consistent; MS (ES) *m/z* 486.1 (M+H).

Examples 636-656

Examples 636 – 656 were prepared from different benzyl bromides by using a procedure similar to that of Example 635 and summarized in Table 45.

Table 45: Compounds Prepared According to the Procedure of Example 635.

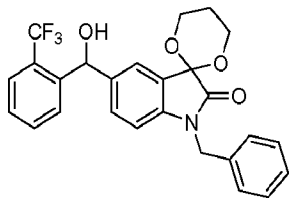
Example	Compound Name	MS
636	1'-benzyl-5'-{[2-(trifluoromethyl)phenyl]carbonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	(ES) *m/z* 468.1 (M+H)
637	1'-(3-fluorobenzyl)-5'-{[2-(trifluoromethyl)phenyl]carbonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	(ES) *m/z* 486.2 (M+H)
638	1'-(2-chlorobenzyl)-5'-{[2-(trifluoromethyl)phenyl]carbonyl}spiro[1,3-dioxane-	(ES) *m/z* 502.1 (M+H)

	2,3'-indol]-2'(1'H)-one	
639	1'-(4-chlorobenzyl)-5'-{[2-(trifluoromethyl)phenyl]carbonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	(ES) *m/z* 502.1 (M+H)
640	1'-(2-methylbenzyl)-5'-{[2-(trifluoromethyl)phenyl]carbonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	(ES) *m/z* 482.1 (M+H)
641	1'-(3-methylbenzyl)-5'-{[2-(trifluoromethyl)phenyl]carbonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	(ES) *m/z* 482.1 (M+H)
642	1'-(4-methylbenzyl)-5'-{[2-(trifluoromethyl)phenyl]carbonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	(ES) *m/z* 482.1 (M+H)
643	3-{[2'-oxo-5'-{[2-(trifluoromethyl)phenyl]carbonyl}spiro[1,3-dioxane-2,3'-indol]-1'(2'H)-yl]methyl}benzonitrile	(ES) *m/z* 493.1 (M+H)
644	4-{[2'-oxo-5'-{[2-(trifluoromethyl)phenyl]carbonyl}spiro[1,3-dioxane-2,3'-indol]-1'(2'H)-yl]methyl}benzonitrile	(ES) *m/z* 493.1 (M+H)
645	1'-[2-(trifluoromethoxy)benzyl]-5'-{[2-(trifluoromethyl)phenyl]carbonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	(ES) *m/z* 552.1 (M+H)
646	1'-[3-(trifluoromethoxy)benzyl]-5'-{[2-(trifluoromethyl)phenyl]carbonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	(ES) *m/z* 552.1 (M+H)
647	1'-[4-(trifluoromethoxy)benzyl]-5'-{[2-(trifluoromethyl)phenyl]carbonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	(ES) *m/z* 552.1 (M+H)
648	1'-[2-(trifluoromethyl)benzyl]-5'-{[2-(trifluoromethyl)phenyl]carbonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	(ES) *m/z* 536.1 (M+H)
649	1'-[3-(trifluoromethyl)benzyl]-5'-{[2-(trifluoromethyl)phenyl]carbonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	(ES) *m/z* 536.1 (M+H)
650	1'-[4-(trifluoromethyl)benzyl]-5'-{[2-(trifluoromethyl)phenyl]carbonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	(ES) *m/z* 536.1 (M+H)

651	1'-(4-fluorobenzyl)-5'-{[2-(trifluoromethyl)phenyl]carbonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	(ES) *m/z* 486.1 (M+H)
652	1'-(3-chlorobenzyl)-5'-{[2-(trifluoromethyl)phenyl]carbonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	(ES) *m/z* 502.0 (M+H)
653	2-{[2'-oxo-5'-{[2-(trifluoromethyl)phenyl]carbonyl}spiro[1,3-dioxane-2,3'-indol]-1'(2'H)-yl]methyl}benzonitrile	(ES) *m/z* 493.1 (M+H)
654	1'-(2-methoxybenzyl)-5'-{[2-(trifluoromethyl)phenyl]carbonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	(ES) *m/z* 498.1 (M+H)
655	1'-(3-methoxybenzyl)-5'-{[2-(trifluoromethyl)phenyl]carbonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	(ES) *m/z* 498.1 (M+H)
656	1'-(4-methoxybenzyl)-5'-{[2-(trifluoromethyl)phenyl]carbonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	(ES) *m/z* 498.2 (M+H)

Example 657

1'-benzyl-5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



The compound 1'-benzyl-5'-{[2-(trifluoromethyl)phenyl]carbonyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one one (0.24g, 0.51mmol) was dissolved in THF (5.00mL) and to this solution was added $NaBH_4$ (0.039g, 1.54mmol). After stirring for 1 hour, TLC analysis indicated reaction to be complete, so reaction mixture was diluted with EtOAc, washed with H_2O, followed by brine. Organic layer was dried over Na_2SO_4, concentrated and purified by flash chromatography on silica gel to afford product as a white solid (0.12g, 50%). ^1H NMR (400 MHz, $CDCl_3$): consistent; MS (ESI) *m/z* 470.2 (M+H).

Examples 658-677

Examples 658-678 were prepared from Examples 636-656 by using a procedure similar to that of Example 657 and are summarized in Table 46.

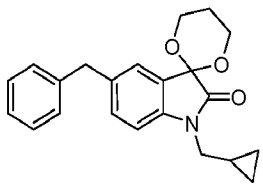
Table 46: Compounds Prepared According to the Procedure of Example 657.

Example	Compound Name	MS
658	1'-(2-fluorobenzyl)-5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 488.1 (M+H)
659	1'-(3-fluorobenzyl)-5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 488.2 (M+H)
660	1'-(4-fluorobenzyl)-5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 488.1 (M+H)
661	1'-(2-chlorobenzyl)-5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 504.1 (M+H)
662	1'-(3-chlorobenzyl)-5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 504.1 (M+H)
663	1'-(4-chlorobenzyl)-5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 504.1 (M+H)
664	5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}-1'-(2-methylbenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 484.1 (M+H)
665	5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}-1'-(3-methylbenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 484.2 (M+H)
666	5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}-1'-(4-methylbenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 484.2 (M+H)
667	3-{[5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'H)-yl]methyl}benzonitrile	MS (ESI) *m/z* 494.9 (M+H)
668	4-{[5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'H)-yl]methyl}benzonitrile	MS (ESI) *m/z* 495.1 (M+H)
669	5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}-1'-[2-	MS (ESI) *m/z* 554.2 (M+H)

	(trifluoromethoxy)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	
670	5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}-1'-[3-(trifluoromethoxy)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 554.1 (M+H)
671	5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}-1'-[4-(trifluoromethoxy)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 554.1 (M+H)
672	5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}-1'-[2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 538.1 (M+H)
673	5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}-1'-[3-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 538.0 (M+H)
674	5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}-1'-[4-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 538.1 (M+H)
675	5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}-1'-(2-methoxybenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 500.1 (M+H)
676	5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}-1'-(3-methoxybenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 500.1 (M+H)
677	5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}-1'-(4-methoxybenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 500.2 (M+H)

Example 678

1'-benzyl-5'-[2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one



The compound 1'-benzyl-5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one(0.098g, 0.21mmol) was dissolved in methylene chloride (3.00mL) and was then treated with Et_3SiH (0.040mL, 0.25mmol). This solution was cooled to 0° C before the drop wise addition of TFA (0.047mL, 0.63mmol). TLC analysis confirmed reaction was complete immediately after the addition of TFA, so reaction mixture was treated with $NaHCO_3$, and diluted with methylene chloride. Organic layer was separated, washed with brine, dried over Na_2SO_4 and purified by flash chromatography on silica gel to afford product as a clear, colorless oil (0.38g, 40%). ^1H NMR (400 MHz, $CDCl_3$): consistent; MS (ESI) *m/z* 454.1 (M+H).

Examples 679-695

Examples 679-695 were prepared from Examples 658-677 by using a procedure similar to that of Example 678 and are summarized in Table 47.

Table 47: Compounds Prepared According to the Procedure of Example 678.

