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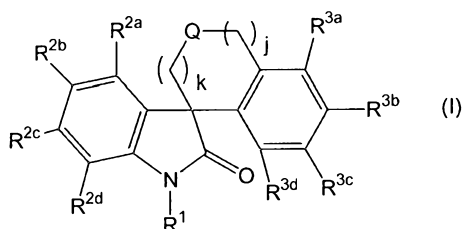
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(54) Title: USE OF SPIRO-OXINDOLE COMPOUNDS AS THERAPEUTIC AGENTS



(57) Abstract: This invention is directed to methods of using spiro-oxindole compounds of formula (I); wherein k, j, Q, R¹, R^{2a}, R^{2b}, R^{2c}, R^{2d}, R^{3a}, R^{3b}, R^{3c}, and R^{3d} are as defined herein, as a stereoisomer, enantiomer, tautomer thereof or mixtures thereof; or a pharmaceutically acceptable salt, solvate or prodrug thereof, for the treatment and/or prevention of hypercholesterolemia, benign prostatic hyperplasia, pruritis and cancer.

USE OF SPIRO-OXINDOLE COMPOUNDS AS THERAPEUTIC AGENTS

FIELD OF THE INVENTION

The present invention is directed to methods of using spiro-oxindole compounds as therapeutic agents. In particular, this invention is directed to the use of
5 certain spiro-oxindole compounds in treating diseases or conditions such as hypercholesterolemia, benign prostatic hyperplasia, pruritis and cancer.

BACKGROUND OF THE INVENTION

Voltage-gated sodium channels, transmembrane proteins that initiate action potentials in nerve, muscle and other electrically excitable cells, are a necessary
10 component of normal sensation, emotions, thoughts and movements (Catterall, W.A., *Nature* (2001), Vol. 409, pp. 988-990). These channels consist of a highly processed alpha subunit that is associated with auxiliary beta subunits. The pore-forming alpha subunit is sufficient for channel function, but the kinetics and voltage dependence of channel gating are in part modified by the beta subunits (Goldin et al., *Neuron* (2000),
15 Vol. 28, pp. 365-368). Each alpha-subunit contains four homologous domains, I to IV, each with six predicted transmembrane segments. The alpha-subunit of the sodium channel, forming the ion-conducting pore and containing the voltage sensors regulating sodium ion conduction has a relative molecular mass of 260,000. Electrophysiological recording, biochemical purification, and molecular cloning have identified ten different
20 sodium channel alpha subunits and four beta subunits (Yu, F.H., et al., *Sci. STKE* (2004), 253; and Yu, F.H., et al., *Neurosci.* (2003), 20:7577-85).

The hallmarks of sodium channels include rapid activation and inactivation when the voltage across the plasma membrane of an excitable cell is depolarized (voltage-dependent gating), and efficient and selective conduction of sodium ions
25 through conducting pores intrinsic to the structure of the protein (Sato, C., et al., *Nature* (2001), 409:1047-1051). At negative or hyperpolarized membrane potentials, sodium channels are closed. Following membrane depolarization, sodium channels open rapidly and then inactivate. Channels only conduct currents in the open state and, once inactivated, have to return to the resting state, favoured by membrane
30 hyperpolarization, before they can reopen. Different sodium channel subtypes vary in the voltage range over which they activate and inactivate as well as their activation and inactivation kinetics.

The sodium channel family of proteins has been extensively studied and shown

to be involved in a number of vital body functions. Research in this area has identified variants of the alpha subunits that result in major changes in channel function and activities, which can ultimately lead to major pathophysiological conditions. Implicit with function, this family of proteins are considered prime points of therapeutic
5 intervention. Na_v1.1 and Na_v1.2 are highly expressed in the brain (Raymond, C.K., et al., *J. Biol. Chem.* (2004), 279(44):46234-41) and are vital to normal brain function. In humans, mutations in Na_v1.1 and Na_v1.2 result in severe epileptic states and in some cases mental decline (Rhodes, T.H., et al., *Proc. Natl. Acad. Sci. USA* (2004), 101(30):11147-52; Kamiya, K., et al., *J. Biol. Chem.* (2004), 279(11):2690-8;
10 Pereira, S., et al., *Neurology* (2004), 63(1):191-2). As such both channels have been considered as validated targets for the treatment of epilepsy (see PCT Published Patent Publication No. WO 01/38564).

Na_v1.3 is broadly expressed throughout the body (Raymond, C.K., et al., *op. cit.*). It has been demonstrated to have its expression upregulated in the dorsal horn
15 sensory neurons of rats after nervous system injury (Hains, B.D., et al., *J. Neurosci.* (2003), 23(26):8881-92). Many experts in the field have considered Na_v1.3 as a suitable target for pain therapeutics (Lai, J., et al., *Curr. Opin. Neurobiol.* (2003), (3):291-7; Wood, J.N., et al., *J. Neurobiol.* (2004), 61(1):55-71; Chung, J.M., et al., *Novartis Found Symp.* (2004), 261:19-27; discussion 27-31, 47-54).

Na_v1.4 expression is essentially limited to muscle (Raymond, C.K., et al., *op. cit.*). Mutations in this gene have been shown to have profound effects on muscle
20 function including paralysis, (Tamaoka A., *Intern. Med.* (2003), (9):769-70). Thus, this channel can be considered a target for the treatment of abnormal muscle contractility, spasm or paralysis.

The cardiac sodium channel, Na_v1.5, is expressed mainly in the heart ventricles and atria (Raymond, C.K., et al., *op. cit.*), and can be found in the sinoatrial node, ventricular node and possibly Purkinje cells. The rapid upstroke of the cardiac action potential and the rapid impulse conduction through cardiac tissue is due to the opening of Na_v1.5. As such, Na_v1.5 is central to the genesis of cardiac arrhythmias. Mutations
25 in human Na_v1.5 result in multiple arrhythmic syndromes, including, for example, long QT3 (LQT3), Brugada syndrome (BS), an inherited cardiac conduction defect, sudden unexpected nocturnal death syndrome (SUNDS) and sudden infant death syndrome (SIDS) (Liu, H. et al., *Am. J. Pharmacogenomics* (2003), 3(3):173-9). Sodium channel blocker therapy has been used extensively in treating cardiac arrhythmias. The first
30 antiarrhythmic drug, quinidine, discovered in 1914, is classified as a sodium channel

blocker.

Na_v1.6 encodes an abundant, widely distributed voltage-gated sodium channel found throughout the central and peripheral nervous systems, clustered in the nodes of Ranvier of neural axons (Caldwell, J.H., et al., *Proc. Natl. Acad. Sci. USA* (2000), 97(10): 5616-20). Although no mutations in humans have been detected, Na_v1.6 is thought to play a role in the manifestation of the symptoms associated with multiple sclerosis and has been considered as a target for the treatment of this disease (Craner, M.J., et al., *Proc. Natl. Acad. Sci. USA* (2004), 101(21):8168-73).

Na_v1.7 was first cloned from the pheochromocytoma PC12 cell line (Toledo-Aral, J. J., et al., *Proc. Natl. Acad. Sci. USA* (1997), 94:1527-1532). Its presence at high levels in the growth cones of small-diameter neurons suggested that it could play a role in the transmission of nociceptive information. Although this has been challenged by experts in the field as Na_v1.7 is also expressed in neuroendocrine cells associated with the autonomic system (Klugbauer, N., et al., *EMBO J.* (1995), 14(6):1084-90) and as such has been implicated in autonomic processes. The implicit role in autonomic functions was demonstrated with the generation of Na_v1.7 null mutants; deleting Na_v1.7 in all sensory and sympathetic neurons resulted in a lethal perinatal phenotype. (Nassar, et al., *Proc. Natl. Acad. Sci. USA* (2004), 101(34):12706-11.). In contrast, by deleting the Na_v1.7 expression in a subset of sensory neurons that are predominantly nociceptive, a role in pain mechanisms, was demonstrated (Nassar, et al., *op. cit.*). Further support for Na_v1.7 blockers active in a subset of neurons is supported by the finding that two human heritable pain conditions, primary erythralgia and familial rectal pain, have been shown to map to Na_v1.7 (Yang, Y., et al., *J. Med. Genet.* (2004), 41(3):171-4).

The expression of Na_v1.8 is essentially restricted to the DRG (Raymond, C.K., et al., *op. cit.*). There are no identified human mutations for Na_v1.8. However, Na_v1.8-null mutant mice were viable, fertile and normal in appearance. A pronounced analgesia to noxious mechanical stimuli, small deficits in noxious thermoreception and delayed development of inflammatory hyperalgesia suggested to the researchers that Na_v1.8 plays a major role in pain signalling (Akopian, A. N., et al., *Nat. Neurosci.* (1999), 2(6): 541-8). Blocking of this channel is widely accepted as a potential treatment for pain (Lai, J, et al., *op. cit.*; Wood, J.N., et al., *op. cit.*; Chung, J.M., et al., *op. cit.*). PCT Published Patent Application No. WO03/037274A2 describes pyrazole-amides and sulfonamides for the treatment of central or peripheral nervous system conditions, particularly pain and chronic pain by blocking sodium channels associated

with the onset or recurrence of the indicated conditions. PCT Published Patent Application No. WO03/037890A2 describes piperidines for the treatment of central or peripheral nervous system conditions, particularly pain and chronic pain by blocking sodium channels associated with the onset or recurrence of the indicated conditions.

- 5 The compounds, compositions and methods of these inventions are of particular use for treating neuropathic or inflammatory pain by the inhibition of ion flux through a channel that includes a PN3 (Na_v1.8) subunit.

- The tetrodotoxin insensitive, peripheral sodium channel Na_v1.9, disclosed by Dib-Hajj, S.D., et al. (see Dib-Hajj, S.D., et al., *Proc. Natl. Acad. Sci. USA* (1998), 10 95(15):8963-8) was shown to reside solely in the dorsal root ganglia. It has been demonstrated that Na_v1.9 underlies neurotrophin (BDNF)-evoked depolarization and excitation, and is the only member of the voltage gated sodium channel superfamily to be shown to be ligand mediated (Blum, R., Kafitz, K.W., Konnerth, A., *Nature* (2002), 419 (6908):687-93). The limited pattern of expression of this channel has made it a 15 candidate target for the treatment of pain (Lai, J, et al., *op. cit.*; Wood, J.N., et al., *op. cit.*; Chung, J.M. et al., *op. cit.*).

- NaX is a putative sodium channel, which has not been shown to be voltage gated. In addition to expression in the lung, heart, dorsal root ganglia, and Schwann cells of the peripheral nervous system, NaX is found in neurons and ependymal cells in 20 restricted areas of the CNS, particularly in the circumventricular organs, which are involved in body-fluid homeostasis (Watanabe, E., et al., *J. Neurosci.* (2000), 20(20):7743-51). NaX-null mice showed abnormal intakes of hypertonic saline under both water- and salt-depleted conditions. These findings suggest that the NaX plays an important role in the central sensing of body-fluid sodium level and regulation of salt 25 intake behaviour. Its pattern of expression and function suggest it as a target for the treatment of cystic fibrosis and other related salt regulating maladies.

- Studies with the sodium channel blocker tetrodotoxin (TTX) used to lower neuron activity in certain regions of the brain, indicate its potential use in the treatment of addiction. Drug-paired stimuli elicit drug craving and relapse in addicts and drug- 30 seeking behavior in rats. The functional integrity of the basolateral amygdala (BLA) is necessary for reinstatement of cocaine-seeking behaviour elicited by cocaine-conditioned stimuli, but not by cocaine itself. BLA plays a similar role in reinstatement of heroin-seeking behavior. TTX-induced inactivation of the BLA on conditioned and heroin-primed reinstatement of extinguished heroin-seeking behaviour in a rat model 35 (Fuchs, R.A. and See, R.E., *Psychopharmacology* (2002) 160(4):425-33).

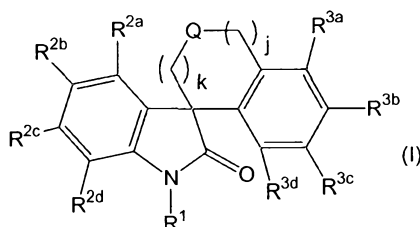
This closely related family of proteins has long been recognised as targets for therapeutic intervention. Sodium channels are targeted by a diverse array of pharmacological agents. These include neurotoxins, antiarrhythmics, anticonvulsants and local anesthetics (Clare, J.J., et al., *Drug Discovery Today* (2000) 5:506-520). All of the current pharmacological agents that act on sodium channels have receptor sites on the alpha subunits. At least six distinct receptor sites for neurotoxins and one receptor site for local anesthetics and related drugs have been identified (Cestèle, S. et al., *Biochimie* (2000), Vol. 82, pp. 883-892).

The small molecule sodium channel blockers or the local anesthetics and related antiepileptic and antiarrhythmic drugs, interact with overlapping receptor sites located in the inner cavity of the pore of the sodium channel (Catterall, W.A., *Neuron* (2000), 26:13-25). Amino acid residues in the S6 segments from at least three of the four domains contribute to this complex drug receptor site, with the IVS6 segment playing the dominant role. These regions are highly conserved and as such most sodium channel blockers known to date interact with similar potency with all channel subtypes. Nevertheless, it has been possible to produce sodium channel blockers with therapeutic selectivity and a sufficient therapeutic window for the treatment of epilepsy (e.g. lamotrigine, phenytoin and carbamazepine) and certain cardiac arrhythmias (e.g. lignocaine, tocainide and mexiletine). However, the potency and therapeutic index of these blockers is not optimal and have limited the usefulness of these compounds in a variety of therapeutic areas where a sodium channel blocker would be ideally suited.