Example	Compound Name	MS
679	1'-(2-fluorobenzyl)-5'-[2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 472.1 (M+H)
680	1'-(3-fluorobenzyl)-5'-[2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 472.1 (M+H)
681	1'-(4-fluorobenzyl)-5'-[2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 472.1 (M+H)
682	1'-(2-chlorobenzyl)-5'-[2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 488.1 (M+H)
683	1'-(3-chlorobenzyl)-5'-[2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 488.1 (M+H)
684	1'-(2-methylbenzyl)-5'-[2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 468.2 (M+H)

685	1'-(3-methylbenzyl)-5'-[2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 468.2 (M+H)
686	1'-(4-methylbenzyl)-5'-[2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 468.1 (M+H)
687	3-({2'-oxo-5'-[2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-1'(2'H)-yl}methyl)benzonitrile	MS (ESI) *m/z* 501.1 (M+Na)
688	4-({2'-oxo-5'-[2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-1'(2'H)-yl}methyl)benzonitrile	MS (ESI) *m/z* 479.2 (M+H)
689	1'-[2-(trifluoromethoxy)benzyl]-5'-[2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 538.1 (M+H)
690	1'-[4-(trifluoromethoxy)benzyl]-5'-[2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 538.1 (M+H)
691	5'-[2-(trifluoromethyl)benzyl]-1'-[3-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 522.2 (M+H)
692	5'-[2-(trifluoromethyl)benzyl]-1'-[4-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 522.1 (M+H)
693	1'-(2-methoxybenzyl)-5'-[2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 484.2 (M+H)
694	1'-(3-methoxybenzyl)-5'-[2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 484.1 (M+H)
695	1'-(4-methoxybenzyl)-5'-[2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one	MS (ESI) *m/z* 484.2 (M+H)

5

Example A

Functional Assessment of Human CB2 and CB1 Cannabinoid Receptor Activity

Cell Culture

CHO K1 cells expressing the human CB1 or CB2 receptor were cultured at 37° C, in Ham's F12 (Invitrogen 21765-037 or equivalent) containing 10% fetal bovine serum (US biotechnologies or the equivalent), 100 μg/ml penicillin and 100 μg/ml streptomycin (Gibco 10131-035), 400 μg/ml G418 (Gibco 10131-035).

Adherent cell culture cells were maintained by seeding at 2-3 x 10^6 cells in 30 mL medium in a T175.

For assays using frozen aliquots of cells, cells were thawed at 37° C, added to 15 mL complete medium, centrifuged at 1200 rpm for 2 minutes. The cell pellet was resuspended in 5 ml medium and then added to a T175 containing 25 ml of medium.

Frozen cells were also thawed as above and maintained in culture by adding the resuspended cells to 100 ml of medium in a sterilized 250 mL Erlenmeyer flask that was gassed with 5% CO_2, capped, and placed on an orbital shaker at low RPM (50-100).

cAMP Assay

Cells were lifted from the plate with dissociation buffer centrifuged and resuspended in a small volume of PBS. Cells were plated (15,000/well; 96 well plate, 7,500/well; 384 well plate) and incubated in the presence of 10 μM forskolin and compound in Krebs bicarbonate buffer (118 mM NaCl, 5 mM KCl, 1.2 mM $MgSO_4$, 2.4 mM $CaCl_2$, 1.2 mM KH_2PO_4, 25 mM $NaHCO_3$, 11.1 mM glucose) at 37° C for 30 minutes. cAMP content was determined using the HitHunter cAMP XS assay (Discoverx 90-0041, 90-0041L). For the antagonist assay, compound is incubated in the presence of 10 μM forskolin and 100nM WIN-55212-2 at 37 °C for 30 minutes.

The HitHunter assay was performed according to the manufacturer's instructions. Briefly, 20 μL cAMP antibody/lysis mix (1:1 ratio) were added to stimulated cells and incubated at room temperature for 1 hour. 20 μL of cAMP XS ED reagent was added and incubated at room temperature for 1 hour. 20 μL of cAMP XS EA reagent and 20 μL of CL substrate (1 part Galacton-Star, 5 parts Emerald-II, 19 parts substrate diluent) were added and then incubated at room temperature for 3 hours. Chemiluminescence was read on a Victor II at 1 s/well. A standard curve was also established with cAMP concentrations ranging from 10^{-10} to 10^{-5} M, diluted in Krebs.

Analysis of Results

For agonists activating Gi coupled receptors (i.e. those which couple to the inhibition of cAMP formation) results were expressed as % inhibition of forskolin stimulated cAMP levels. Raw

chemiluminescent data was converted to pMol cAMP using the standard curve and then % inhibition calculated as follows:

$$1 - \left(\frac{\text{Forskolin} - \text{Test}}{\text{Forskolin}} \right) \times 100$$

IC_{50} and EC_{50} values were calculated using Prism GraphPad using a 4-parameter logistic equation. An active agonist displays greater than 40% inhibition of cAMP. An antagonist typically displays greater than 40% reversal of 100 nM WIN55212-2 response.

EC_{50} values and binding constants for selected inventive compounds are provided in Table 48 below.

Table 48

Example	Ki (uM)	EC_{50} (nM)
1	0.258	34.126
2	0.368	97.426
3	0.557	149.662
4	0.607	149.138
5	0.087	189.131
6	0.938	967.818
7	3.754	—
8	0.235	78.213
9	0.670	748.837
10	0.368	97.426
11	0.201	92.826
12	0.484	404.448
13	0.591	1155.565
14	0.418	147.189
15	0.532	316.535
16	0.429	952.877
17	—	—
18	—	—
19	0.368	99.792
20	0.072	11.585
21	0.079	401.245
22	0.042	33.755
23	0.096	131.277
24	0.129	78.066
25	0.300	114.788
26	0.803	713.962

27	**0.042**	**62.589**
28	**0.114**	**324.425**
29	**2.067**	**1516.455**
30	**0.128**	**284.748**
31	**0.052**	**127.457**
32	**0.068**	**211.203**
33	**0.035**	**61.821**
34	**0.060**	**476.041**
35	**0.114**	**230.967**
36	**0.105**	**249.256**
37	**0.029**	**37.820**
38	**0.319**	**281.291**
39	**0.181**	**279.425**
40		
41	**0.086**	**7.416**
42	**0.164**	**26.892**
43	**0.437**	**55.390**
44	**0.057**	**8.489**
45	**0.103**	**100.521**
46	**2.434**	**2604.901**
47	**0.038**	**8.908**
48	**0.621**	**60.047**
49	**0.426**	**1252.521**
50	**0.080**	**14.464**
51	**0.154**	**167.789**
52	**3.322**	**1394.081**
53	**0.207**	**30.999**
54	**1.177**	**317.406**
55	**0.192**	**837.232**
56	**1.471**	**1845.162**
57	**1.458**	**66.736**
58	**0.466**	**220.469**
59	**0.208**	**22.840**
60	**0.107**	**117.954**
61	**0.272**	**150.478**
62	**0.547**	**881.044**
63	**0.084**	**82.977**
64	**0.080**	**132.177**
65	**0.549**	**1115.404**

66	0.214	300.469
67	0.273	477.716
68	1.587	8753.457
69	2.916	8135.851
70	0.067	111.948
71	0.101	251.980
72	0.089	129.378
73	0.670	950.646
74	0.564	15256.478
75	0.586	632.193
76	0.088	92.388
77	0.234	216.185
78		
79	0.014	9.324
80	0.065	24.084
81	0.098	38.520
82	0.287	116.453
83	0.084	149.766
84	0.986	442.848
85	0.035	15.655
86	0.094	13.352
87	0.314	82.417
88	0.044	22.356
89	0.073	57.791
90	0.463	371.701
91	0.083	63.691
92	0.264	526.424
93	1.325	—
94	0.163	48.471
95	0.081	70.849
96	0.017	3.745
97	0.026	7.255
98	0.071	50.705
99	0.042	5.380
100	0.067	5.195
101	0.202	49.480
102	0.075	3.315
103	0.118	32.070
104	0.731	141.925

105	**0.560**	**155.505**
106	**0.026**	**11.625**
107	**0.038**	**9.680**
108	**0.032**	**7.465**
109	**0.131**	**31.425**
110	**0.082**	**3.645**
111	**0.052**	**12.030**
112		
113	**0.013**	—
114	**0.019**	**6.339**
115	**0.015**	**2.976**
116	**0.013**	**7.207**
117	**0.042**	**10.064**
118	**0.031**	**7.637**
119	**0.670**	**62.465**
120	**0.304**	**17.539**
121	**0.063**	**8.055**
122	**0.072**	**6.922**
123	**0.144**	**14.869**
124	**0.671**	**535.068**
125	**0.291**	**66.114**
126	**0.077**	**3.149**
127	**0.113**	**4.766**
128	**0.100**	**56.616**
129	**0.092**	**11.498**
130	**0.045**	**12.802**
131	**0.081**	**28.932**
132	**0.402**	**6.934**
133	**0.901**	**52.040**
134	**0.099**	**210.149**
135	**0.717**	—
136	**0.410**	—
137	**0.423**	**1303.280**
138	**0.528**	—
139		
140	**0.026**	**49.518**
141		
142		
143		

144	**0.066**	**91.142**
145	**0.166**	**395.874**
146	**0.044**	**39.619**
147	**0.015**	**64.747**
148	**0.021**	**32.682**
149	**0.032**	**71.190**
150	**0.119**	**51.215**
151		
152		
153		
154		
155		
156		
157	**0.262**	—
158	**0.144**	**1774.399**
159	**0.375**	—
160	**0.661**	—
161	**0.040**	**228.183**
162	**0.019**	**6.339**
163	**0.015**	**2.976**
164	**0.009**	**75.979**
165	**0.013**	**7.207**
166		
167		
168		
169		
170	**0.018**	**21.423**
171	**0.058**	**17.834**
172	**0.011**	**6.350**
173	**0.033**	**6.637**
174	**0.058**	**916.308**
175	**0.129**	**965.312**
176	**0.006**	**13.208**
177	**0.058**	**17.834**
178		
179	**0.005**	—
180	**0.111**	—
181	**0.004**	—
182	**0.086**	—

183	0.007	—
184	0.039	—
185	1.200	142.512
186	1.332	265.841
187	1.101	22.452
188	3.176	614.855
189	—	103.527
190	0.486	—
191	3.986	1346.500
192	2.877	1829.752
193	4.936	—
194	1.775	294.813
195	—	—
196	—	—
197	0.770	1892.966
198	1.891	1182.523
199	1.421	394.607
200		103.527
201	1.796	—
202		
203	0.879	440.685
204		
205	0.334	193.870
206	0.252	405.092
207		
208	—	5335.404
209		
210	—	11435.629
211		
212		
213	0.007	5.950
214	0.404	382.001
215	0.072	—
216	0.031	140.791
217	0.211	309.577
218	0.039	8.970
219	0.016	30.148
220	0.054	—
221	0.007	2570.056

222	**0.021**	—
223	**0.006**	—
224		
225		
226	**0.004**	—
227	**0.025**	—
228	**0.036**	—
229	**0.255**	—
230	**0.037**	—
231	**0.145**	—
232	**0.352**	—
233	**0.007**	—
234	**0.458**	—
235	**0.411**	—
236	**0.006**	—
237	**0.006**	—
238	**0.004**	—
239	**0.039**	—
240	**0.503**	—
241	**0.055**	—
242	**0.037**	—
243	**0.130**	—
244	**0.125**	—
245	**0.064**	—
246	**0.075**	—
247	**0.014**	—
248	**0.253**	—
249	**0.029**	—
250	**0.028**	**45.883**
251	**0.068**	**82.402**
252		
253	**0.002**	**11.875**
254	**0.004**	**3.772**
255	**0.002**	**4.069**
256	**0.006**	**7.803**
257	**0.008**	**7.985**
258	**0.005**	**9.171**
259	**0.003**	**3.535**
260	**0.005**	**6.371**

261	**0.011**	**32.922**
262	**0.015**	**2.773**
263	**0.036**	—
264	**0.159**	—
265	**0.110**	—
266	**0.113**	—
267	**0.126**	—
268	**0.013**	—
269	**0.036**	—
270	**0.008**	—
271	**0.007**	—
272	**0.031**	—
273	**0.160**	—
274	**0.230**	—
275	**0.116**	—
276	**0.004**	—
277	**0.110**	—
278	**0.079**	—
279		
280	**0.020**	—
281	**0.030**	—
282	**0.716**	—
283	**0.067**	—
284	**0.126**	—
285	**0.012**	—
286	**0.014**	—
287	**0.049**	—
288	**0.096**	—
289	**0.179**	—
290	**0.066**	—
291	**0.005**	—
292	**0.005**	—
293	**0.028**	—
294	**0.043**	—
295	**0.011**	—
296		
297	**0.022**	—
298	**0.004**	—
299	**0.092**	—

300	0.022	—
301	0.012	—
302	0.002	—
303	0.003	—
304	0.002	—
305	0.007	—
306	0.020	—
307	0.017	—
308	0.003	—
309	0.018	—
310	0.019	—
311	0.004	—
312	0.517	377.048
313	0.161	46.520
314	0.424	54.813
315	3.235	1220.681
316	1.574	—
317	0.102	81.166
318	0.240	146.665
319	0.094	
320	0.01	1.479
321	0.201	0.193
322		>10.000
323	3.641	2.069
324		>10.000
325		>10.000
326	1.488	>10.000
327	3.059	1.233
328	0.272	0.232
329	0.052	0.248
330	0.044	0.084
331	0.041	0.051
332	0.168	0.125
333	0.102	0.149
334	0.076	0.12
335	4.156	>10.000
336	0.038	0.006
337	0.048	0.007
338	0.079	0.008

339	0.279	0.026
340	0.183	0.031
341		>10.000
342	0.08	0.084
343	0.015	0.027
344	0.022	0.034
345	0.009	0.022
346	0.023	0.042
347	0.008	0.014
348	0.103	0.328
349	0.023	0.026
350	0.239	0.221
351	0.004	0.01
352	0.004	0.008
353	0.003	0.009
354	0.046	0.103
355	0.006	0.008
356	0.08	0.025
357	0.036	0.005
358	0.408	1.773
359	2.334	>10.000
360		>10.000
361	0.003	0.012
362	0.003	0.064
363	0.011	0.058
364	0.093	1.901
365	0.446	0.346
366	0.389	0.406
367	0.599	0.303
368	1.352	0.717
369	0.66	0.558
370	0.425	0.593
371	0.915	>10.000
372		>10.000
373	0.002	0.008
374	0.002	0.009
375	0.002	0.009
376	0.004	0.009
377	0.007	0.009

378	0.501	0.77
379	0.029	0.033
380	0.046	0.1
381	0.075	0.077
382	0.087	0.124
383	0.081	0.139
384	1.588	>10.000
385	0.091	0.051
386	0.12	0.083
387	0.216	0.112
388	0.145	0.141
389	0.131	0.196
390		0.935
391	1.024	>10.000
392	0.54	1.334
393	0.014	0.015
394	0.028	0.831
395	0.047	0.02
396	0.041	0.202
397	0.07	0.04
398	2.471	>10.000
399	0.069	0.028
400	0.053	0.014
401	0.009	0.005
402	0.017	0.011
403	0.005	0.003
404	0.024	0.013
405	0.041	0.032
406	0.006	>10.000
407	0.089	0.324
408	0.017	>10.000
409	0.237	0.483
410	0.004	0.009
411	0.002	0.007
412	0.002	0.003
413	0.033	0.027
414	0.037	0.042
415	0.038	0.247
416	0.064	0.152

417	0.264	>10.000
418	0.138	0.259
419	0.16	>10.000
420	0.398	0.164
421	0.366	1.688
422		>10.000
423	0.002	>10.000
424	0.022	0.045
425	0.368	>10.000
426	0.056	>10.000
427	0.146	0.118
428	0.003	0.008
429	2.061	2.052
430	0.435	0.287
431	0.7	0.23
432	0.136	0.677
433	0.321	>10.000
434	0.137	>10.000
435	1.942	>10.000
436	0.94	>10.000
437		>10.000
438	0.107	0.254
439	0.034	2.705
440	0.037	2.26
441	0.315	0.606
442	0.082	0.325
443	0.168	0.334
444	0.061	>10.000
445	0.152	>10.000
446	0.062	>10.000
447	0.37	>10.000
448	0.177	>10.000
449	0.033	0.016
450	0.018	>10.000
451	0.024	>10.000
452	0.016	0.182
453	0.029	0.051
454	0.004	0.012
455	0.003	0.007

456	0.222	0.11
457	0.516	0.308
458	0.108	0.09
459	0.196	0.139
460	0.042	0.234
461	0.081	0.125
462	0.013	0.382
463	0.061	0.382
464	0.016	>10.000
465	0.359	>10.000
466	0.167	>10.000
467	1.446	3.312
468	0.017	0.058
469	0.004	>10.000
470	0.007	0.243
471	0.231	0.162
472	0.133	0.217
473	0.005	0.009
474	0.002	0.157
475	0.006	0.013
476	0.001	0.009
477	0.196	>10.000
478	0.031	0.028
479	0.036	0.085
480		>10.000
481	0.298	>10.000
482	1.755	>10.000
483	0.274	>10.000
484	0.159	0.505
485	0.083	0.222
486	0.396	>10.000
487	0.116	0.131
488	0.582	>10.000
489	1.321	>10.000
490	3.218	>10.000
491		>10.000
492	0.417	1.065
493	0.285	>10.000
494	0.334	>10.000