SUMMARY OF THE INVENTION

The present invention is directed to the use of spiro-oxindole compounds for the treatment and/or prevention of diseases or conditions, such as hypercholesterolemia, benign prostatic hyperplasia, pruritis, and cancer.

Accordingly, in one aspect, the invention provides compounds of formula (I):



wherein:

j and k are each independently 0, 1, 2 or 3;

Q is $-C(R^{1a})H-$, $-C(O)-$, $-O-$, $-S(O)_m-$ (where m is 0, 1 or 2), $-CF_2-$, $-C(O)O-$, $-C(O)N(R^5)-$ or $-N(R^5)C(O)-$;

R^{1a} is hydrogen or $-OR^5$;

R^1 is hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl,

5 heteroaryl, heterocyclyl, $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$, $-R^9-S(O)_m-R^5$ (where m is 0, 1 or 2), $-R^8-OR^5$, $-R^8-CN$, $-R^9-P(O)(OR^5)_2$, or $-R^9-O-R^9-OR^5$;

or R^1 is aralkyl substituted by $-C(O)N(R^6)R^7$ where:

R^6 is hydrogen, alkyl, aryl or aralkyl; and

10 R^7 is hydrogen, alkyl, haloalkyl, $-R^9-CN$, $-R^9-OR^5$, $-R^9-N(R^4)R^5$, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl;

or R^6 and R^7 , together with the nitrogen to which they are attached, form a heterocyclyl or heteroaryl;

15 and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroaryl groups for R^6 and R^7 may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, $-R^8-CN$, $-R^8-OR^5$, heterocyclyl and heteroaryl;

20 or R^1 is aralkyl optionally substituted by one or more substituents selected from the group consisting of $-R^8-OR^5$, $-C(O)OR^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

or R^1 is $-R^9-N(R^{10})R^{11}$, $-R^9-N(R^{12})C(O)R^{11}$ or $-R^9-N(R^{10})C(O)N(R^{10})R^{11}$ where:

each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

25 each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$;

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

30 and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, $-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

35 or R^1 is heterocyclylalkyl or heteroarylalkyl where the heterocyclylalkyl or the

heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, -R⁸-OR⁵, -R⁸-C(O)OR⁵, -R⁸-N(R⁴)R⁵, -R⁸-C(O)N(R⁴)R⁵,
5 -R⁸-N(R⁵)C(O)R⁴, -R⁸-S(O)_mR⁴ (where m is 0, 1 or 2), -R⁸-CN, or -R⁸-NO₂;
R^{2a}, R^{2b}, R^{2c} and R^{2d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, -R⁸-CN, -R⁸-NO₂, -R⁸-OR⁵,
10 -R⁸-N(R⁴)R⁵, -N=C(R⁴)R⁵, -S(O)_mR⁴, -OS(O)₂CF₃, -R⁸-C(O)R⁴, -C(S)R⁴, -C(R⁴)₂C(O)R⁵, -R⁸-C(O)OR⁴, -C(S)OR⁴, -R⁸-C(O)N(R⁴)R⁵, -C(S)N(R⁴)R⁵, -N(R⁵)C(O)R⁴, -N(R⁵)C(S)R⁴, -N(R⁵)C(O)OR⁴, -N(R⁵)C(S)OR⁴, -N(R⁵)C(O)N(R⁴)R⁵, -N(R⁵)C(S)N(R⁴)R⁵, -N(R⁵)S(O)_nR⁴, -N(R⁵)S(O)_nN(R⁴)R⁵, -R⁸-S(O)_nN(R⁴)R⁵, -N(R⁵)C(=NR⁵)N(R⁴)R⁵, and -N(R⁵)C(=N-CN)N(R⁴)R⁵,
15 wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2; and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{2a}, R^{2b}, R^{2c} and R^{2d} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, -R⁸-CN, -R⁸-NO₂, -R⁸-OR⁵, -R⁸-N(R⁴)R⁵, -S(O)_mR⁴, -R⁸-S(O)_nN(R⁴)R⁵, -R⁸-C(O)R⁴, -R⁸-C(O)OR⁴, -R⁸-C(O)N(R⁴)R⁵, -N(R⁵)C(O)R⁴, and -N(R⁵)S(O)_nR⁴, wherein each m is
20 independently 0, 1, or 2 and each n is independently 1 or 2;
or R^{2a} and R^{2b}, together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;
or R^{2b} and R^{2c}, together with the carbon ring atoms to which they are directly attached,
30 may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2d} are as defined above;
or R^{2c} and R^{2d}, together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;
35 R^{3a}, R^{3b}, R^{3c} and R^{3d} are each independently selected from the group consisting of

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hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;

or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3d} are as defined above;

or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3b} are as defined above;

each R^4 and R^5 is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;

or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl;

each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and

each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain;

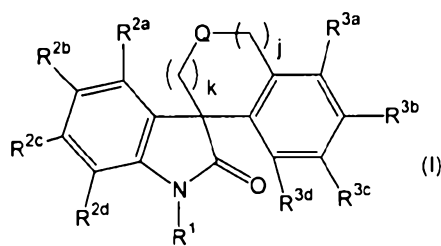
or a stereoisomer, enantiomer, tautomer thereof or mixtures thereof;

or a pharmaceutically acceptable salt, solvate or prodrug thereof.

In one aspect the present invention provides a method of treating hypercholesterolemia in a mammal, wherein the method comprises administering to the mammal in need thereof a therapeutically effective amount of a compound of formula (I):

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wherein:

j and k are each independently 0, 1, 2 or 3;

Q is $-C(R^{1a})H-$, $-O-$, $-S(O)_m-$ (where m is 1 or 2), $-CF_2-$, $-C(O)O-$, $-C(O)N(R^5)-$ or $-N(R^5)C(O)-$;

R^{1a} is $-OR^5$;

R^1 is hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$, $-R^9-S(O)_m-R^5$ (where m is 0, 1 or 2), $-R^8-OR^5$, $-R^8-CN$, $-R^9-P(O)(OR^5)_2$, or $-R^9-O-R^9-OR^5$;

or R^1 is aralkyl substituted by $-C(O)N(R^6)R^7$ where:

R^6 is hydrogen, alkyl, aryl or aralkyl; and

R^7 is hydrogen, alkyl, haloalkyl, $-R^9-CN$, $-R^9-OR^5$, $-R^9-N(R^4)R^5$, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

or R^6 and R^7 , together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^6 and R^7 may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, $-R^8-CN$, $-R^8-OR^5$, heterocyclyl and heteroaryl;

or R^1 is aralkyl optionally substituted by one or more substituents selected from the group consisting of $-R^8-OR^5$, $-C(O)OR^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

or R^1 is $-R^9-N(R^{10})R^{11}$, $-R^9-N(R^{12})C(O)R^{11}$ or $-R^9-N(R^{10})C(O)N(R^{10})R^{11}$ where:

each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$,

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$-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl,

heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, $-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

or R^1 is heterocyclylalkyl or heteroarylalkyl where the heterocyclylalkyl or the

heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$ (where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of

hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl,

heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$, $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

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- and provided that R^{2c} is not $-C(O)OCH_3$, $-C(O)NH_2$, iodo or cyano;
- or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;
- or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2d} are as defined above;
- or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;
- R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;
- or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;
- or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3d} are as defined above;
- or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3b} are as defined above;
- each R^4 and R^5 is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;
- or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a heterocyclyl or

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heteroaryl;

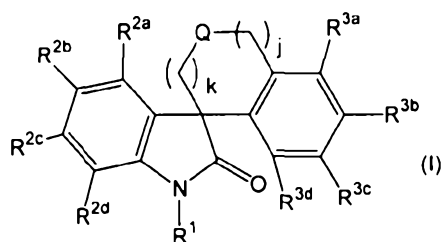
each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and

each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain;

or a stereoisomer, enantiomer or tautomer thereof;

or a pharmaceutically acceptable salt or solvate thereof.

In one aspect the present invention provides a method of treating benign prostatic hyperplasia in a mammal, wherein the method comprises administering to the mammal in need thereof a therapeutically effective amount of a compound of formula (I):



wherein:

j and k are each independently 0, 1, 2 or 3;

Q is $-C(R^{1a})H-$, $-O-$, $-S(O)_m-$ (where m is 1 or 2), $-CF_2-$, $-C(O)O-$, $-C(O)N(R^5)-$ or $-N(R^5)C(O)-$;

R^{1a} is $-OR^5$;

R^1 is hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$, $-R^9-S(O)_m-R^5$ (where m is 0, 1 or 2), $-R^8-OR^5$, $-R^8-CN$, $-R^9-P(O)(OR^5)_2$, or $-R^9-O-R^9-OR^5$;

or R^1 is aralkyl substituted by $-C(O)N(R^6)R^7$ where:

R^6 is hydrogen, alkyl, aryl or aralkyl; and

R^7 is hydrogen, alkyl, haloalkyl, $-R^9-CN$, $-R^9-OR^5$, $-R^9-N(R^4)R^5$, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

or R^6 and R^7 , together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^6 and R^7 may

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be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, $-R^8-CN$, $-R^8-OR^5$, heterocyclyl and heteroaryl;

or R^1 is aralkyl optionally substituted by one or more substituents selected from the group consisting of $-R^8-OR^5$, $-C(O)OR^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

or R^1 is $-R^9-N(R^{10})R^{11}$, $-R^9-N(R^{12})C(O)R^{11}$ or $-R^9-N(R^{10})C(O)N(R^{10})R^{11}$ where:

each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, $-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

or R^1 is heterocyclylalkyl or heteroarylalkyl where the heterocyclylalkyl or the heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$ (where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

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and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl and heteroarylalkyl groups for R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$, $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not $-C(O)OCH_3$, $-C(O)NH_2$, iodo or cyano;

or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2d} are as defined above;

or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;

R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;

or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached,

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may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3d} are as defined above;

or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3b} are as defined above;

each R^4 and R^5 is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl, and heteroarylalkyl;

or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl;

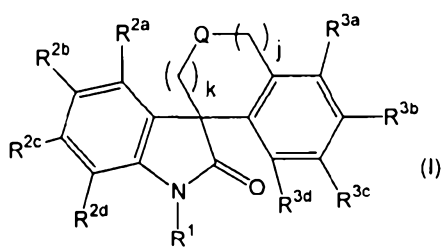
each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and

each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain;

or a stereoisomer, enantiomer or tautomer thereof;

or a pharmaceutically acceptable salt or solvate thereof.

In one aspect the present invention provides a method of treating pruritis in a mammal, wherein the method comprises administering to the mammal in need thereof a therapeutically effective amount of a compound of formula (I):



wherein:

j and k are each independently 0, 1, 2 or 3;

Q is $-C(R^{1a})H-$, $-O-$, $-S(O)_m-$ (where m is 1 or 2), $-CF_2-$, $-C(O)O-$, $-C(O)N(R^5)-$ or $-N(R^5)C(O)-$;

R^{1a} is $-OR^5$;

R^1 is hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$, $-R^9-S(O)_m-R^5$ (where m is 0, 1 or 2), $-R^8-OR^5$, $-R^8-CN$, $-R^9-P(O)(OR^5)_2$, or

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$-R^9-O-R^9-OR^5$;

or R^1 is aralkyl substituted by $-C(O)N(R^6)R^7$ where:

R^6 is hydrogen, alkyl, aryl or aralkyl; and

R^7 is hydrogen, alkyl, haloalkyl, $-R^9-CN$, $-R^9-OR^5$, $-R^9-N(R^4)R^5$, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

or R^6 and R^7 , together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^6 and R^7 may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, $-R^8-CN$, $-R^8-OR^5$, heterocyclyl and heteroaryl;

or R^1 is aralkyl optionally substituted by one or more substituents selected from the group consisting of $-R^8-OR^5$, $-C(O)OR^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

or R^1 is $-R^9-N(R^{10})R^{11}$, $-R^9-N(R^{12})C(O)R^{11}$ or $-R^9-N(R^{10})C(O)N(R^{10})R^{11}$ where:

each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, $-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

or R^1 is heterocyclylalkyl or heteroarylalkyl where the heterocyclylalkyl or the heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$ (where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

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R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$, $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not $-C(O)OCH_3$, $-C(O)NH_2$, iodo or cyano;

or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2d} are as defined above;

or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;

R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$,

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-S(O)_mR⁴, -OS(O)₂CF₃, -R⁸-C(O)R⁴, -C(S)R⁴, -C(R⁴)₂C(O)R⁵, -R⁸-C(O)OR⁴,
 -C(S)OR⁴, -R⁸-C(O)N(R⁴)R⁵, -C(S)N(R⁴)R⁵, -N(R⁵)C(O)R⁴, -N(R⁵)C(S)R⁴,
 -N(R⁵)C(O)OR⁴, -N(R⁵)C(S)OR⁴, -N(R⁵)C(O)N(R⁴)R⁵, -N(R⁵)C(S)N(R⁴)R⁵,
 -N(R⁵)S(O)_nR⁴, -N(R⁵)S(O)_nN(R⁴)R⁵, -R⁸-S(O)_nN(R⁴)R⁵, -N(R⁵)C(=NR⁵)N(R⁴)R⁵,
 and -N(R⁵)C(N=C(R⁴)R⁵)N(R⁴)R⁵, wherein each m is independently 0, 1, or 2 and
 each n is independently 1 or 2;

or R^{3a} and R^{3b}, together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and
 R^{3c} and R^{3d} are as defined above;

or R^{3b} and R^{3c}, together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and
 R^{3a} and R^{3d} are as defined above;

or R^{3c} and R^{3d}, together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and
 R^{3a} and R^{3b} are as defined above;

each R⁴ and R⁵ is independently selected from the group consisting of hydrogen, alkyl,
 alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl,
 heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;

or when R⁴ and R⁵ are each attached to the same nitrogen atom, then R⁴ and R⁵, together
 with the nitrogen atom to which they are attached, may form a heterocyclyl or
 heteroaryl;

each R⁸ is a direct bond or a straight or branched alkylene chain, a straight or branched
 alkenylene chain or a straight or branched alkynylene chain; and

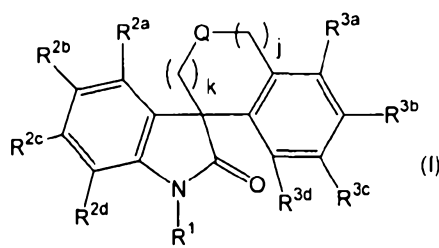
each R⁹ is a straight or branched alkylene chain, a straight or branched alkenylene chain
 or a straight or branched alkynylene chain;

or a stereoisomer, enantiomer or tautomer thereof;

or a pharmaceutically acceptable salt or solvate thereof.