495	**0.057**	**0.058**
496	**0.119**	**0.103**
497	**0.008**	**0.013**
498	**0.409**	**0.345**
499	**1.157**	**>10.000**
500		**>10.000**
501	**0.014**	**0.016**
502	**1.383**	**0.373**
503	**3.964**	**>10.000**
504	**0.004**	**0.013**
505	**0.066**	**0.06**
506	**0.014**	**0.015**
507	**0.002**	**0.007**
508	**0.363**	**0.174**
509	**0.048**	**0.054**
510	**0.041**	**0.056**
511		**>10.000**
512	**0.39**	**0.509**
513	**1.075**	**>10.000**
514	**0.564**	**0.376**
515	**0.398**	**0.239**
516	**0.158**	**0.187**
517	**0.159**	**0.026**
518	**0.848**	**>10.000**
519	**0.347**	**0.37**
520	**0.771**	**>10.000**
521	**1.872**	**>10.000**
522	**1.402**	**>10.000**
523	**1.49**	**>10.000**
524	**1.398**	**0.968**
525	**0.889**	**1.802**
526	**0.772**	**1.166**
527	**1.089**	**1.297**
528	**1.578**	**3.658**
529	**1.212**	**>10.000**
530	**0.358**	**0.061**
531	**0.038**	**0.005**
532	**0.086**	**0.073**
533	**0.016**	**>10.000**

534	0.268	0.145
535	0.009	0.002
536	0.118	0.06
537	0.024	0.004
538	0.185	0.069
539	0.35	0.145
540	0.049	0.011
541	0.335	0.206
542	1.332	0.175
543		>10.000
544		4.404
545	0.301	0.072
546	0.093	0.012
547	0.855	0.31
548	0.538	0.143
549		>10.000
550	0.012	0.021
551	0.333	0.136
552	0.103	0.021
553	0.208	0.062
554	0.038	0.035
555	0.373	0.049
556	1.677	0.259
557	0.146	0.013
558		0.02
559	0.004	0.007
560	0.068	0.11
561	0.001	0.01
562	0.074	0.059
563	0.047	0.058
564	0.001	0.006
565	1.27	0.905
566	0.006	0.009
567	0.013	0.014
568	0.001	0.004
569	0.007	0.01
570	0.004	0.009
571	0.002	0.003
572	0.055	0.025

573	0.046	0.043
574		2.929
575	2.786	3.128
576	0.299	0.094
577	0.821	>10.000
578	1.373	0.051
579	0.486	0.596
580	0.106	0.118
581	0.008	0.025
582	0.007	0.021
583	0.006	0.004
584	0.18	1.882
585	0.006	0.019
586	0.002	0.014
587	0.037	0.056
588	0.178	>10.000
589	0.588	0.042
590	0.747	>10.000
591	0.048	0.059
592	0.692	1.602
593		>10.000
594	0.128	0.09
595	0.156	0.564
596	0.005	0.005
597	0.027	0.002
598		>10.000
599	0.035	0.169
600	0.022	0.021
601	0.028	0.098
602	0.002	0.014
603	0.001	0.009
604	0.054	0.081
605		2.901
606		2.252
607	0.828	>10.000
608	1.586	>10.000
609	1.1	0.427
610	0.417	1.384
611		>10.000

612	**0.006**	**0.334**
613	**0.163**	**0.139**
614	**0.017**	**0.039**
615	**0.007**	**0.02**
616	**0.008**	**0.014**
617	**0.126**	**1.875**
618	**0.005**	**0.08**
619	**0.004**	**0.007**
620	**0.052**	**0.073**
621	**0.07**	**>10.000**
622	**0.349**	**>10.000**
623	**0.03**	**>10.000**
624	**0.486**	**>10.000**
625	**0.063**	**0.038**
626	**0.09**	**>10.000**
627	**1.524**	**>10.000**
628		**>10.000**
629	**0.149**	**>10.000**
630	**0.004**	**0.009**
631	**0.04**	**0.007**
632	**0.023**	**0.108**
633	**0.114**	**0.136**
634	**0.007**	**0.012**
635	**0.079**	**0.362**
636	**0.056**	**0.194**
637	**0.066**	**0.112**
638	**0.331**	**>10.000**
639	**0.123**	**0.191**
640	**0.64**	**>10.000**
641	**0.786**	**>10.000**
642	**2.278**	**>10.000**
643		**>10.000**
644	**0.157**	**0.474**
645		**>10.000**
646		**>10.000**
647		**>10.000**
648		**>10.000**
649	**2.137**	**>10.000**
650		**>10.000**

651	0.009	0.05
652	0.218	0.599
653	3.631	>10.000
654	2.889	>10.000
655	2.015	>10.000
656		>10.000
657	0.142	0.097
658	0.234	>10.000
659	0.021	0.147
660	0.01	0.055
661	0.318	>10.000
662	0.226	>10.000
663	0.231	0.99
664	0.933	>10.000
665	0.403	>10.000
666	0.426	>10.000
667	0.394	>10.000
668	0.205	>10.000
669		>10.000
670	4.678	>10.000
671	2.636	>10.000
672		>10.000
673	0.357	>10.000
674	2.296	>10.000
675	4.421	>10.000
676	0.973	>10.000
677	0.996	>10.000
678	0.014	0.043
679	0.067	>10.000
680	0.023	0.062
681	0.003	0.023
682	0.097	>10.000
683	0.062	0.332
684	0.177	>10.000
685	0.184	>10.000
686	0.353	>10.000
687	0.085	0.625
688	0.077	0.525
689	0.379	>10.000

690	**0.252**	**>10.000**
691	**0.367**	**>10.000**
692	**1.039**	**>10.000**
693	**0.99**	**>10.000**
694	**0.349**	**>10.000**
695	**0.42**	**>10.000**

Example B

Assessment of Compound Affinity at the Human CB2 and CB1 Cannabinoid Receptors

Cell Culture and Membrane Preparation

CHO K1 cells expressing the human CB1 or CB2 receptor were cultured at 37 °C, in Ham's F12 (Invitrogen 21765-037 or equivalent) containing 10% fetal bovine serum (US biotechnologies or equivalent), 100 μg/mL penicillin and 100 μg/mL streptomycin (Gibco 10131-035), 400 μg/mL G418 (Gibco 10131-035).

Cells were harvested from plates by scraping in a small volume of ice-cold 20 mM HEPES, 20mM EDTA, pH 7.5. The cells were homogenized and pelleted by centrifugation at 100,000 g for 30 minutes at 4° C. Membranes were resuspended at a concentration of 1-5mg/mL.

Radioligand Binding Assay

30 μg Membranes were incubated in 0.5 mL binding buffer (50 mM Tris pH 5.7, 2.5 mM EDTA pH 8.0, 0.25% essentially fatty acid free BSA (Sigma A6003)) in the presence of 4 nM [^{3}H] SR141716 (CB1 antagonist) or 0.6 nM [^{3}H] CP 55,940 (non-selective agonist) nM and cold displacing ligand for 1 hour at 30° C. The assay was terminated by filtration on a brandel harvester through Whatman GFB filter paper, previously soaked in 0.15% polyethyleneamine. Samples were washed with 4 x 5 mL ice cold binding buffer and radioactivity was determined by liquid scintillation counting. Non-specific binding values were determined by either 1 μM CP 55, 940 or 1 μM WIN 55212-2.

Analysis of Results

IC_{50} values are calculated using GraphPad by fitting to a 1 or 2 site-binding model. Ki values are calculated from the apparent IC_{50} values using the Cheng-Prussof equation:

$$Ki = \frac{IC_{50}}{1 + ([L]/Kd)}$$

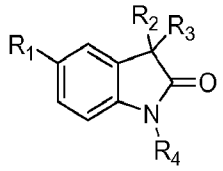
where [L] = concentration of free radioligand and Kd = dissociation constant of radioligand for the receptor.

Compounds in this invention were found to have CB2 IC_{50}s ranging from 0.062 to 20 μM.

Various modifications of the invention, in addition to those described herein, will be apparent to those skilled in the art from the foregoing description. Such modifications are also intended to fall within the scope of the appended claims. Each reference, including all patent, patent applications, and publications, cited in the present application is incorporated herein by reference in its entirety.