In one aspect the present invention provides a method of treating hormone
 sensitive cancer in a mammal, wherein the method comprises administering to the
 mammal in need thereof a therapeutically effective amount of a compound of formula (I):

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wherein:

j and k are each independently 0, 1, 2 or 3;

Q is $-C(R^{1a})H-$, $-O-$, $-S(O)_m-$ (where m is 1 or 2), $-CF_2-$, $-C(O)O-$, $-C(O)N(R^5)-$ or $-N(R^5)C(O)-$;

R^{1a} is $-OR^5$;

R^1 is hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$, $-R^9-S(O)_m-R^5$ (where m is 0, 1 or 2), $-R^8-OR^5$, $-R^8-CN$, $-R^9-P(O)(OR^5)_2$, or $-R^9-O-R^9-OR^5$;

or R^1 is aralkyl substituted by $-C(O)N(R^6)R^7$ where:

R^6 is hydrogen, alkyl, aryl or aralkyl; and

R^7 is hydrogen, alkyl, haloalkyl, $-R^9-CN$, $-R^9-OR^5$, $-R^9-N(R^4)R^5$, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

or R^6 and R^7 , together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^6 and R^7 may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, $-R^8-CN$, $-R^8-OR^5$, heterocyclyl and heteroaryl;

or R^1 is aralkyl optionally substituted by one or more substituents selected from the group consisting of $-R^8-OR^5$, $-C(O)OR^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

or R^1 is $-R^9-N(R^{10})R^{11}$, $-R^9-N(R^{12})C(O)R^{11}$ or $-R^9-N(R^{10})C(O)N(R^{10})R^{11}$ where:

each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or

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$-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl,

heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may

be optionally substituted by one or more substituents selected from the

group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro,

$-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

or R^1 is heterocyclylalkyl or heteroarylalkyl where the heterocyclylalkyl or the

heteroarylalkyl group is optionally substituted by one or more substituents selected

from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl,

aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$,

$-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$

(where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of

hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy,

cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl,

heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$,

$-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$,

$-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$,

$-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$,

$-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$,

and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each

n is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl,

heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for

R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more

substituents selected from the group consisting of alkyl, alkenyl, alkynyl,

alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl,

aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl,

heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$,

$-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$,

$-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1,

or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not $-C(O)OCH_3$, $-C(O)NH_2$, iodo or cyano;

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or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2d} are as defined above;

or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;

R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;

or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3d} are as defined above;

or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3b} are as defined above;

each R^4 and R^5 is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;

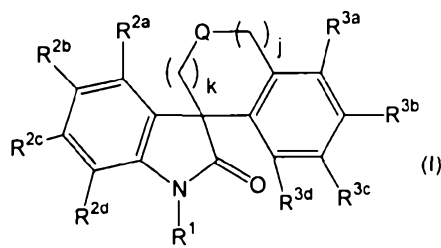
or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl;

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each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and
 each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain;
 or a stereoisomer, enantiomer or tautomer thereof;
 or a pharmaceutically acceptable salt or solvate thereof.

In one aspect the present invention provides a method of treating hypercholesterolemia in a mammal, wherein the method comprises administering to the mammal in need thereof a therapeutically effective amount of a compound of formula (I):



wherein:

j is 0 and k is 1 or 2;

Q is $-C(R^{1a})H-$, $-C(O)-$, $-CF_2-$, $-C(O)O-$ or $-N(R^5)C(O)-$;

R^{1a} is hydrogen or $-OR^5$;

R^1 is ethyl, *n*-propyl, 1-methylethyl, *n*-butyl, *n*-pentyl, 1,1-dimethylethyl, 3-methylhexyl, 2-methylhexyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$, $-R^9-S(O)_m-R^5$ (where m is 0, 1 or 2), $-R^8-OR^5$, $-R^8-CN$, $-R^9-P(O)(OR^5)_2$, or $-R^9-O-R^9-OR^5$;

or R^1 is aralkyl substituted by $-C(O)N(R^6)R^7$ where:

R^6 is hydrogen, alkyl, aryl or aralkyl; and

R^7 is hydrogen, alkyl, haloalkyl, $-R^9-CN$, $-R^9-OR^5$, $-R^9-N(R^4)R^5$, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

or R^6 and R^7 , together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^6 and R^7 may be optionally substituted by one or more substituents selected from the

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group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, $-R^8-CN$, $-R^8-OR^5$, heterocyclyl and heteroaryl;

or R^1 is aralkyl optionally substituted by one or more substituents selected from the group consisting of $-R^8-OR^5$, $-C(O)OR^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

or R^1 is $-R^9-N(R^{10})R^{11}$, $-R^9-N(R^{12})C(O)R^{11}$ or $-R^9-N(R^{10})C(O)N(R^{10})R^{11}$ where:

each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, $-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

or R^1 is heterocyclylalkyl or heteroarylalkyl where the heterocyclylalkyl or the heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$ (where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl,

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heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$, $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not $-C(O)OCH_3$, $-C(O)NH_2$, iodo or cyano;

or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2d} are as defined above;

or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;

R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;

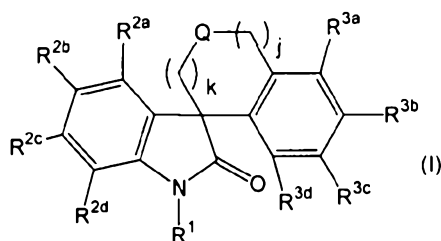
or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and

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R^{3a} and R^d are as defined above;
 or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and
 R^{3a} and R^{3b} are as defined above;
 each R^4 and R^5 is independently selected from the group consisting of hydrogen, alkyl,
 alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl,
 heterocyclyl, heterocyclalkyl, heteroaryl, and heteroarylalkyl;
 or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together
 with the nitrogen atom to which they are attached, may form a heterocyclyl or
 heteroaryl;
 each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched
 alkenylene chain or a straight or branched alkynylene chain; and
 each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain
 or a straight or branched alkynylene chain;
 or a stereoisomer, enantiomer or tautomer thereof;
 or a pharmaceutically acceptable salt or solvate thereof.

In one aspect the present invention provides a method of treating benign prostatic
 hyperplasia in a mammal, wherein the method comprises administering to the mammal in
 need thereof a therapeutically effective amount of a compound of formula (I):



wherein:

j is 0 and k is 1 or 2;

Q is $-C(R^{1a})H-$, $-C(O)-$, $-CF_2-$, $-C(O)O-$ or $-N(R^5)C(O)-$;

R^{1a} is hydrogen or $-OR^5$;

R^1 is ethyl, *n*-propyl, 1-methylethyl, *n*-butyl, *n*-pentyl, 1,1-dimethylethyl, 3-methylhexyl,
 2-methylhexyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl,
 heteroaryl, heterocyclyl, $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$,
 $-R^9-S(O)_m-R^5$ (where m is 0, 1 or 2), $-R^8-OR^5$, $-R^8-CN$, $-R^9-P(O)(OR^5)_2$, or
 $-R^9-O-R^9-OR^5$;

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or R¹ is aralkyl substituted by -C(O)N(R⁶)R⁷ where:

R⁶ is hydrogen, alkyl, aryl or aralkyl; and

R⁷ is hydrogen, alkyl, haloalkyl, -R⁹-CN, -R⁹-OR⁵, -R⁹-N(R⁴)R⁵, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclalkyl, heteroaryl, or heteroarylalkyl;

or R⁶ and R⁷, together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclalkyl, heteroaryl and heteroarylalkyl groups for R⁶ and R⁷ may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, -R⁸-CN, -R⁸-OR⁵, heterocyclyl and heteroaryl;

or R¹ is aralkyl optionally substituted by one or more substituents selected from the group consisting of -R⁸-OR⁵, -C(O)OR⁵, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

or R¹ is -R⁹-N(R¹⁰)R¹¹, -R⁹-N(R¹²)C(O)R¹¹ or -R⁹-N(R¹⁰)C(O)N(R¹⁰)R¹¹ where:

each R¹⁰ is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each R¹¹ is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, -R⁹-OC(O)R⁵, -R⁹-C(O)OR⁵, -R⁹-C(O)N(R⁴)R⁵, -R⁹-C(O)R⁵, -R⁹-N(R⁴)R⁵, -R⁹-OR⁵, or -R⁹-CN; and

R¹² is hydrogen, alkyl, aryl, aralkyl or -C(O)R⁵;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclalkyl, heteroaryl and heteroarylalkyl groups for R¹⁰ and R¹¹ may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, -R⁸-CN, -R⁸-OR⁵, -R⁸-C(O)R⁵, heterocyclyl and heteroaryl;

or R¹ is heterocyclalkyl or heteroarylalkyl where the heterocyclalkyl or the heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, -R⁸-OR⁵, -R⁸-C(O)OR⁵, -R⁸-N(R⁴)R⁵, -R⁸-C(O)N(R⁴)R⁵, -R⁸-N(R⁵)C(O)R⁴, -R⁸-S(O)_mR⁴ (where m is 0, 1 or 2), -R⁸-CN, or -R⁸-NO₂;

R^{2a}, R^{2b}, R^{2c} and R^{2d} are each independently selected from the group consisting of

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hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl,

heterocyclyl, heterocyclalkyl, heteroaryl and heteroarylalkyl groups for R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$, $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not $-C(O)OCH_3$, $-C(O)NH_2$, iodo or cyano;

or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2d} are as defined above;

or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;

R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$,

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-C(S)OR⁴, -R⁸-C(O)N(R⁴)R⁵, -C(S)N(R⁴)R⁵, -N(R⁵)C(O)R⁴, -N(R⁵)C(S)R⁴,
 -N(R⁵)C(O)OR⁴, -N(R⁵)C(S)OR⁴, -N(R⁵)C(O)N(R⁴)R⁵, -N(R⁵)C(S)N(R⁴)R⁵,
 -N(R⁵)S(O)_nR⁴, -N(R⁵)S(O)_nN(R⁴)R⁵, -R⁸-S(O)_nN(R⁴)R⁵, -N(R⁵)C(=NR⁵)N(R⁴)R⁵,
 and -N(R⁵)C(N=C(R⁴)R⁵)N(R⁴)R⁵, wherein each m is independently 0, 1, or 2 and
 each n is independently 1 or 2;

or R^{3a} and R^{3b}, together with the carbon ring atoms to which they are directly attached,
 form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c}
 and R^{3d} are as defined above;

or R^{3b} and R^{3c}, together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and
 R^{3a} and R^d are as defined above;

or R^{3c} and R^{3d}, together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and
 R^{3a} and R^{3b} are as defined above;

each R⁴ and R⁵ is independently selected from the group consisting of hydrogen, alkyl,
 alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl,
 heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;

or when R⁴ and R⁵ are each attached to the same nitrogen atom, then R⁴ and R⁵, together
 with the nitrogen atom to which they are attached, may form a heterocyclyl or
 heteroaryl;

each R⁸ is a direct bond or a straight or branched alkylene chain, a straight or branched
 alkenylene chain or a straight or branched alkynylene chain; and

each R⁹ is a straight or branched alkylene chain, a straight or branched alkenylene chain
 or a straight or branched alkynylene chain;

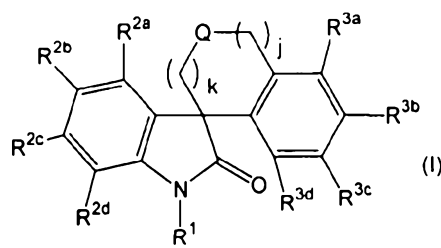
or a stereoisomer, enantiomer or tautomer thereof;

or a pharmaceutically acceptable salt or solvate thereof.

In one aspect the present invention provides a method of treating pruritis in a
 mammal, wherein the method comprises administering to the mammal in need thereof a
 therapeutically effective amount of a compound of formula (I):

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wherein:

j is 0 and k is 1 or 2;

Q is -C(R^{1a})H-, -C(O)-, -CF₂-, -C(O)O- or -N(R⁵)C(O)-;

R^{1a} is hydrogen or -OR⁵;

R¹ is ethyl, *n*-propyl, 1-methylethyl, *n*-butyl, *n*-pentyl, 1,1-dimethylethyl, 3-methylhexyl, 2-methylhexyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, -R⁸-C(O)R⁵, -R⁸-C(O)OR⁵, -R⁸-C(O)N(R⁴)R⁵, -S(O)₂-R⁵, -R⁹-S(O)_m-R⁵ (where m is 0, 1 or 2), -R⁸-OR⁵, -R⁸-CN, -R⁹-P(O)(OR⁵)₂, or -R⁹-O-R⁹-OR⁵;

or R¹ is aralkyl substituted by -C(O)N(R⁶)R⁷ where:

R⁶ is hydrogen, alkyl, aryl or aralkyl; and

R⁷ is hydrogen, alkyl, haloalkyl, -R⁹-CN, -R⁹-OR⁵, -R⁹-N(R⁴)R⁵, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

or R⁶ and R⁷, together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R⁶ and R⁷ may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, -R⁸-CN, -R⁸-OR⁵, heterocyclyl and heteroaryl;

or R¹ is aralkyl optionally substituted by one or more substituents selected from the group consisting of -R⁸-OR⁵, -C(O)OR⁵, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

or R¹ is -R⁹-N(R¹⁰)R¹¹, -R⁹-N(R¹²)C(O)R¹¹ or -R⁹-N(R¹⁰)C(O)N(R¹⁰)R¹¹ where:

each R¹⁰ is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each R¹¹ is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, -R⁹-OC(O)R⁵, -R⁹-C(O)OR⁵, -R⁹-C(O)N(R⁴)R⁵, -R⁹-C(O)R⁵, -R⁹-N(R⁴)R⁵, -R⁹-OR⁵, or

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$-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl,

heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may

be optionally substituted by one or more substituents selected from the

group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro,

$-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

or R^1 is heterocyclylalkyl or heteroarylalkyl where the heterocyclylalkyl or the

heteroarylalkyl group is optionally substituted by one or more substituents selected

from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl,

aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$,

$-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$

(where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of

hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy,

cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl,

heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$,

$-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$,

$-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$,

$-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$,

$-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$,

and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl,

heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for

R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more

substituents selected from the group consisting of alkyl, alkenyl, alkynyl,

alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl,

aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl,

heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$,

$-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$,

$-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1,

or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not $-C(O)OCH_3$, $-C(O)NH_2$, iodo or cyano;

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or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2d} are as defined above;

or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;

R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;

or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3d} are as defined above;

or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3b} are as defined above;

each R^4 and R^5 is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;

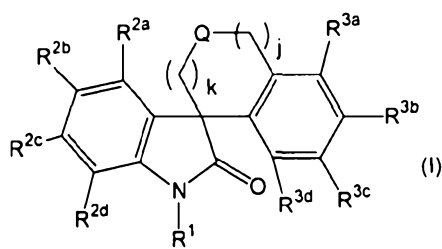
or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl;

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each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and
 each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain;
 or a stereoisomer, enantiomer or tautomer thereof;
 or a pharmaceutically acceptable salt or solvate thereof.

In one aspect the present invention provides a method of treating hormone sensitive cancer in a mammal, wherein the method comprises administering to the mammal in need thereof a therapeutically effective amount of a compound of formula (I):



wherein:

j is 0 and k is 1 or 2;

Q is $-C(R^{1a})H-$, $-C(O)-$, $-CF_2-$, $-C(O)O-$ or $-N(R^5)C(O)-$;

R^{1a} is hydrogen or $-OR^5$;

R^1 is ethyl, *n*-propyl, 1-methylethyl, *n*-butyl, *n*-pentyl, 1,1-dimethylethyl, 3-methylhexyl, 2-methylhexyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$, $-R^9-S(O)_m-R^5$ (where m is 0, 1 or 2), $-R^8-OR^5$, $-R^8-CN$, $-R^9-P(O)(OR^5)_2$, or $-R^9-O-R^9-OR^5$;

or R^1 is aralkyl substituted by $-C(O)N(R^6)R^7$ where:

R^6 is hydrogen, alkyl, aryl or aralkyl; and

R^7 is hydrogen, alkyl, haloalkyl, $-R^9-CN$, $-R^9-OR^5$, $-R^9-N(R^4)R^5$, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

or R^6 and R^7 , together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^6 and R^7 may be optionally substituted by one or more substituents selected from the

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group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, $-R^8-CN$, $-R^8-OR^5$, heterocyclyl and heteroaryl;

or R^1 is aralkyl optionally substituted by one or more substituents selected from the group consisting of $-R^8-OR^5$, $-C(O)OR^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

or R^1 is $-R^9-N(R^{10})R^{11}$, $-R^9-N(R^{12})C(O)R^{11}$ or $-R^9-N(R^{10})C(O)N(R^{10})R^{11}$ where:

each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl,

heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, $-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

or R^1 is heterocyclylalkyl or heteroarylalkyl where the heterocyclylalkyl or the heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$ (where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl,

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heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$, $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not $-C(O)OCH_3$, $-C(O)NH_2$, iodo or cyano;

or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2d} are as defined above;

or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;

R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;

or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and

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R^{3a} and R^d are as defined above;

or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3b} are as defined above;

each R^4 and R^5 is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl, and heteroarylalkyl;

or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl;

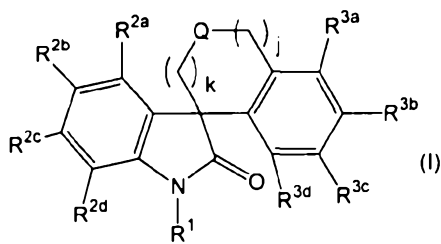
each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and

each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain;

or a stereoisomer, enantiomer or tautomer thereof;

or a pharmaceutically acceptable salt or solvate thereof.

In one aspect the present invention provides use of a compound of formula (I):



wherein:

j and k are each independently 0, 1, 2 or 3;

Q is $-C(R^{1a})H-$, $-O-$, $-S(O)_m-$ (where m is 1 or 2), $-CF_2-$, $-C(O)O-$, $-C(O)N(R^5)-$ or $-N(R^5)C(O)-$;

R^{1a} is $-OR^5$;

R^1 is hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$, $-R^9-S(O)_m-R^5$ (where m is 0, 1 or 2), $-R^8-OR^5$, $-R^8-CN$, $-R^9-P(O)(OR^5)_2$, or $-R^9-O-R^9-OR^5$;

or R^1 is aralkyl substituted by $-C(O)N(R^6)R^7$ where:

R^6 is hydrogen, alkyl, aryl or aralkyl; and

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R^7 is hydrogen, alkyl, haloalkyl, $-R^9-CN$, $-R^9-OR^5$, $-R^9-N(R^4)R^5$, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

or R^6 and R^7 , together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^6 and R^7 may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, $-R^8-CN$, $-R^8-OR^5$, heterocyclyl and heteroaryl;

or R^1 is aralkyl optionally substituted by one or more substituents selected from the group consisting of $-R^8-OR^5$, $-C(O)OR^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

or R^1 is $-R^9-N(R^{10})R^{11}$, $-R^9-N(R^{12})C(O)R^{11}$ or $-R^9-N(R^{10})C(O)N(R^{10})R^{11}$ where:

each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, $-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

or R^1 is heterocyclylalkyl or heteroarylalkyl where the heterocyclylalkyl or the heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$ (where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl,

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heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl,

heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$, $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not $-C(O)OCH_3$, $-C(O)NH_2$, iodo or cyano;

or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2d} are as defined above;

or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;

R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$,

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$-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$,
and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and
each n is independently 1 or 2;

or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached,
may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and
 R^{3c} and R^{3d} are as defined above;

or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached,
may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and
 R^{3a} and R^{3d} are as defined above;

or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached,
may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and
 R^{3a} and R^{3b} are as defined above;

each R^4 and R^5 is independently selected from the group consisting of hydrogen, alkyl,
alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl,
heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;

or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together
with the nitrogen atom to which they are attached, may form a heterocyclyl or
heteroaryl;

each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched
alkenylene chain or a straight or branched alkynylene chain; and

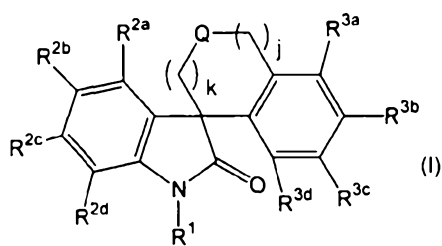
each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain
or a straight or branched alkynylene chain;

or a stereoisomer, enantiomer or tautomer thereof;

or a pharmaceutically acceptable salt or solvate thereof,

in the manufacture of a medicament for the treatment of hypercholesterolemia.

In one aspect the present invention provides use of a compound of formula (I):



wherein:

j and k are each independently 0, 1, 2 or 3;

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Q is $-C(R^{1a})H-$, $-O-$, $-S(O)_m-$ (where m is 1 or 2), $-CF_2-$, $-C(O)O-$, $-C(O)N(R^5)-$ or $-N(R^5)C(O)-$;

R^{1a} is $-OR^5$;

R^1 is hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$, $-R^9-S(O)_m-R^5$ (where m is 0, 1 or 2), $-R^8-OR^5$, $-R^8-CN$, $-R^9-P(O)(OR^5)_2$, or $-R^9-O-R^9-OR^5$;

or R^1 is aralkyl substituted by $-C(O)N(R^6)R^7$ where:

R^6 is hydrogen, alkyl, aryl or aralkyl; and

R^7 is hydrogen, alkyl, haloalkyl, $-R^9-CN$, $-R^9-OR^5$, $-R^9-N(R^4)R^5$, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

or R^6 and R^7 , together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^6 and R^7 may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, $-R^8-CN$, $-R^8-OR^5$, heterocyclyl and heteroaryl;

or R^1 is aralkyl optionally substituted by one or more substituents selected from the group consisting of $-R^8-OR^5$, $-C(O)OR^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

or R^1 is $-R^9-N(R^{10})R^{11}$, $-R^9-N(R^{12})C(O)R^{11}$ or $-R^9-N(R^{10})C(O)N(R^{10})R^{11}$ where:

each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, $-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

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or R^1 is heterocyclalkyl or heteroarylalkyl where the heterocyclalkyl or the heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocycl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$ (where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocycl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocycl, heterocyclalkyl, heteroaryl and heteroarylalkyl groups for R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocycl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$, $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1; or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not $-C(O)OCH_3$, $-C(O)NH_2$, iodo or cyano;

or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocycl and heteroaryl, and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocycl and heteroaryl, and R^{2a} and R^{2d} are as defined above;

or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached,

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may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;

R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;

or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3d} are as defined above;

or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3b} are as defined above;

each R^4 and R^5 is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;

or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl;

each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and

each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain;

or a stereoisomer, enantiomer or tautomer thereof;

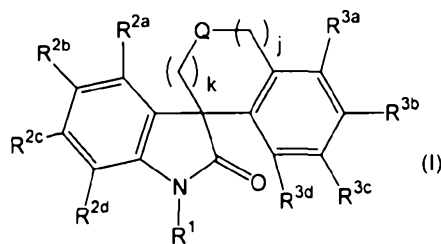
or a pharmaceutically acceptable salt or solvate thereof,

in the manufacture of a medicament for the treatment of benign prostatic hyperplasia.

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In one aspect the present invention provides use of a compound of formula (I):



wherein:

j and k are each independently 0, 1, 2 or 3;

Q is -C(R¹ᵃ)H-, -O-, -S(O)ₘ- (where m is 1 or 2), -CF₂-, -C(O)O-, -C(O)N(R⁵)- or -N(R⁵)C(O)-;

R¹ᵃ is -OR⁵;

R¹ is hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, -R⁸-C(O)R⁵, -R⁸-C(O)OR⁵, -R⁸-C(O)N(R⁴)R⁵, -S(O)₂-R⁵, -R⁹-S(O)ₘ-R⁵ (where m is 0, 1 or 2), -R⁸-OR⁵, -R⁸-CN, -R⁹-P(O)(OR⁵)₂, or -R⁹-O-R⁹-OR⁵;

or R¹ is aralkyl substituted by -C(O)N(R⁶)R⁷ where:

R⁶ is hydrogen, alkyl, aryl or aralkyl; and

R⁷ is hydrogen, alkyl, haloalkyl, -R⁹-CN, -R⁹-OR⁵, -R⁹-N(R⁴)R⁵, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

or R⁶ and R⁷, together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R⁶ and R⁷ may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, -R⁸-CN, -R⁸-OR⁵, heterocyclyl and heteroaryl;

or R¹ is aralkyl optionally substituted by one or more substituents selected from the group consisting of -R⁸-OR⁵, -C(O)OR⁵, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

or R¹ is -R⁹-N(R¹⁰)R¹¹, -R⁹-N(R¹²)C(O)R¹¹ or -R⁹-N(R¹⁰)C(O)N(R¹⁰)R¹¹ where:

each R¹⁰ is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each R¹¹ is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl,

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heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl,

heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, $-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

or R^1 is heterocyclylalkyl or heteroarylalkyl where the heterocyclylalkyl or the

heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$ (where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl,

heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$, $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1,

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or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not $-C(O)OCH_3$, $-C(O)NH_2$, iodo or cyano;

or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2d} are as defined above;

or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;

R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;

or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3d} are as defined above;

or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3b} are as defined above;

each R^4 and R^5 is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;

or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together

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with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl;

each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and

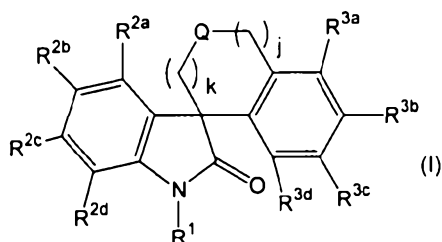
each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain;

or a stereoisomer, enantiomer or tautomer thereof;

or a pharmaceutically acceptable salt or solvate thereof,

in the manufacture of a medicament for the treatment of pruritis.