WHAT IS CLAIMED IS:

1. A compound of Formula I:



I

or pharmaceutically acceptable salts thereof, wherein:

R^1 is selected from $-(CH_2)_nR^a$, $-CH(OH)R^a$, $-CH(OR^b)R^a$, and $-C(O)R^a$, or is selected from OR^a, SR^a, SOR^a, SO_2R^a and NR^aR^b;

R^2 and R^3 are independently selected from H, halogen, OH, OR^a, OWR^a, C_{1-6} alkyl, and WC_{1-6} alkyl, wherein C_{1-6} alkyl or OR^a, is optionally substituted with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl;

or R^2 and R^3, together with the carbon atom to which they are attached, join to form a ring selected from 3-8 membered cycloalkyl, 3-8 membered heterocycloalkyl, C_5-C_7 oxycycloalkyl, C_{5-7} dioxycycloalkyl and oxazolidinyl ring, each ring optionally substituted with 1, 2, or 3 substituents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl;

R^4 is independently selected from H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n$-benzodioxane, $-(CH_2)_n$- oxazolidinone and $-(CH_2)_n$-C_{1-6} haloalkyl, each of which is optionally substituted with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, WC_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl;

at each occurrence W is $-(CH_2)_n$- or -C(O)-;

at each occurrence, R^a and R^b are independently selected from H, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, C_{3-8} cycloalkyl, C_{3-8} heterocycloalkyl, C_{3-8} heterocycloalkenyl C_{7-14} arylalkyl, C_{4-14} heteroarylalkyl, C_{5-12} cycloalkylalkyl and C_{5-12} heterocycloalkylalkyl, each of which is optionally substituted with OR^a, cyano, amino, halo, C_{1-6} alkyl, C_{6-10} aryl, C_{4-10} heteroaryl, C_{3-8} cycloalkyl, C_{3-8} heterocycloalkyl, C_{3-8} heterocycloalkenyl C_{7-14} arylalkyl, C_{4-14} heteroarylalkyl, C_{5-12} cycloalkylalkyl and C_{5-12} heterocycloalkylalkyl;

at each occurrence, halogen is selected from F, Cl, Br and I; and

at each occurrence, n is 0, 1, 2, or 3.

2. The compound of claim 1, wherein R^1 is $-N(R^a)R^b$; R^2 and R^3, together with the carbon atom to which they are attached, join to form a ring selected from 3-8 membered cycloalkyl, 3-8 membered heterocycloalkyl, C_5-C_7 oxycycloalkyl, C_{5-7} dioxycycloalkyl and oxazolidinyl ring, each ring optionally substituted with 1, 2, or 3 substituents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_1-$_6$ alkyl, C_2-$_6$ alkenyl, C_2-$_6$ alkynyl, C_{3-8} cycloalkyl, WC_{3-8} cycloalkyl, C_{6-10} aryl, C_{4-10} heteroaryl, -$(CH_2)_n$-benzodioxane, -$(CH_2)_n$-oxazolidinone and -$(CH_2)_n$-C_{1-6} haloalkyl, each of which is optionally substituted with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl.

3. The compound of claim 2, wherein R^1 is $-N(R^a)R^b$ and at least one of R^a and R^b are hydrogen or R^a and R^b, together with the N atom to which they are attached, join to form a 4-6 memebered heterocycloalkyl ring.

4. The compound of claim 2, wherein R^1 is a methylene radical -$(CH_2)_n$- further attached to substituents selected from C_{6-10} aryl, C_{4-10} heteroaryl, benzodioxanyl, oxazolidinonyl, -$(CH_2)_n$-C_{1-6} haloalkyl, C_{3-8} cycloalkyl and C_{1-6} haloalkyl, each of which is optionally substituted with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, and C_{1-6} haloalkyl, C_{3-8} cycloalkyl, WC_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl.

5. The compound of claim 1, wherein R^1 is $-OR^a$; R^2 and R^3, together with the carbon atom to which they are attached, join to form a ring selected from 3-8 membered cycloalkyl, 3-8 membered heterocycloalkyl, C_5-C_7 oxycycloalkyl, C_{5-7} dioxycycloalkyl and oxazolidinyl ring, each ring optionally substituted with 1, 2, or 3 substituents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{6-10} heteroaryl; and R^4 is independently selected from H, C_1-$_6$ alkyl, C_2-$_6$ alkenyl, C_2-$_6$ alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, -$(CH_2)_n$-benzodioxane, -$(CH_2)_n$- oxazolidinone, -$(CH_2)_n$-C_{1-6} haloalkyl, -$(CH_2)_n$-C_{3-8} cycloalkyl and C_{1-6} haloalkyl, each of which is optionally substituted with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl.

6. The compound of claim 5, wherein R^1 is -O-, substituted with substituents selected from C_1-$_6$ alkyl, C_2-$_6$ alkenyl, C_2-$_6$ alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, -$(CH_2)_n$-benzodioxane, -$(CH_2)_n$-oxazolidinone, each of which is optionally substituted with 1, 2, 3 or 4 substitutents

independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n-C_{3-8}$ cycloalkyl, $-(CH_2)_n-C_{3-8}$ heterocycloalkyl, $-(CH_2)_n-C_{1-6}$ haloalkyl, $-(CH_2)_n-$ and C_{1-6} haloalkyl.

7. The compound of claim 1, wherein R^1 is $-SR^a$; R^2 and R^3, together with the carbon atom to which they are attached, join to form a ring selected from 3-8 membered cycloalkyl, 3-8 membered heterocycloalkyl, C_5-C_7 oxycycloalkyl, C_{5-7} dioxycycloalkyl and oxazolidinyl ring, each ring optionally substituted with 1, 2, or 3 substituents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n$-benzodioxane, $-(CH_2)_n-$ oxazolidinone, $-(CH_2)_n-C_{1-6}$ haloalkyl, $-(CH_2)_n-C_{3-8}$ cycloalkyl and C_{1-6} haloalkyl, each of which is optionally substituted with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl.

8. The compound of claim 7, wherein R^1 is -S-, substituted with substituents selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n$-benzodioxane, $-(CH_2)_n$-oxazolidinone, each of which is optionally substituted with 1, 2, 3 or 4 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n-C_{3-8}$ cycloalkyl, $-(CH_2)_n-C_{3-8}$ heterocycloalkyl, $-(CH_2)_n-C_{1-6}$ haloalkyl, $-(CH_2)_n-$ and C_{1-6} haloalkyl.

9. The compound of claim 1, wherein R^1 is $-S(=O)R^a$; R^2 and R^3, together with the carbon atom to which they are attached, join to form a ring selected from 3-8 membered cycloalkyl, 3-8 membered heterocycloalkyl, C_5-C_7 oxycycloalkyl, C_{5-7} dioxycycloalkyl and oxazolidinyl ring, each ring optionally substituted with 1, 2, or 3 substituents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n$-benzodioxane, $-(CH_2)_n-$ oxazolidinone, $-(CH_2)_n-C_{1-6}$ haloalkyl, $-(CH_2)_n-C_{3-8}$ cycloalkyl and C_{1-6} haloalkyl, each of which is optionally substituted with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl.

10. The compound of claim 9, wherein R^1 is -S(=O)-, substituted with substituents selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n$-benzodioxane, $-(CH_2)_n$-oxazolidinone, each of which is optionally substituted with 1, 2, 3 or 4 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n$- C_{3-8} cycloalkyl, $-(CH_2)_n$- C_{3-8} heterocycloalkyl, $-(CH_2)_n$-C_{1-6} haloalkyl, $-(CH_2)_n$- and C_{1-6} haloalkyl.

11. The compound of claim 1, wherein R^1 is $-S(=O)(O)R^a$; R^2 and R^3, together with the carbon atom to which they are attached, join to form a ring selected from 3-8 membered cycloalkyl, 3-8 membered heterocycloalkyl, C_5-C_7 oxycycloalkyl, C_{5-7} dioxycycloalkyl and oxazolidinyl ring, each ring optionally substituted with 1, 2, or 3 substituents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n$-benzodioxane, $-(CH_2)_n$- oxazolidinone, $-(CH_2)_n$-C_{1-6} haloalkyl, $-(CH_2)_n$- C_{3-8} cycloalkyl and C_{1-6} haloalkyl, each of which is optionally substituted with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl.

12. The compound of claim 11, wherein R^1 is -S(=O)(O)-, substituted with substituents selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n$-benzodioxane, $-(CH_2)_n$-oxazolidinone, each of which is optionally substituted with 1, 2, 3 or 4 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n$- C_{3-8} cycloalkyl, $-(CH_2)_n$- C_{3-8} heterocycloalkyl, $-(CH_2)_n$-C_{1-6} haloalkyl, $-(CH_2)_n$- and C_{1-6} haloalkyl.

13. The compound of claim 1, wherein R^1 is $-C(=O)R^a$; R^2 and R^3, together with the carbon atom to which they are attached, join to form a ring selected from 3-8 membered cycloalkyl, 3-8 membered heterocycloalkyl, C_5-C_7 oxycycloalkyl, C_{5-7} dioxycycloalkyl and oxazolidinyl ring, each ring optionally substituted with 1, 2, or 3 substituents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n$-benzodioxane, $-(CH_2)_n$- oxazolidinone, $-(CH_2)_n$-C_{1-6} haloalkyl, $-(CH_2)_n$- C_{3-8} cycloalkyl and C_{1-6} haloalkyl, each of which is optionally substituted

with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl.

14. The compound of claim 13, wherein R^1 is -C(=O)- , substituted with substituents selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n$-benzodioxane, $-(CH_2)_n$-oxazolidinone, each of which is optionally substituted with 1, 2, 3 or 4 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n$- C_{3-8} cycloalkyl, $-(CH_2)_n$- C_{3-8} heterocycloalkyl, $-(CH_2)_n$-C_{1-6} haloalkyl, $-(CH_2)_n$- and C_{1-6} haloalkyl.