In one aspect the present invention provides use of a compound of formula (I):



wherein:

j and k are each independently 0, 1, 2 or 3;

Q is $-C(R^{1a})H-$, $-O-$, $-S(O)_m-$ (where m is 1 or 2), $-CF_2-$, $-C(O)O-$, $-C(O)N(R^5)-$ or $-N(R^5)C(O)-$;

R^{1a} is $-OR^5$;

R^1 is hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$, $-R^9-S(O)_m-R^5$ (where m is 0, 1 or 2), $-R^8-OR^5$, $-R^8-CN$, $-R^9-P(O)(OR^5)_2$, or $-R^9-O-R^9-OR^5$;

or R^1 is aralkyl substituted by $-C(O)N(R^6)R^7$ where:

R^6 is hydrogen, alkyl, aryl or aralkyl; and

R^7 is hydrogen, alkyl, haloalkyl, $-R^9-CN$, $-R^9-OR^5$, $-R^9-N(R^4)R^5$, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

or R^6 and R^7 , together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^6 and R^7 may

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be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, $-R^8-CN$, $-R^8-OR^5$, heterocyclyl and heteroaryl;

or R^1 is aralkyl optionally substituted by one or more substituents selected from the group consisting of $-R^8-OR^5$, $-C(O)OR^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

or R^1 is $-R^9-N(R^{10})R^{11}$, $-R^9-N(R^{12})C(O)R^{11}$ or $-R^9-N(R^{10})C(O)N(R^{10})R^{11}$ where:

each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, $-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

or R^1 is heterocyclylalkyl or heteroarylalkyl where the heterocyclylalkyl or the heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$ (where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

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and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl and heteroarylalkyl groups for R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$, $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not $-C(O)OCH_3$, $-C(O)NH_2$, iodo or cyano;

or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2d} are as defined above;

or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;

R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;

or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached,

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may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3d} are as defined above;

or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3b} are as defined above;

each R^4 and R^5 is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl, and heteroarylalkyl;

or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl;

each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and

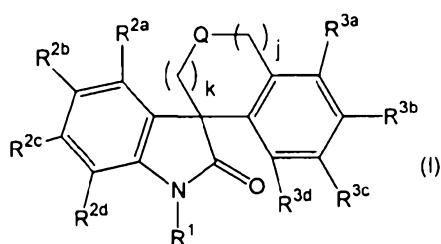
each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain;

or a stereoisomer, enantiomer or tautomer thereof;

or a pharmaceutically acceptable salt or solvate thereof,

in the manufacture of a medicament for the treatment of hormone sensitive cancer.

In one aspect the present invention provides use of a compound of formula (I):



wherein:

j is 0 and k is 1 or 2;

Q is $-C(R^{1a})H-$, $-C(O)-$, $-CF_2-$, $-C(O)O-$ or $-N(R^5)C(O)-$;

R^{1a} is hydrogen or $-OR^5$;

R^1 is ethyl, *n*-propyl, 1-methylethyl, *n*-butyl, *n*-pentyl, 1,1-dimethylethyl, 3-methylhexyl, 2-methylhexyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$, $-R^9-S(O)_m-R^5$ (where m is 0, 1 or 2), $-R^8-OR^5$, $-R^8-CN$, $-R^9-P(O)(OR^5)_2$, or $-R^9-O-R^9-OR^5$;

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or R^1 is aralkyl substituted by $-C(O)N(R^6)R^7$ where:

R^6 is hydrogen, alkyl, aryl or aralkyl; and

R^7 is hydrogen, alkyl, haloalkyl, $-R^9-CN$, $-R^9-OR^5$, $-R^9-N(R^4)R^5$, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclalkyl, heteroaryl, or heteroarylalkyl;

or R^6 and R^7 , together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclalkyl, heteroaryl and heteroarylalkyl groups for R^6 and R^7 may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, $-R^8-CN$, $-R^8-OR^5$, heterocyclyl and heteroaryl;

or R^1 is aralkyl optionally substituted by one or more substituents selected from the group consisting of $-R^8-OR^5$, $-C(O)OR^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

or R^1 is $-R^9-N(R^{10})R^{11}$, $-R^9-N(R^{12})C(O)R^{11}$ or $-R^9-N(R^{10})C(O)N(R^{10})R^{11}$ where:

each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, $-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

or R^1 is heterocyclalkyl or heteroarylalkyl where the heterocyclalkyl or the heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$ (where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of

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hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl,

heterocyclyl, heterocyclalkyl, heteroaryl and heteroarylalkyl groups for R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$, $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not $-C(O)OCH_3$, $-C(O)NH_2$, iodo or cyano;

or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2d} are as defined above;

or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;

R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$,

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-C(S)OR⁴, -R⁸-C(O)N(R⁴)R⁵, -C(S)N(R⁴)R⁵, -N(R⁵)C(O)R⁴, -N(R⁵)C(S)R⁴,
 -N(R⁵)C(O)OR⁴, -N(R⁵)C(S)OR⁴, -N(R⁵)C(O)N(R⁴)R⁵, -N(R⁵)C(S)N(R⁴)R⁵,
 -N(R⁵)S(O)_nR⁴, -N(R⁵)S(O)_nN(R⁴)R⁵, -R⁸-S(O)_nN(R⁴)R⁵, -N(R⁵)C(=NR⁵)N(R⁴)R⁵,
 and -N(R⁵)C(N=C(R⁴)R⁵)N(R⁴)R⁵, wherein each m is independently 0, 1, or 2 and
 each n is independently 1 or 2;

or R^{3a} and R^{3b}, together with the carbon ring atoms to which they are directly attached,
 form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c}
 and R^{3d} are as defined above;

or R^{3b} and R^{3c}, together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and
 R^{3a} and R^d are as defined above;

or R^{3c} and R^{3d}, together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and
 R^{3a} and R^{3b} are as defined above;

each R⁴ and R⁵ is independently selected from the group consisting of hydrogen, alkyl,
 alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl,
 heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;

or when R⁴ and R⁵ are each attached to the same nitrogen atom, then R⁴ and R⁵, together
 with the nitrogen atom to which they are attached, may form a heterocyclyl or
 heteroaryl;

each R⁸ is a direct bond or a straight or branched alkylene chain, a straight or branched
 alkenylene chain or a straight or branched alkynylene chain; and

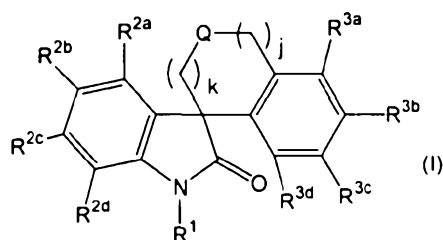
each R⁹ is a straight or branched alkylene chain, a straight or branched alkenylene chain
 or a straight or branched alkynylene chain;

or a stereoisomer, enantiomer or tautomer thereof;

or a pharmaceutically acceptable salt or solvate thereof,

in the manufacture of a medicament for the treatment of hypercholesterolemia.

In one aspect the present invention provides use of a compound of formula (I):



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wherein:

j is 0 and k is 1 or 2;

Q is $-C(R^{1a})H-$, $-C(O)-$, $-CF_2-$, $-C(O)O-$ or $-N(R^5)C(O)-$;

R^{1a} is hydrogen or $-OR^5$;

R^1 is ethyl, *n*-propyl, 1-methylethyl, *n*-butyl, *n*-pentyl, 1,1-dimethylethyl, 3-methylhexyl, 2-methylhexyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$, $-R^9-S(O)_m-R^5$ (where m is 0, 1 or 2), $-R^8-OR^5$, $-R^8-CN$, $-R^9-P(O)(OR^5)_2$, or $-R^9-O-R^9-OR^5$;

or R^1 is aralkyl substituted by $-C(O)N(R^6)R^7$ where:

R^6 is hydrogen, alkyl, aryl or aralkyl; and

R^7 is hydrogen, alkyl, haloalkyl, $-R^9-CN$, $-R^9-OR^5$, $-R^9-N(R^4)R^5$, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

or R^6 and R^7 , together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^6 and R^7 may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, $-R^8-CN$, $-R^8-OR^5$, heterocyclyl and heteroaryl;

or R^1 is aralkyl optionally substituted by one or more substituents selected from the group consisting of $-R^8-OR^5$, $-C(O)OR^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

or R^1 is $-R^9-N(R^{10})R^{11}$, $-R^9-N(R^{12})C(O)R^{11}$ or $-R^9-N(R^{10})C(O)N(R^{10})R^{11}$ where:

each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the

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group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, $-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

or R^1 is heterocyclylalkyl or heteroarylalkyl where the heterocyclylalkyl or the

heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$ (where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl,

heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$, $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not $-C(O)OCH_3$, $-C(O)NH_2$, iodo or cyano;

or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl,

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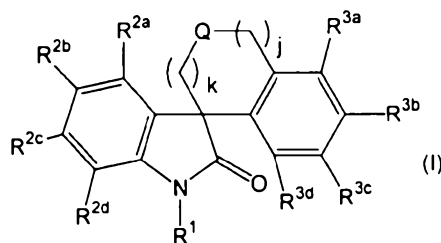
- and R^{2a} and R^{2d} are as defined above;
- or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;
- R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;
- or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;
- or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^d are as defined above;
- or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3b} are as defined above;
- each R^4 and R^5 is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;
- or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl;
- each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and
- each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain;
- or a stereoisomer, enantiomer or tautomer thereof;

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or a pharmaceutically acceptable salt or solvate thereof,
in the manufacture of a medicament for the treatment of benign prostatic hyperplasia.

In one aspect the present invention provides use of a compound of formula (I):



wherein:

j is 0 and k is 1 or 2;

Q is $-\text{C}(\text{R}^{1a})\text{H}-$, $-\text{C}(\text{O})-$, $-\text{CF}_2-$, $-\text{C}(\text{O})\text{O}-$ or $-\text{N}(\text{R}^5)\text{C}(\text{O})-$;

R^{1a} is hydrogen or $-\text{OR}^5$;

R^1 is ethyl, *n*-propyl, 1-methylethyl, *n*-butyl, *n*-pentyl, 1,1-dimethylethyl, 3-methylhexyl, 2-methylhexyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, $-\text{R}^8-\text{C}(\text{O})\text{R}^5$, $-\text{R}^8-\text{C}(\text{O})\text{OR}^5$, $-\text{R}^8-\text{C}(\text{O})\text{N}(\text{R}^4)\text{R}^5$, $-\text{S}(\text{O})_2-\text{R}^5$, $-\text{R}^9-\text{S}(\text{O})_m-\text{R}^5$ (where m is 0, 1 or 2), $-\text{R}^8-\text{OR}^5$, $-\text{R}^8-\text{CN}$, $-\text{R}^9-\text{P}(\text{O})(\text{OR}^5)_2$, or $-\text{R}^9-\text{O}-\text{R}^9-\text{OR}^5$;

or R^1 is aralkyl substituted by $-\text{C}(\text{O})\text{N}(\text{R}^6)\text{R}^7$ where:

R^6 is hydrogen, alkyl, aryl or aralkyl; and

R^7 is hydrogen, alkyl, haloalkyl, $-\text{R}^9-\text{CN}$, $-\text{R}^9-\text{OR}^5$, $-\text{R}^9-\text{N}(\text{R}^4)\text{R}^5$, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

or R^6 and R^7 , together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^6 and R^7 may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, $-\text{R}^8-\text{CN}$, $-\text{R}^8-\text{OR}^5$, heterocyclyl and heteroaryl;

or R^1 is aralkyl optionally substituted by one or more substituents selected from the group consisting of $-\text{R}^8-\text{OR}^5$, $-\text{C}(\text{O})\text{OR}^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

or R^1 is $-\text{R}^9-\text{N}(\text{R}^{10})\text{R}^{11}$, $-\text{R}^9-\text{N}(\text{R}^{12})\text{C}(\text{O})\text{R}^{11}$ or $-\text{R}^9-\text{N}(\text{R}^{10})\text{C}(\text{O})\text{N}(\text{R}^{10})\text{R}^{11}$ where:

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each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, $-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

or R^1 is heterocyclylalkyl or heteroarylalkyl where the heterocyclylalkyl or the heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$ (where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$,

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$-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$,
 $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1,
 or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not $-C(O)OCH_3$, $-C(O)NH_2$, iodo or cyano;

or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl,
 and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl,
 and R^{2a} and R^{2d} are as defined above;

or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl,
 and R^{2a} and R^{2b} are as defined above;

R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of
 hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy,
 cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl,
 heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$,
 $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$,
 $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$,
 $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$,
 $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$,
 and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and
 each n is independently 1 or 2;

or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached,
 form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c}
 and R^{3d} are as defined above;

or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and
 R^{3a} and R^{3d} are as defined above;

or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and
 R^{3a} and R^{3b} are as defined above;

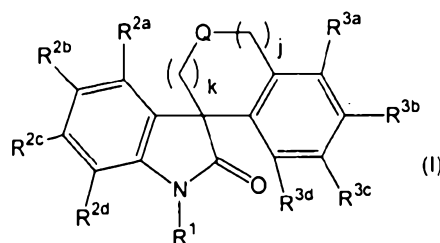
each R^4 and R^5 is independently selected from the group consisting of hydrogen, alkyl,
 alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl,

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heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;
 or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl;
 each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and
 each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain;
 or a stereoisomer, enantiomer or tautomer thereof;
 or a pharmaceutically acceptable salt or solvate thereof,
 in the manufacture of a medicament for the treatment of pruritis.

In one aspect the present invention provides use of a compound of formula (I):



wherein:

j is 0 and k is 1 or 2;

Q is $-C(R^{1a})H-$, $-C(O)-$, $-CF_2-$, $-C(O)O-$ or $-N(R^5)C(O)-$;

R^{1a} is hydrogen or $-OR^5$;

R^1 is ethyl, *n*-propyl, 1-methylethyl, *n*-butyl, *n*-pentyl, 1,1-dimethylethyl, 3-methylhexyl, 2-methylhexyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$, $-R^9-S(O)_m-R^5$ (where m is 0, 1 or 2), $-R^8-OR^5$, $-R^8-CN$, $-R^9-P(O)(OR^5)_2$, or $-R^9-O-R^9-OR^5$;

or R^1 is aralkyl substituted by $-C(O)N(R^6)R^7$ where:

R^6 is hydrogen, alkyl, aryl or aralkyl; and

R^7 is hydrogen, alkyl, haloalkyl, $-R^9-CN$, $-R^9-OR^5$, $-R^9-N(R^4)R^5$, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

or R^6 and R^7 , together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

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and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^6 and R^7 may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, $-R^8-CN$, $-R^8-OR^5$, heterocyclyl and heteroaryl;

or R^1 is aralkyl optionally substituted by one or more substituents selected from the group consisting of $-R^8-OR^5$, $-C(O)OR^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

or R^1 is $-R^9-N(R^{10})R^{11}$, $-R^9-N(R^{12})C(O)R^{11}$ or $-R^9-N(R^{10})C(O)N(R^{10})R^{11}$ where:

each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, $-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

or R^1 is heterocyclylalkyl or heteroarylalkyl where the heterocyclylalkyl or the heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$ (where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$,

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and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl,

heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$, $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not $-C(O)OCH_3$, $-C(O)NH_2$, iodo or cyano;

or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2d} are as defined above;

or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;

R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c}

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and R^{3d} are as defined above;
or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached,
may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and
 R^{3a} and R^d are as defined above;
or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached,
may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and
 R^{3a} and R^{3b} are as defined above;
each R^4 and R^5 is independently selected from the group consisting of hydrogen, alkyl,
alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl,
heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;
or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together
with the nitrogen atom to which they are attached, may form a heterocyclyl or
heteroaryl;
each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched
alkenylene chain or a straight or branched alkynylene chain; and
each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain
or a straight or branched alkynylene chain;
or a stereoisomer, enantiomer or tautomer thereof;
or a pharmaceutically acceptable salt or solvate thereof,
in the manufacture of a medicament for the treatment of hormone sensitive cancer.

In another aspect, the invention provides methods of treating or preventing

benign prostatic hyperplasia in a mammal, preferably a human, wherein the methods comprise administering to the mammal in need thereof a therapeutically effective amount of a compound of the invention as set forth above.

5 In another aspect, the invention provides methods of treating or preventing pruritis in a mammal, preferably a human, wherein the methods comprise administering to the mammal in need thereof a therapeutically effective amount of a compound of the invention as set forth above.

10 In another aspect, the invention provides methods of treating or preventing cancer in a mammal, preferably a human, wherein the methods comprise administering to the mammal in need thereof a therapeutically effective amount of a compound of the invention as set forth above.

In another aspect, the invention provides pharmaceutical compositions comprising the compounds of the invention, as set forth above, and pharmaceutically acceptable excipients.

15 In another aspect, the invention provides pharmaceutical therapy in combination with one or more other compounds of the invention or one or more other accepted therapies or as any combination thereof to increase the potency of an existing or future drug therapy or to decrease the adverse events associated with the accepted therapy. In one embodiment, the present invention relates to a
20 pharmaceutical composition combining compounds of the present invention with established or future therapies for the indications listed in the invention.

In another aspect, this invention is directed to the use of a compound of the invention, as set forth above, as a stereoisomer, enantiomer or tautomer or mixtures thereof, or a pharmaceutically acceptable salt, solvate or prodrug thereof, or the use of
25 a pharmaceutical composition of the invention, comprising a pharmaceutically acceptable excipient and a compound of the invention, as set forth above, as a stereoisomer, enantiomer or tautomer or mixtures thereof, or a pharmaceutically acceptable salt, solvate or prodrug thereof, in the preparation of a medicament for the treatment and/or prevention of hypercholesterolemia, benign prostatic hyperplasia,
30 pruritis, and/or cancer in a mammal.

DETAILED DESCRIPTION OF THE INVENTION

DEFINITIONS

Certain chemical groups named herein are preceded by a shorthand notation

indicating the total number of carbon atoms that are to be found in the indicated chemical group. For example; C₇-C₁₂alkyl describes an alkyl group, as defined below, having a total of 7 to 12 carbon atoms, and C₄-C₁₂cycloalkylalkyl describes a cycloalkylalkyl group, as defined below, having a total of 4 to 12 carbon atoms. The total number of carbons in the shorthand notation does not include carbons that may exist in substituents of the group described. For example, the following terms have the meaning indicated:

"C₁-C₁₀alkyl" refers to an alkyl radical as defined below containing one to ten carbon atoms. The C₁-C₁₀alkyl radical may be optionally substituted as defined below for an alkyl group.

"C₂-C₁₂alkynyl" refers to an alkynyl radical as defined below containing two to twelve carbon atoms. The C₂-C₁₂alkynyl radical may be optionally substituted as defined below for an alkenyl group.

"C₁-C₁₂alkoxy" refers to an alkoxy radical as defined below containing one to twelve carbon atoms. The alkyl part of the C₁-C₁₂alkoxy radical may be optionally substituted as defined below for an alkyl group.

"C₂-C₁₂alkoxyalkyl" refers to an alkoxyalkyl radical as defined below containing two to twelve carbon atoms. Each alkyl part of the C₂-C₁₂alkoxyalkyl radical may be optionally substituted as defined below for an alkyl group.

"C₇-C₁₂aralkyl" refers to an aralkyl group as defined below containing seven to twelve carbon atoms. The aryl part of the C₇-C₁₂aralkyl radical may be optionally substituted as described below for an aryl group. The alkyl part of the C₇-C₁₂aralkyl radical may be optionally substituted as defined below for an alkyl group.

"C₇-C₁₂aralkenyl" refers to an aralkenyl group as defined below containing seven to twelve carbon atoms. The aryl part of the C₇-C₁₂aralkenyl radical may be optionally substituted as described below for an aryl group. The alkenyl part of the C₇-C₁₂aralkenyl radical may be optionally substituted as defined below for an alkenyl group.

"C₃-C₁₂cycloalkyl" refers to a cycloalkyl radical as defined below having three to twelve carbon atoms. The C₃-C₁₂cycloalkyl radical may be optionally substituted as defined below for a cycloalkyl group.

"C₄-C₁₂cycloalkylalkyl" refers to a cycloalkylalkyl radical as defined below having four to twelve carbon atoms. The C₄-C₁₂cycloalkylalkyl radical may be optionally substituted as defined below for a cycloalkylalkyl group.

In addition to the foregoing, as used in the specification and appended claims,

unless specified to the contrary, the following terms have the meaning indicated:

"Amino" refers to the -NH_2 radical.

"Cyano" refers to the -CN radical.

"Hydroxyl" refers to the -OH radical.

5 "Imino" refers to the =NH substituent.

"Nitro" refers to the -NO_2 radical.

"Oxo" refers to the =O substituent.

"Thioxo" refers to the =S substituent.

"Trifluoromethyl" refers to the -CF_3 radical.

10 "Alkyl" refers to a straight or branched hydrocarbon chain radical consisting solely of carbon and hydrogen atoms, containing no unsaturation, having from one to twelve carbon atoms, preferably one to eight carbon atoms or one to six carbon atoms, and which is attached to the rest of the molecule by a single bond, e.g., methyl, ethyl, *n*-propyl, 1-methylethyl (*iso*-propyl), *n*-butyl, *n*-pentyl, 1,1-dimethylethyl (*t*-butyl),
 15 3-methylhexyl, 2-methylhexyl, and the like. Unless stated otherwise specifically in the specification, an alkyl group may be optionally substituted by one of the following groups: alkyl, alkenyl, halo, haloalkenyl, cyano, nitro, aryl, cycloalkyl, heterocyclyl, heteroaryl, oxo, trimethylsilyl, -OR^{14} , -OC(O)-R^{14} , $\text{-N(R}^{14})_2$, -C(O)R^{14} , -C(O)OR^{14} , $\text{-C(O)N(R}^{14})_2$, $\text{-N(R}^{14})\text{C(O)OR}^{16}$, $\text{-N(R}^{14})\text{C(O)R}^{16}$, $\text{-N(R}^{14})\text{S(O)}_t\text{R}^{16}$ (where *t* is 1 to 2),
 20 $\text{-S(O)}_t\text{OR}^{16}$ (where *t* is 1 to 2), $\text{-S(O)}_t\text{R}^{16}$ (where *t* is 0 to 2), and $\text{-S(O)}_t\text{N(R}^{14})_2$ (where *t* is 1 to 2) where each R^{14} is independently hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl (optionally substituted with one or more halo groups), aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl; and each R^{16} is alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl,
 25 heteroaryl or heteroarylalkyl.

"Alkenyl" refers to a straight or branched hydrocarbon chain radical group consisting solely of carbon and hydrogen atoms, containing at least one double bond, having from two to twelve carbon atoms, preferably one to eight carbon atoms and which is attached to the rest of the molecule by a single bond, e.g., ethenyl,
 30 prop-1-enyl, but-1-enyl, pent-1-enyl, penta-1,4-dienyl, and the like. Unless stated otherwise specifically in the specification, an alkenyl group may be optionally substituted by one of the following groups: alkyl, alkenyl, halo, haloalkenyl, cyano, nitro, aryl, cycloalkyl, heterocyclyl, heteroaryl, oxo, trimethylsilyl, -OR^{14} , -OC(O)-R^{14} , $\text{-N(R}^{14})_2$, -C(O)R^{14} , -C(O)OR^{14} , $\text{-C(O)N(R}^{14})_2$, $\text{-N(R}^{14})\text{C(O)OR}^{16}$, $\text{-N(R}^{14})\text{C(O)R}^{16}$,
 35 $\text{-N(R}^{14})\text{S(O)}_t\text{R}^{16}$ (where *t* is 1 to 2), $\text{-S(O)}_t\text{OR}^{16}$ (where *t* is 1 to 2), $\text{-S(O)}_t\text{R}^{16}$ (where *t* is

0 to 2), and $-S(O)_tN(R^{14})_2$ (where t is 1 to 2) where each R^{14} is independently hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl (optionally substituted with one or more halo groups), aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl or heteroarylalkyl; and each R^{16} is alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl,

5 heterocyclalkyl, heteroaryl or heteroarylalkyl.

"Alkylene" or "alkylene chain" refers to a straight or branched divalent hydrocarbon chain linking the rest of the molecule to a radical group, consisting solely of carbon and hydrogen, containing no unsaturation and having from one to twelve carbon atoms, *e.g.*, methylene, ethylene, propylene, *n*-butylene, and the like. The
 10 alkylene chain is attached to the rest of the molecule through a single bond and to the radical group through a single bond. The points of attachment of the alkylene chain to the rest of the molecule and to the radical group can be through one carbon or any two carbons within the chain. Unless stated otherwise specifically in the specification, an alkylene chain may be optionally substituted by one of the following groups: alkyl,
 15 alkenyl, halo, haloalkenyl, cyano, nitro, aryl, cycloalkyl, heterocyclyl, heteroaryl, oxo, trimethylsilanyl, $-OR^{14}$, $-OC(O)-R^{14}$, $-N(R^{14})_2$, $-C(O)R^{14}$, $-C(O)OR^{14}$, $-C(O)N(R^{14})_2$, $-N(R^{14})C(O)OR^{16}$, $-N(R^{14})C(O)R^{16}$, $-N(R^{14})S(O)_tR^{16}$ (where t is 1 to 2), $-S(O)_tOR^{16}$ (where t is 1 to 2), $-S(O)_tR^{16}$ (where t is 0 to 2), and $-S(O)_tN(R^{14})_2$ (where t is 1 to 2) where each R^{14} is independently hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl,
 20 aryl (optionally substituted with one or more halo groups), aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl or heteroarylalkyl; and each R^{16} is alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl or heteroarylalkyl.

"Alkenylene" or "alkenylene chain" refers to a straight or branched divalent
 25 hydrocarbon chain linking the rest of the molecule to a radical group, consisting solely of carbon and hydrogen, containing at least one double bond and having from two to twelve carbon atoms, *e.g.*, ethenylene, propenylene, *n*-butenylene, and the like. The alkenylene chain is attached to the rest of the molecule through a single bond and to the radical group through a double bond or a single bond. The points of attachment of
 30 the alkenylene chain to the rest of the molecule and to the radical group can be through one carbon or any two carbons within the chain. Unless stated otherwise specifically in the specification, an alkenylene chain may be optionally substituted by one of the following groups: alkyl, alkenyl, halo, haloalkenyl, cyano, nitro, aryl, cycloalkyl, heterocyclyl, heteroaryl, oxo, trimethylsilanyl, $-OR^{14}$, $-OC(O)-R^{14}$, $-N(R^{14})_2$,
 35 $-C(O)R^{14}$, $-C(O)OR^{14}$, $-C(O)N(R^{14})_2$, $-N(R^{14})C(O)OR^{16}$, $-N(R^{14})C(O)R^{16}$, $-N(R^{14})S(O)_tR^{16}$

(where t is 1 to 2), $-S(O)_tOR^{16}$ (where t is 1 to 2), $-S(O)_tR^{16}$ (where t is 0 to 2), and $-S(O)_tN(R^{14})_2$ (where t is 1 to 2) where each R^{14} is independently hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl (optionally substituted with one or more halo groups), aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl; and each

5 R^{16} is alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl.

"Alkynylene" or "alkynylene chain" refers to a straight or branched divalent hydrocarbon chain linking the rest of the molecule to a radical group, consisting solely of carbon and hydrogen, containing at least one triple bond and having from two to

10 twelve carbon atoms, e.g., propynylene, *n*-butynylene, and the like. The alkynylene chain is attached to the rest of the molecule through a single bond and to the radical group through a double bond or a single bond. The points of attachment of the alkynylene chain to the rest of the molecule and to the radical group can be through one carbon or any two carbons within the chain. Unless stated otherwise specifically in

15 the specification, an alkynylene chain may be optionally substituted by one of the following groups: alkyl, alkenyl, halo, haloalkenyl, cyano, nitro, aryl, cycloalkyl, heterocyclyl, heteroaryl, oxo, trimethylsilanyl, $-OR^{14}$, $-OC(O)-R^{14}$, $-N(R^{14})_2$, $-C(O)R^{14}$, $-C(O)OR^{14}$, $-C(O)N(R^{14})_2$, $-N(R^{14})C(O)OR^{16}$, $-N(R^{14})C(O)R^{16}$, $-N(R^{14})S(O)_tR^{16}$ (where t is 1 to 2), $-S(O)_tOR^{16}$ (where t is 1 to 2), $-S(O)_tR^{16}$ (where t is 0 to 2), and $-S(O)_tN(R^{14})_2$

20 (where t is 1 to 2) where each R^{14} is independently hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl (optionally substituted with one or more halo groups), aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl; and each R^{16} is alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl.