15. The compound of claim 13, wherein R^4 is $-(CH_2)_n$-C_{3-7} cycloalkyl or C_{6-10} aryl and C_{6-10} heteroaryl, wherein each of C_{6-10} aryl and C_{4-10} heteroaryl is substituted with 1-4 substituents selected from H, CN, OH, OR^a, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n$-C_{1-6} haloalkyl, $-(CH_2)_n$-, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl.

16. The compound of claim 13, wherein R^4 is $-(CH_2)$-cyclopropyl, OR^a, C_{6-10} aryl, C_{4-10} heteroaryl, substituted C_{6-10} aryl, or substituted C_{4-10} heteroaryl.

17. The compound of claim 13, wherein R^4 is C_{6-10} aryl or C_{4-10} heteroaryl substituted with 1, 2, 3 or 4 substitutents independently selected from halogen, CN, OH, OR^a and C_{1-6} alkyl.

18. The compound of claim 17, wherein R^a is C_{1-6} haloalkyl.

19. The compound of claim 17, wherein halogen or halogen of C_{1-6} haloalkyl is fluoro.

20. The compound of claim 17, wherein R^a is CF_3 or OCF_3.

21. The compound of claim 1, wherein R^1 is $-CH(OH)R^a$; R^2 and R^3, together with the carbon atom to which they are attached, join to form a ring selected from 3-8 membered cycloalkyl, 3-8 membered heterocycloalkyl, C_5-C_7 oxycycloalkyl, C_{5-7} dioxycycloalkyl and oxazolidinyl ring, each ring optionally substituted with 1, 2, or 3 substituents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-}

$_{10}$ aryl, C_{4-10} heteroaryl, -$(CH_2)_n$-benzodioxane, -$(CH_2)_n$- oxazolidinone, -$(CH_2)_n$-C_{1-6} haloalkyl, -$(CH_2)_n$- C_{3-8} cycloalkyl and C_{1-6} haloalkyl, each of which is optionally substituted with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl.

22. The compound of claim 21, wherein R^1 is -CH(OH)-, substituted with substituents selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, -$(CH_2)_n$-benzodioxane, -$(CH_2)_n$-oxazolidinone, each of which is optionally substituted with 1, 2, 3 or 4 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{6-10} aryl, C_{4-10} heteroaryl, -$(CH_2)_n$- C_{3-8} cycloalkyl, -$(CH_2)_n$- C_{3-8} heterocycloalkyl, -$(CH_2)_n$-C_{1-6} haloalkyl, -$(CH_2)_n$- and C_{1-6} haloalkyl.

23. The compound of claim 21, wherein R^4 is -$(CH_2)_n$-C_{3-7} cycloalkyl, C_{6-10} aryl or C_{6-10} heteroaryl, wherein each of C_{6-10} aryl and C_{4-10} heteroaryl is substituted with 1-4 substituents selected from H, CN, OH, OR^a, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, -$(CH_2)_n$-C_{1-6} haloalkyl, -$(CH_2)_n$-, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl.

24. The compound of claim 21, wherein R^4 is -(CH_2)-cyclopropyl, OR^a, C_{6-10} aryl, C_{4-10} heteroaryl, substituted C_{6-10} aryl, or substituted C_{4-10} heteroaryl.

25. The compound of claim 21, wherein R^4 is C_{6-10} aryl or C_{4-10} heteroaryl substituted with 1, 2, 3 or 4 substitutents independently selected from halogen, CN, OH, OR^a and C_{1-6} alkyl.

26. The compound of claim 25, wherein R^a is C_{1-6} haloalkyl.

27. The compound of claim 25, wherein halogen or halogen of C_{1-6} haloalkyl is fluoro.

28. The compound of claim 25, wherein R^a is CF_3 or OCF_3.

29. The compound of claim 1, wherein R^1 is -$CH(OR^b)R^a$; R^2 and R^3, together with the carbon atom to which they are attached, join to form a ring selected from 3-8 membered cycloalkyl, 3-8 membered heterocycloalkyl, C_5-C_7 oxycycloalkyl, C_{5-7} dioxycycloalkyl and oxazolidinyl ring, each ring optionally substituted with 1, 2, or 3 substituents independently

selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n$-benzodioxane, $-(CH_2)_n$- oxazolidinone, $-(CH_2)_n$-C_{1-6} haloalkyl, $-(CH_2)_n$- C_{3-8} cycloalkyl and C_{1-6} haloalkyl, each of which is optionally substituted with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl.

30. The compound of claim 29, wherein R^1 is $-CH(OR^b)-$, substituted with substituents selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n$-benzodioxane, $-(CH_2)_n$-oxazolidinone, each of which is optionally substituted with 1, 2, 3 or 4 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n$- C_{3-8} cycloalkyl, $-(CH_2)_n$- C_{3-8} heterocycloalkyl, $-(CH_2)_n$-C_{1-6} haloalkyl, $-(CH_2)_n$- and C_{1-6} haloalkyl.

31. The compound of claim 1, wherein R^1 is $-(CH_2)_n-$; R^2 and R^3, together with the carbon atom to which they are attached, join to form a ring selected from 3-8 membered cycloalkyl, 3-8 membered heterocycloalkyl, C_5-C_7 oxycycloalkyl, C_{5-7} dioxycycloalkyl and oxazolidinyl ring, each ring optionally substituted with 1, 2, or 3 substituents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n$-benzodioxane, $-(CH_2)_n$- oxazolidinone, $-(CH_2)_n$-C_{1-6} haloalkyl, $-(CH_2)_n$- C_{3-8} cycloalkyl and C_{1-6} haloalkyl, each of which is optionally substituted with 1, 2, or 3 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl.

32. The compound of claim 31, wherein R^1 is $-(CH_2)_n-$, substituted with substituents selected from C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n$-benzodioxane, $-(CH_2)_n$-oxazolidinone, each of which is optionally substituted with 1, 2, 3 or 4 substitutents independently selected from halogen, CN, OH, OR^a, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{4-10} heteroaryl; and R^4 is independently selected from H, C_{1-6} alkyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n$- C_{3-8} cycloalkyl, $-(CH_2)_n$- C_{3-8} heterocycloalkyl, $-(CH_2)_n$-C_{1-6} haloalkyl, $-(CH_2)_n$- and C_{1-6} haloalkyl.

33. The compound of claim 31, wherein R^4 is $-(CH_2)_n$-C_{3-7} cycloalkyl or C_{6-10} aryl and C_{4-10} heteroaryl, wherein each of C_{6-10} aryl and C_{4-10} heteroaryl is substituted with 1-4

substituents selected from H, CN, OH, OR^a, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{6-10} aryl, C_{4-10} heteroaryl, $-(CH_2)_n-C_{1-6}$ haloalkyl, $-(CH_2)_n-$, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{6-10} aryl and C_{6-10} heteroaryl.

34. The compound of claim 31, wherein R^4 is $-(CH_2)$-cyclopropyl, OR^a, C_{6-10} aryl, C_{6-10} heteroaryl, substituted C_{6-10} aryl, or substituted C_{4-10} heteroaryl.

35. The compound of claim 31, wherein R^4 is C_{6-10} aryl or C_{4-10} heteroaryl substituted with 1, 2, 3 or 4 substitutents independently selected from halogen, CN, OH, OR^a and C_{1-6} alkyl.

36. The compound of claim 35, wherein R^a is C_{1-6} haloalkyl.

37. The compound of claim 35, wherein halogen or halogen of C_{1-6} haloalkyl is fluoro.

38. The compound of claim 35, wherein R^a is CF_3 or OCF_3.

39. A compound selected from: 5'-benzoyl-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2-fluorobenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(3-fluorobenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(4-fluorobenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[3-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[3-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[4-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2-methoxybenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(3-methoxybenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(4-methoxybenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(2-chlorobenzoyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(3-chlorobenzoyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(4-chlorobenzoyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(3-methylbenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(4-methylbenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[3-(trifluoromethoxy)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[4-(trifluoromethoxy)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(3-furoyl)spiro[1,3-dioxane-2,3'-

indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(3-thienylcarbonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2-methylbenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[4-fluoro-2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[5-fluoro-2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-[4-chloro-2-(trifluoromethyl)benzoyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2,3-difluorobenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(cyclopropylmethyl)-5'-(2,5-difluorobenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(3-chloro-4-fluorobenzoyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2,3-dichlorobenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2,5-dichlorobenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(3,4-dichlorobenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2,3-dimethoxybenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2-methoxy-5-methylbenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(5-chloro-2-methoxybenzoyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(5-fluoro-2-methoxybenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2,3-dimethylbenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2,6-dimethylbenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(5-chloro-2-methylbenzoyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[2-(trifluoromethoxy)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2,4-difluorobenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2,6-dimethoxybenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[hydroxy(phenyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[(2-fluorophenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[(3-fluorophenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[(4-fluorophenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 2-[5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}-2'-oxospiro[1,3-dioxane-2,3'- indol]-1'(2'H)-yl]benzonitrile, (-)-2-[5'-{(S)-hydroxy[2-(trifluoromethyl)phenyl]methyl}-2'-oxospiro[1,3-dioxane- 2,3'-indol]-1'(2'H)-yl]benzonitrile, (+)2-[5'-{(R)-hydroxy[2-(trifluoromethyl)phenyl]methyl}-2'-oxospiro[1,3-dioxane- 2,3'-indol]-1'(2'H)-yl]benzonitrile, (+)-1'-(3,4-difluorophenyl)-5'-{(R)-hydroxy[2-(trifluoromethyl)phenyl]-methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, (-)-1'-(3,4-difluorophenyl)-5'-{(S)-hydroxy[2-(trifluoromethyl)phenyl]-methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(cyclopropylmethyl)-5'-{1-hydroxy-1-[2-(trifluoromethyl)phenyl]ethyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(3,4-

difluorophenyl)-5'-{1-hydroxy-1-[2-(trifluoromethyl)phenyl]ethyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(cyclopropylmethyl)-5'-{hydroxy[2-(trifluoromethyl)phenyl]methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-{hydroxy[3-(trifluoromethyl)phenyl]methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-{hydroxy[4-(trifluoromethyl)phenyl]methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[hydroxy(2-methoxyphenyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[hydroxy(3-methoxyphenyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[hydroxy(4-methoxyphenyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-[(2-chlorophenyl)(hydroxy)methyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-[(3-chlorophenyl)(hydroxy)methyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-[(4-chlorophenyl)(hydroxy)methyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[hydroxy(3-methylphenyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[hydroxy(4-methylphenyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-{hydroxy[3-(trifluoromethoxy)phenyl]methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-{hydroxy[4-(trifluoromethoxy)phenyl]methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[3-furyl(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[hydroxy(3-thienyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[hydroxy(2-methylphenyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-{[4-fluoro-2-(trifluoromethyl)phenyl](hydroxy)methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-{[5-fluoro-2-(trifluoromethyl)phenyl](hydroxy)methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-{[4-chloro-2-(trifluoromethyl)phenyl](hydroxy)methyl}-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[(2,3-difluorophenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[(2,5-difluorophenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-[(3-chloro-4-fluorophenyl)(hydroxy)methyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[(2,3-dichlorophenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[(2,5-dichlorophenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[(3,4-dichlorophenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[(2,3-dimethoxyphenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-

(cyclopropylmethyl)-5'-[hydroxy(2-methoxy-5-methylphenyl)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-[(5-chloro-2-methoxyphenyl)(hydroxy)methyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[(5-fluoro-2-methoxyphenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[(2,3-dimethylphenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[(2,6-dimethylphenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-[(5-chloro-2-methylphenyl)(hydroxy)methyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-{hydroxy[2-(trifluoromethoxy)phenyl]methyl}spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[(2,4-difluorophenyl)(hydroxy)methyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-benzyl-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2-fluorobenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(3-fluorobenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(4-fluorobenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[3-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[4-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2-methoxybenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(3-methoxybenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(4-methoxybenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(2-chlorobenzyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(3-chlorobenzyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(4-chlorobenzyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(3-methylbenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(4-methylbenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[4-(trifluoromethoxy)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(3-thienylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2-methylbenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[4-fluoro-2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[5-fluoro-2-(trifluoromethyl)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-[4-chloro-2-(trifluoromethyl)benzyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2,3-difluorobenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2,5-difluorobenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(3-chloro-4-fluorobenzyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2,3-dichlorobenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2,5-

dichlorobenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(3,4-dichlorobenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2,3-dimethoxybenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2-methoxy-5-methylbenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(5-chloro-2-methoxybenzyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(5-fluoro-2-methoxybenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2,3-dimethylbenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(5-chloro-2-methylbenzyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-[2-(trifluoromethoxy)benzyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(cyclopropylmethyl)-5'-(2,4-difluorobenzyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-phenyl-5'-[2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-benzoyl-1'-phenylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(2-fluorobenzoyl)-1'-phenylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(2-methoxybenzoyl)-1'-phenylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(2-chlorobenzoyl)-1'-phenylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(2-methylbenzoyl)-1'-phenylspiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 2-(5'-benzoyl-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl)benzonitrile, 2-[5'-(2-fluorobenzoyl)-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl]benzonitrile, 2-{2'-oxo-5'-[2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl}benzonitrile, 2-[5'-(2-methoxybenzoyl)-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl]benzonitrile, 2-[5'-(2-chlorobenzoyl)-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl]benzonitrile, 5'-benzoyl-1'-(3,4-difluorophenyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(3,4-difluorophenyl)-5'-(2-fluorobenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(3,4-difluorophenyl)-5'-[2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(3,4-difluorophenyl)-5'-(2-methoxybenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(2-chlorobenzoyl)-1'-(3,4-difluorophenyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(3,4-difluorophenyl)-5'-(2-methylbenzoyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(2,5-difluorophenyl)-5'-[2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(2-chlorobenzoyl)-1'-(2,5-difluorophenyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(3-thienyl)-5'-[2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-(2-chlorobenzoyl)-1'-(3-thienyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 2-[5'-(2-methylbenzoyl)-2'-oxospiro[1,3-dioxane-2,3'-indol]-1'(2'*H*)-yl]benzonitrile,

5'-benzoyl-1'-(3,3,3-trifluoropropyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-propyl-5'-[2-(trifluoromethyl)benzoyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(3,4-Difluorophenyl)-5'-phenethylspiro[[1,3]dioxane-2,3'-indolin]-2'-one, 5'-(Benzylamino)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(2-furylmethyl)amino]spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(2-

thienylmethyl)amino]spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 5'-{[(5-Chloro-2-thienyl)methyl]amino}-1'-(cyclopropylmethyl)spiro[1,3-dioxane- 2,3'-indol]-2'(1'H)-one, 5'-{[(2-Butyl-1-benzofuran-3-yl)methyl]amino}-1'-(cyclopropylmethyl)spiro[1,3- dioxane-2,3'-indol]-2'(1'H)-one, 5'-[(4-Chlorobenzyl)amino]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(4-methoxybenzyl)amino]spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(4-methylbenzyl)amino]spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(3,4-dichlorobenzyl)amino]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 5'-[(3-Chlorobenzyl)amino]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-{[4-(trifluoromethyl)benzyl]amino}spiro[1,3-dioxane- 2,3'-indol]-2'(1'H)-one, 5'-{[4-Chloro-3-(trifluoromethyl)benzyl]amino}-1'-(cyclopropylmethyl)spiro[1,3- dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(1-naphthylmethyl)amino]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(2,3-dihydro-1,4-benzodioxin-6- ylmethyl)amino]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(4-fluorobenzyl)amino]spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 5'-[(1-Benzothiophen-2-ylmethyl)amino]-1'-(cyclopropylmethyl)spiro[1,3-dioxane- 2,3'-indol]-2'(1'H)-one,

5'-[Bis(cyclohexylmethyl)amino]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(dimethylamino)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-Butyl-5'-(methylamino)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[methyl(phenyl)amino]spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-piperidin-1-ylspiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 5'-(Phenylthio)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 5'-(Phenylsulfinyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 5'-(Phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 5'-(Phenylthio)spiro[1,3-dioxolane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(phenylthio)spiro[1,3-dioxolane-2,3'-indol]-2'(1'H)-one, 5'-(Phenylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(phenylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]- 2'(1'H)-one, 1'-Phenyl-5'-(phenylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'H)-one, 5'-(Phenylsulfonyl)-1'-[3-(trifluoromethyl)phenyl]spiro[1,3-dioxolane-2,3'- indol]-2'(1'H)-one, 1'-(3,4-Difluorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxolane-2,3'-indol]-2'(1'H)-one, 1'-Phenyl-5'-(phenylthio)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-Phenyl-5'-(phenylthio)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(3,4-Difluorophenyl)-5'-(phenylthio)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-Phenyl-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 5'-(Phenylsulfonyl)-1'-[3-(trifluoromethyl)phenyl]spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 1'-(3,4-difluorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(2,5-difluorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-