25 "Alkynyl" refers to a straight or branched hydrocarbon chain radical group consisting solely of carbon and hydrogen atoms, containing at least one triple bond, having from two to twelve carbon atoms, preferably one to eight carbon atoms and which is attached to the rest of the molecule by a single bond, e.g., ethynyl, propynyl, butynyl, pentynyl, hexynyl, and the like. Unless stated otherwise specifically in the

30 specification, an alkynyl group may be optionally substituted by one of the following groups: alkyl, alkenyl, halo, haloalkyl, haloalkenyl, cyano, nitro, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-OR^{14}$, $-OC(O)-R^{14}$, $-N(R^{14})_2$, $-C(O)R^{14}$, $-C(O)OR^{14}$, $-C(O)N(R^{14})_2$, $-N(R^{14})C(O)OR^{16}$, $-N(R^{14})C(O)R^{16}$, $-N(R^{14})S(O)_tR^{16}$ (where t is 1 to 2), $-S(O)_tOR^{16}$ (where t is 1 to 2),

35 $-S(O)_tR^{16}$ (where t is 0 to 2), and $-S(O)_tN(R^{14})_2$ (where t is 1 to 2) where each R^{14} is

independently hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl or heteroarylalkyl; and each R^{16} is alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl or heteroarylalkyl.

5 "Alkoxy" refers to a radical of the formula $-OR_a$ where R_a is an alkyl radical as defined above containing one to twelve carbon atoms. The alkyl part of the alkoxy radical may be optionally substituted as defined above for an alkyl radical.

"Alkoxyalkyl" refers to a radical of the formula $-R_a-O-R_a$ where each R_a is independently an alkyl radical as defined above. The oxygen atom may be bonded to
10 any carbon in either alkyl radical. Each alkyl part of the alkoxyalkyl radical may be optionally substituted as defined above for an alkyl group.

"Aryl" refers to aromatic monocyclic or multicyclic hydrocarbon ring system consisting only of hydrogen and carbon and containing from 6 to 18 carbon atoms, where the ring system may be partially saturated. Aryl groups include, but are not
15 limited to, groups such as fluorenyl, phenyl and naphthyl. Unless stated otherwise specifically in the specification, the term "aryl" or the prefix "ar-" (such as in "aralkyl") is meant to include aryl radicals optionally substituted by one or more substituents independently selected from the group consisting of alkyl, akenyl, halo, haloalkyl, haloalkenyl, cyano, nitro, aryl, heteroaryl, heteroarylalkyl, $-R^{15}-OR^{14}$, $-R^{15}-OC(O)-R^{14}$,
20 $-R^{15}-N(R^{14})_2$, $-R^{15}-C(O)R^{14}$, $-R^{15}-C(O)OR^{14}$, $-R^{15}-C(O)N(R^{14})_2$, $-R^{15}-N(R^{14})C(O)OR^{16}$, $-R^{15}-N(R^{14})C(O)R^{16}$, $-R^{15}-N(R^{14})S(O)_tR^{16}$ (where t is 1 to 2), $-R^{15}-S(O)_tOR^{16}$ (where t is 1 to 2), $-R^{15}-S(O)_tR^{16}$ (where t is 0 to 2), and $-R^{15}-S(O)_tN(R^{14})_2$ (where t is 1 to 2) where each R^{14} is independently hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl or heteroarylalkyl; each R^{15} is
25 independently a direct bond or a straight or branched alkylene or alkenylene chain; and each R^{16} is alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl or heteroarylalkyl.

"Aralkyl" refers to a radical of the formula $-R_aR_b$ where R_a is an alkyl radical as defined above and R_b is one or more aryl radicals as defined above, e.g., benzyl,
30 diphenylmethyl and the like. The aryl radical(s) may be optionally substituted as described above.

"Aryloxy" refers to a radical of the formula $-OR_b$ where R_b is an aryl group as defined above. The aryl part of the aryloxy radical may be optionally substituted as defined above.

35 "Aralkenyl" refers to a radical of the formula $-R_cR_b$ where R_c is an alkenyl radical

as defined above and R_b is one or more aryl radicals as defined above, which may be optionally substituted as described above. The aryl part of the aralkenyl radical may be optionally substituted as described above for an aryl group. The alkenyl part of the aralkenyl radical may be optionally substituted as defined above for an alkenyl group.

5 "Aralkyloxy" refers to a radical of the formula $-OR_b$ where R_b is an aralkyl group as defined above. The aralkyl part of the aralkyloxy radical may be optionally substituted as defined above.

"Cycloalkyl" refers to a stable non-aromatic monocyclic or polycyclic hydrocarbon radical consisting solely of carbon and hydrogen atoms, which may include fused or bridged ring systems, having from three to fifteen carbon atoms, preferably having from three to ten carbon atoms, and which is saturated or unsaturated and attached to the rest of the molecule by a single bond. Monocyclic radicals include, for example, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and cyclooctyl. Polycyclic radicals include, for example, adamantyl, norbornyl, decalinyl, and the like. Unless otherwise stated specifically in the specification, the term "cycloalkyl" is meant to include cycloalkyl radicals which are optionally substituted by one or more substituents independently selected from the group consisting of alkyl, alkenyl, halo, haloalkyl, haloalkenyl, cyano, nitro, oxo, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^{15}-OR^{14}$, $-R^{15}-OC(O)-R^{14}$, $-R^{15}-N(R^{14})_2$, $-R^{15}-C(O)R^{14}$, $-R^{15}-C(O)OR^{14}$, $-R^{15}-C(O)N(R^{14})_2$, $-R^{15}-N(R^{14})C(O)OR^{16}$, $-R^{15}-N(R^{14})C(O)R^{16}$, $-R^{15}-N(R^{14})S(O)_tR^{16}$ (where t is 1 to 2), $-R^{15}-S(O)_tOR^{16}$ (where t is 1 to 2), $-R^{15}-S(O)_tR^{16}$ (where t is 0 to 2), and $-R^{15}-S(O)_tN(R^{14})_2$ (where t is 1 to 2) where each R^{14} is independently hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl; each R^{15} is independently a direct bond or a straight or branched alkylene or alkenylene chain; and each R^{16} is alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl.

30 "Cycloalkylalkyl" refers to a radical of the formula $-R_aR_d$ where R_a is an alkyl radical as defined above and R_d is a cycloalkyl radical as defined above. The alkyl radical and the cycloalkyl radical may be optionally substituted as defined above.

"Halo" refers to bromo, chloro, fluoro or iodo.

"Haloalkyl" refers to an alkyl radical, as defined above, that is substituted by one or more halo radicals, as defined above, e.g., trifluoromethyl, difluoromethyl, trichloromethyl, 2,2,2-trifluoroethyl, 1-fluoromethyl-2-fluoroethyl,

3-bromo-2-fluoropropyl, 1-bromomethyl-2-bromoethyl, and the like. The alkyl part of the haloalkyl radical may be optionally substituted as defined above for an alkyl group.

"Heterocyclyl" refers to a stable 3- to 18-membered non-aromatic ring radical which consists of two to twelve carbon atoms and from one to six heteroatoms

- 5 selected from the group consisting of nitrogen, oxygen and sulfur. Unless stated otherwise specifically in the specification, the heterocyclyl radical may be a monocyclic, bicyclic, tricyclic or tetracyclic ring system, which may include fused or bridged ring systems; and the nitrogen, carbon or sulfur atoms in the heterocyclyl radical may be optionally oxidized; the nitrogen atom may be optionally quaternized; and the
- 10 heterocyclyl radical may be partially or fully saturated. Examples of such heterocyclyl radicals include, but are not limited to, dioxolanyl, thienyl[1,3]dithianyl, decahydroisoquinolyl, imidazolyl, imidazolidinyl, isothiazolidinyl, isoxazolidinyl, morpholyl, octahydroindolyl, octahydroisoindolyl, 2-oxopiperazinyl, 2-oxopiperidinyl, 2-oxopyrrolidinyl, oxazolidinyl, piperidinyl, piperazinyl, 4-piperidonyl, pyrrolidinyl,
- 15 pyrazolidinyl, thiazolidinyl, tetrahydrofuryl, trithianyl, tetrahydropyranyl, thiomorpholyl, thiomorpholyl, 1-oxo-thiomorpholyl, and 1,1-dioxo-thiomorpholyl. Unless stated otherwise specifically in the specification, the term "heterocyclyl" is meant to include heterocyclyl radicals as defined above which are optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, halo, haloalkyl,
- 20 haloalkenyl, cyano, oxo, thioxo, nitro, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^{15}-OR^{14}$, $-R^{15}-OC(O)-R^{14}$, $-R^{15}-N(R^{14})_2$, $-R^{15}-C(O)R^{14}$, $-R^{15}-C(O)OR^{14}$, $-R^{15}-C(O)N(R^{14})_2$, $-R^{15}-N(R^{14})C(O)OR^{16}$, $-R^{15}-N(R^{14})C(O)R^{16}$, $-R^{15}-N(R^{14})S(O)_tR^{16}$ (where t is 1 to 2), $-R^{15}-S(O)_tOR^{16}$ (where t is 1 to 2), $-R^{15}-S(O)_tR^{16}$ (where t is 0 to 2), and $-R^{15}-S(O)_tN(R^{14})_2$ (where t is 1 to 2) where
- 25 each R^{14} is independently hydrogen, alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl; each R^{15} is independently a direct bond or a straight or branched alkylene or alkenylene chain; and each R^{16} is alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl.

- 30 "Heterocyclylalkyl" refers to a radical of the formula $-R_aR_e$ where R_a is an alkyl radical as defined above and R_e is a heterocyclyl radical as defined above, and if the heterocyclyl is a nitrogen-containing heterocyclyl, the heterocyclyl may be attached to the alkyl radical at the nitrogen atom. The alkyl part of the heterocyclylalkyl radical may be optionally substituted as defined above for an alkyl group. The heterocyclyl
- 35 part of the heterocyclylalkyl radical may be optionally substituted as defined above for

a heterocyclyl group.

"Heteroaryl" refers to a 5- to 18-membered aromatic ring radical which consists of one to seventeen carbon atoms and from one to ten heteroatoms selected from the group consisting of nitrogen, oxygen and sulfur. For purposes of this invention, the heteroaryl radical may be a monocyclic, bicyclic, tricyclic or tetracyclic ring system, which may include fused or bridged ring systems; and the nitrogen, carbon or sulfur atoms in the heteroaryl radical may be optionally oxidized; the nitrogen atom may be optionally quaternized. Examples include, but are not limited to, azepinyl, acridinyl, benzimidazolyl, benzthiazolyl, benzindolyl, benzodioxolyl, benzofuranyl, benzooxazolyl, benzothiazolyl, benzothiadiazolyl, benzo[*b*][1,4]dioxepinyl, 1,4-benzodioxanyl, benzonaphthofuranyl, benzoxazolyl, benzodioxolyl, benzodioxinyl, benzopyranyl, benzopyranonyl, benzofuranyl, benzofuranonyl, benzothienyl (benzothiophenyl), benzotriazolyl, benzo[4,6]imidazo[1,2-*a*]pyridinyl, carbazolyl, cinnolinyl, dibenzofuranyl, dibenzothiophenyl, furanyl, furanonyl, isothiazolyl, imidazolyl, indazolyl, indolyl, indazolyl, isoindolyl, indolinyl, isoindolinyl, isoquinolyl, indoliziny, isoxazolyl, naphthyridinyl, oxadiazolyl, 2-oxoazepinyl, oxazolyl, oxiranyl, 1-phenyl-1*H*-pyrrolyl, phenazinyl, phenothiazinyl, phenoxazinyl, phthalazinyl, pteridinyl, purinyl, pyrrolyl, pyrazolyl, pyridinyl, pyrazinyl, pyrimidinyl, pyridazinyl, pyrrolyl, quinazolinyl, quinoxalinyl, quinolinyl, quinuclidinyl, isoquinolinyl, tetrahydroquinolinyl, thiazolyl, thiadiazolyl, triazolyl, tetrazolyl, triazinyl, and thiophenyl (i.e. thienyl). Unless stated otherwise specifically in the specification, the term "heteroaryl" is meant to include heteroaryl radicals as defined above which are optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkoxy, halo, haloalkyl, haloalkenyl, cyano, oxo, thioxo, nitro, oxo, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^{15}-OR^{14}$, $-R^{15}-OC(O)-R^{14}$, $-R^{15}-N(R^{14})_2$, $-R^{15}-C(O)R^{14}$, $-R^{15}-C(O)OR^{14}$, $-R^{15}-C(O)N(R^{14})_2$, $-R^{15}-N(R^{14})C(O)OR^{16}$, $-R^{15}-N(R^{14})C(O)R^{16}$, $-R^{15}-N(R^{14})S(O)_tR^{16}$ (where *t* is 1 to 2), $-R^{15}-S(O)_tOR^{16}$ (where *t* is 1 to 2), $-R^{15}-S(O)_tR^{16}$ (where *t* is 0 to 2), and $-R^{15}-S(O)_tN(R^{14})_2$ (where *t* is 1 to 2) where each R^{14} is independently hydrogen, alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl; each R^{15} is independently a direct bond or a straight or branched alkylene or alkenylene chain; and each R^{16} is alkyl, alkenyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl or heteroarylalkyl.