2,3'-indol]-2'(1'H)-one, 1'-(3-fluorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(3,5-dichlorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(3-chloro-4-fluorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(4-chlorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 5'-(phenylsulfonyl)-1'-[2-(trifluoromethyl)phenyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(2-methoxyphenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(4-fluorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(2,3-difluorophenyl)-5'-(phenylsulfonyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(phenylsulfinyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 5'-(Phenylthio)-1'-(2,2,2-trifluoroethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(phenylthio)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(2-fluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(2-methoxyphenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 5'-[(2-Chlorophenyl)sulfonyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 5'-[(3-Chlorophenyl)sulfonyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(2-methylphenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(3-fluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(4-fluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-{[2-(trifluoromethyl)phenyl]sulfinyl}spiro[1,3- dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(2,5-dichlorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 5'-[(4-Chlorophenyl)sulfonyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(3-methoxyphenyl)sulfonyl]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(3,4-dichlorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(3-methylphenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(4-methoxyphenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 5'-(1,3-Benzothiazol-2-ylsulfonyl)-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(3,4-difluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(pyridin-4-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(pyridin-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(pyridin-4-ylthio)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(3,4-dichlorophenyl)thio]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(3,4-difluorophenyl)thio]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-{[3-(trifluoromethyl)phenyl]sulfanyl}spiro[1,3- dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(pyridin-2-ylsulfanyl)spiro[1,3-dioxane-2,3'-

indol]- 2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(pyridin-4-ylsulfinyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(pyridin-2-ylsulfinyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(3,4-difluorophenyl)sulfinyl]-spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(pyridin-3-ylsulfanyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(4-methylphenyl)sulfanyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-{[4-(trifluoromethyl)phenyl]sulfanyl}spiro[1,3- dioxane-2,3'-indol]-2'(1'H)-one, 5'-[(3-Chloro-4-fluorophenyl)sulfanyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane- 2,3'-indol]-2'(1'H)-one, 5'-[(6-Chloropyridin-3-yl)sulfanyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(naphthalen-1-ylsulfanyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(thiophen-2-ylsulfanyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(5-methyl-2-thienyl)thio]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 5'-[(5-Acetyl-2-thienyl)thio]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 5'-[(2-Chloropyridin-4-yl)thio]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(3,5-dichlorophenyl)thio]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(3,5-dichloropyridin-4-yl)thio]spiro[1,3-dioxane- 2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(2,4-dichlorophenyl)thio]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(2,5-dichlorophenyl)thio]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 5'-[(4-Chloro-2-fluorophenyl)thio]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(2,4-difluorophenyl)thio]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(pyridin-3-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-{[3-(trifluoromethyl)phenyl]sulfonyl}spiro[1,3- dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(4-methylphenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-{[4-(trifluoromethyl)phenyl]sulfonyl}spiro[1,3- dioxane-2,3'-indol]-2'(1'H)-one, 5'-[(3-Chloro-4-fluorophenyl)sulfonyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane- 2,3'-indol]-2'(1'H)-one, 5'-[(6-Chloropyridin-3-yl)sulfonyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane- 2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(naphthalen-1-ylsulfonyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(thiophen-2-ylsulfonyl)spiro[1,3-dioxane-2,3'-indol]- 2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(5-methyl-2-thienyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 5'-[(5-Acetyl-2-thienyl)sulfonyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 5'-[(2-Chloropyridin-4-yl)sulfonyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane- 2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(3,5-dichlorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(3,5-dichloropyridin-4-yl)sulfonyl]spiro[1,3-dioxane-

2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(2,4-dichlorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 5'-[(4-Chloro-2-fluorophenyl)sulfonyl]-1'-(cyclopropylmethyl)spiro[1,3-dioxane- 2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(2,4-difluorophenyl)sulfonyl]spiro[1,3-dioxane-2,3'- indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(4-methoxyphenoxy)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-(4-methoxyphenoxy)spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(2,6-difluoropyridin-4-yl)oxy]spiro[1,3-dioxane-2,3'-indol]-2'(1'H)-one, 1'-(Cyclopropylmethyl)-5'-[(2,3,5,6-tetrafluoropyridin-4-yl)oxy]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-[(3-Chloro-2,5,6-trifluoropyridin-4-yl)oxy]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(Cyclopropylmethyl)-5'-[(3,5-difluoro-2,6-dimethoxypyridin-4-yl)oxy]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 5'-[(3-Chloro-5-fluoro-2,6-dimethoxypyridin-4-yl)oxy]-1'-(cyclopropylmethyl)spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one, 1'-(Cyclopropylmethyl)-5'-[(2,3,5-trifluoro-6-methoxypyridin-4-yl)oxy]spiro[1,3-dioxane-2,3'-indol]-2'(1'*H*)-one and pharmaceutically acceptable salts thereof.

40. A pharmaceutical composition comprising a compound of any one of claims 1 to 39, or pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable carrier.

41. A method for treating a CB2-mediated disorder, comprising administering to a subject in need thereof an effective amount of a compound of any one of claims 1 to 39, or a pharmaceutically acceptable salt thereof.

42. The method of claim 41, wherein the CB2-mediated disorder is pain, osteoarthritis, atherosclerosis, osteoporosis, or cancer.

43. The method of claim 42, wherein said cancer is glioma.

44. A method for reducing pain in a subject, comprising administering to the subject an effective amount of a compound of any one of claims 1 to 39, or a pharmaceutically acceptable salt thereof.

45. The method of claim 44, wherein the pain is inflammatory pain, post surgical pain, neuropathic pain, or bone pain.

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2009/067981

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D491/10 A61K31/407
ADD.

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 practical, search terms used)
EPO-Internal, CHEM ABS Data, WPI Data, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2005/250798 A1 (DOLLINGS, PAUL JEFFREY ET AL) 10 November 2005 (2005-11-10) page 11 - page 12; the compounds of the general formulae III, V and VI page 17; the compounds of the general formula XIX page 35, paragraph [0393] - paragraph [0396 page 36, paragraph [0404] - paragraph [0407] page 40, paragraph [0436] - paragraph [0437] page 44, paragraph [0472] page 48, paragraph [0494] page 56, paragraph [0551] - paragraph [0552] page 57, paragraph [0555] - paragraph [0556] ----- -/--	1-3,5-14

[X] Further documents are listed in the continuation of Box C.

[X] 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

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"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	Date of mailing of the international search report
14 April 2010	02/06/2010

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Fink, Dieter

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2009/067981

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

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X	WO 00/66556 A1 (AMERICAN HOME PRODUCTS CORPORATION, USA; LIGAND PHARMACEUTICALS, INC.) 9 November 2000 (2000-11-09) page 106 - page 108; claim 1 page 120 - page 121; claims 13-17 page 34 - page 36; examples 11,12	1,4, 31-34, 40-42
X	WO 95/13807 A1 (PATHOGENESIS CORP., USA) 26 May 1995 (1995-05-26) figure 2; the compounds 6, 7 and 12-14 page 58; example 98B page 61 - page 62; example 100A	1,4,13, 14,21, 22,31,32
X	WO 94/29272 A1 (ASTRA AB, SWED.) 22 December 1994 (1994-12-22) page 36 - page 37; claim 7, the compounds of the general formulae (4) and (5) page 16 - page 18; examples 6,10 page 24; example 27 page 27 - page 28; examples 39,40	1-6,31, 32
X	WO 93/12085 A1 (AKTIEBOLAGET ASTRA, SWED.) 24 June 1993 (1993-06-24) page 58 - page 59; claim 10, the compounds of the general formulae (5) and (6) page 46 - page 47; examples 93-95	1-6,31, 32
X	EP 0 249 407 A2 (PFIZER CORP., PANAMA) 16 December 1987 (1987-12-16) page 6; example 5(A)	1-3
X	GB 1 366 133 A (WYETH JOHN & BROTHER LTD) 11 September 1974 (1974-09-11) page 22; claim 34, the compounds of the general formulae (IV) and (V) page 14; example 32b	1,4,5,31
X	DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 2002, ZHUNGHIETU, GRIGORE: "Isatin .beta.-ethylene ketals as psychotropics" XP002577715 retrieved from STN Database accession no. 2002:619487 the abstract and the compounds with the Registry-Numbers [75822-56-9], [479630-37-0], and [479630-39-2] & ZHUNGHIETU, GRIGORE: "Isatin .beta.-ethylene ketals as psychotropics" REVUE ROUMAINE DE CHIMIE, CODEN: RRCHAX; ISSN: 0035-3930, vol. 46, no. 5, 2002, pages 517-520, -/--	1,5,6,40

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2009/067981

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DIAZ, PHILIPPE ET AL: "Design and Synthesis of a Novel Series of N-Alkyl Isatin Acylhydrazone Derivatives that Act as Selective Cannabinoid Receptor 2 Agonists for the Treatment of Neuropathic Pain" JOURNAL OF MEDICINAL CHEMISTRY, CODEN: JMCMAR; ISSN: 0022-2623, vol. 51, no. 16, 28 August 2008 (2008-08-28), pages 4932-4947, XP002577716 the whole document	1-45

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2009/067981

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