"Heteroarylalkyl" refers to a radical of the formula $-R_aR_f$ where R_a is an alkyl radical as defined above and R_f is a heteroaryl radical as defined above. The

heteroaryl part of the heteroarylalkyl radical may be optionally substituted as defined above for a heteroaryl group. The alkyl part of the heteroarylalkyl radical may be optionally substituted as defined above for an alkyl group.

"Heteroarylalkenyl" refers to a radical of the formula $-R_bR_f$ where R_b is an alkenyl radical as defined above and R_f is a heteroaryl radical as defined above. The heteroaryl part of the heteroarylalkenyl radical may be optionally substituted as defined above for a heteroaryl group. The alkenyl part of the heteroarylalkenyl radical may be optionally substituted as defined above for an alkenyl group.

"Trihaloalkyl" refers to an alkyl radical, as defined above, that is substituted by three halo radicals, as defined above, e.g., trifluoromethyl. The alkyl part of the trihaloalkyl radical may be optionally substituted as defined above for an alkyl group.

"Trihaloalkoxy" refers to a radical of the formula $-OR_g$ where R_g is a trihaloalkyl group as defined above. The trihaloalkyl part of the trihaloalkoxy group may be optionally substituted as defined above for a trihaloalkyl group.

"Prodrugs" is meant to indicate a compound that may be converted under physiological conditions or by solvolysis to a biologically active compound of the invention. Thus, the term "prodrug" refers to a metabolic precursor of a compound of the invention that is pharmaceutically acceptable. A prodrug may be inactive when administered to a subject in need thereof, but is converted *in vivo* to an active compound of the invention. Prodrugs are typically rapidly transformed *in vivo* to yield the parent compound of the invention, for example, by hydrolysis in blood. The prodrug compound often offers advantages of solubility, tissue compatibility or delayed release in a mammalian organism (see, Bundgard, H., Design of Prodrugs (1985), pp. 7-9, 21-24 (Elsevier, Amsterdam)). A discussion of prodrugs is provided in Higuchi, T., *et al.*, "Pro-drugs as Novel Delivery Systems," A.C.S. Symposium Series, Vol. 14, and in Bioreversible Carriers in Drug Design, Ed. Edward B. Roche, American Pharmaceutical Association and Pergamon Press, 1987, both of which are incorporated in full by reference herein.

The term "prodrug" is also meant to include any covalently bonded carriers, which release the active compound of the invention *in vivo* when such prodrug is administered to a mammalian subject. Prodrugs of a compound of the invention may be prepared by modifying functional groups present in the compound of the invention in such a way that the modifications are cleaved, either in routine manipulation or *in vivo*, to the parent compound of the invention. Prodrugs include compounds of the invention wherein a hydroxy, amino or mercapto group is bonded to any group that,

when the prodrug of the compound of the invention is administered to a mammalian subject, cleaves to form a free hydroxy, free amino or free mercapto group, respectively. Examples of prodrugs include, but are not limited to, acetate, formate and benzoate derivatives of alcohol or amide derivatives of amine functional groups in
5 the compounds of the invention and the like.

The invention disclosed herein is also meant to encompass all pharmaceutically acceptable compounds of formula (I) being isotopically-labelled by having one or more atoms replaced by an atom having a different atomic mass or mass number. Examples of isotopes that can be incorporated into the disclosed compounds include
10 isotopes of hydrogen, carbon, nitrogen, oxygen, phosphorous, fluorine, chlorine, and iodine, such as ^2H , ^3H , ^{11}C , ^{13}C , ^{14}C , ^{13}N , ^{15}N , ^{15}O , ^{17}O , ^{18}O , ^{31}P , ^{32}P , ^{35}S , ^{18}F , ^{36}Cl , ^{123}I , and ^{125}I , respectively. These radiolabelled compounds could be useful to help determine or measure the effectiveness of the compounds, by characterizing, for example, the site or mode of action on the sodium channels, or binding affinity to
15 pharmacologically important site of action on the sodium channels. Certain isotopically-labelled compounds of formula (I), for example, those incorporating a radioactive isotope, are useful in drug and/or substrate tissue distribution studies. The radioactive isotopes tritium, *i.e.* ^3H , and carbon-14, *i.e.* ^{14}C , are particularly useful for this purpose in view of their ease of incorporation and ready means of detection.

20 Substitution with heavier isotopes such as deuterium, *i.e.* ^2H , may afford certain therapeutic advantages resulting from greater metabolic stability, for example, increased *in vivo* half-life or reduced dosage requirements, and hence may be preferred in some circumstances.

Substitution with positron emitting isotopes, such as ^{11}C , ^{18}F , ^{15}O and ^{13}N , can
25 be useful in Positron Emission Topography (PET) studies for examining substrate receptor occupancy. Isotopically-labeled compounds of formula (I) can generally be prepared by conventional techniques known to those skilled in the art or by processes analogous to those described in the Examples and Preparations as set out below using an appropriate isotopically-labeled reagent in place of the non-labeled reagent
30 previously employed.

The invention disclosed herein is also meant to encompass the *in vivo* metabolic products of the disclosed compounds. Such products may result from, for example, the oxidation, reduction, hydrolysis, amidation, esterification, and the like of the administered compound, primarily due to enzymatic processes. Accordingly, the
35 invention includes compounds produced by a process comprising contacting a

compound of this invention with a mammal for a period of time sufficient to yield a metabolic product thereof. Such products are typically identified by administering a radiolabelled compound of the invention in a detectable dose to an animal, such as rat, mouse, guinea pig, monkey, or to human, allowing sufficient time for metabolism to occur, and isolating its conversion products from the urine, blood or other biological samples.

"Stable compound" and "stable structure" are meant to indicate a compound that is sufficiently robust to survive isolation to a useful degree of purity from a reaction mixture, and formulation into an efficacious therapeutic agent.

10 "Mammal" includes humans and both domestic animals such as laboratory animals and household pets, (e.g. cats, dogs, swine, cattle, sheep, goats, horses, rabbits), and non-domestic animals such as wildlife and the like.

"Optional" or "optionally" means that the subsequently described event of circumstances may or may not occur, and that the description includes instances where said event or circumstance occurs and instances in which it does not. For example, "optionally substituted aryl" means that the aryl radical may or may not be substituted and that the description includes both substituted aryl radicals and aryl radicals having no substitution. When a functional group is described as "optionally substituted," and in turn, substituents on the functional group are also "optionally substituted" and so on, for the purposes of this invention, such iterations are limited to five.

"Pharmaceutically acceptable carrier, diluent or excipient" includes without limitation any adjuvant, carrier, excipient, glidant, sweetening agent, diluent, preservative, dye/colorant, flavor enhancer, surfactant, wetting agent, dispersing agent, suspending agent, stabilizer, isotonic agent, solvent, or emulsifier which has been approved by the United States Food and Drug Administration as being acceptable for use in humans or domestic animals.

"Pharmaceutically acceptable salt" includes both acid and base addition salts.

"Pharmaceutically acceptable acid addition salt" refers to those salts which retain the biological effectiveness and properties of the free bases, which are not biologically or otherwise undesirable, and which are formed with inorganic acids such as, but are not limited to, hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid and the like, and organic acids such as, but not limited to, acetic acid, 2,2-dichloroacetic acid, adipic acid, alginic acid, ascorbic acid, aspartic acid, benzenesulfonic acid, benzoic acid, 4-acetamidobenzoic acid, camphoric acid,

camphor-10-sulfonic acid, capric acid, caproic acid, caprylic acid, carbonic acid, cinnamic acid, citric acid, cyclamic acid, dodecylsulfuric acid, ethane-1,2-disulfonic acid, ethanesulfonic acid, 2-hydroxyethanesulfonic acid, formic acid, fumaric acid, galactaric acid, gentisic acid, glucoheptonic acid, gluconic acid, glucuronic acid, glutamic acid, glutaric acid, 2-oxo-glutaric acid, glycerophosphoric acid, glycolic acid, hippuric acid, isobutyric acid, lactic acid, lactobionic acid, lauric acid, maleic acid, malic acid, malonic acid, mandelic acid, methanesulfonic acid, mucic acid, naphthalene-1,5-disulfonic acid, naphthalene-2-sulfonic acid, 1-hydroxy-2-naphthoic acid, nicotinic acid, oleic acid, orotic acid, oxalic acid, palmitic acid, pamoic acid, propionic acid, pyroglutamic acid, pyruvic acid, salicylic acid, 4-aminosalicylic acid, sebacic acid, stearic acid, succinic acid, tartaric acid, thiocyanic acid, *p*-toluenesulfonic acid, trifluoroacetic acid, undecylenic acid, and the like.

"Pharmaceutically acceptable base addition salt" refers to those salts which retain the biological effectiveness and properties of the free acids, which are not biologically or otherwise undesirable. These salts are prepared from addition of an inorganic base or an organic base to the free acid. Salts derived from inorganic bases include, but are not limited to, the sodium, potassium, lithium, ammonium, calcium, magnesium, iron, zinc, copper, manganese, aluminum salts and the like. Preferred inorganic salts are the ammonium, sodium, potassium, calcium, and magnesium salts. Salts derived from organic bases include, but are not limited to, salts of primary, secondary, and tertiary amines, substituted amines including naturally occurring substituted amines, cyclic amines and basic ion exchange resins, such as ammonia, isopropylamine, trimethylamine, diethylamine, triethylamine, tripropylamine, diethanolamine, ethanolamine, deanol, 2-dimethylaminoethanol, 2-diethylaminoethanol, dicyclohexylamine, lysine, arginine, histidine, caffeine, procaine, hydrabamine, choline, betaine, benethamine, benzathine, ethylenediamine, glucosamine, methylglucamine, theobromine, triethanolamine, tromethamine, purines, piperazine, piperidine, *N*-ethylpiperidine, polyamine resins and the like. Particularly preferred organic bases are isopropylamine, diethylamine, ethanolamine, trimethylamine, dicyclohexylamine, choline and caffeine.

Often crystallizations produce a solvate of the compound of the invention. As used herein, the term "solvate" refers to an aggregate that comprises one or more molecules of a compound of the invention with one or more molecules of solvent. The solvent may be water, in which case the solvate may be a hydrate. Alternatively, the solvent may be an organic solvent. Thus, the compounds of the present invention may

exist as a hydrate, including a monohydrate, dihydrate, hemihydrate, sesquihydrate, trihydrate, tetrahydrate and the like, as well as the corresponding solvated forms. The compound of the invention may be true solvates, while in other cases, the compound of the invention may merely retain adventitious water or be a mixture of water plus

5 some adventitious solvent.

A "pharmaceutical composition" refers to a formulation of a compound of the invention and a medium generally accepted in the art for the delivery of the biologically active compound to mammals, e.g., humans. Such a medium includes all pharmaceutically acceptable carriers, diluents or excipients therefor.

10 "Therapeutically effective amount" refers to that amount of a compound of the invention which, when administered to a mammal, preferably a human, is sufficient to effect treatment, as defined below, of a disease or condition in the mammal, preferably a human. The amount of a compound of the invention which constitutes a
15 "therapeutically effective amount" will vary depending on the compound, the condition and its severity, the manner of administration, and the age of the mammal to be treated, but can be determined routinely by one of ordinary skill in the art having regard to his own knowledge and to this disclosure.

"Treating" or "treatment" as used herein covers the treatment of the disease or condition of interest in a mammal, preferably a human, having the disease or condition
20 of interest, and includes:

- (i) preventing the disease or condition from occurring in a mammal, in particular, when such mammal is predisposed to the condition but has not yet been diagnosed as having it;
- (ii) inhibiting the disease or condition, *i.e.*, arresting its development;
- 25 (iii) relieving the disease or condition, *i.e.*, causing regression of the disease or condition; or
- (iv) relieving the symptoms resulting from the disease or condition.

As used herein, the terms "disease" and "condition" may be used interchangeably or may be different in that the particular malady or condition may not
30 have a known causative agent (so that etiology has not yet been worked out) and it is therefore not yet recognized as a disease but only as an undesirable condition or syndrome, wherein a more or less specific set of symptoms have been identified by clinicians.

The compounds of the invention, or their pharmaceutically acceptable salts
35 may contain one or more asymmetric centres and may thus give rise to enantiomers,

diastereomers, and other stereoisomeric forms that may be defined, in terms of absolute stereochemistry, as (*R*)- or (*S*)- or, as (*D*)- or (*L*)- for amino acids. The present invention is meant to include all such possible isomers, as well as their racemic and optically pure forms. Optically active (+) and (-), (*R*)- and (*S*)-, or (*D*)- and (*L*)- isomers may be prepared using chiral synthons or chiral reagents, or resolved using conventional techniques, for example, chromatography and fractional crystallisation. Conventional techniques for the preparation/isolation of individual enantiomers include chiral synthesis from a suitable optically pure precursor or resolution of the racemate (or the racemate of a salt or derivative) using, for example, chiral high pressure liquid chromatography (HPLC). When the compounds described herein contain olefinic double bonds or other centres of geometric asymmetry, and unless specified otherwise, it is intended that the compounds include both *E* and *Z* geometric isomers. Likewise, all tautomeric forms are also intended to be included.

A "stereoisomer" refers to a compound made up of the same atoms bonded by the same bonds but having different three-dimensional structures, which are not interchangeable. The present invention contemplates various stereoisomers and mixtures thereof and includes "enantiomers", which refers to two stereoisomers whose molecules are nonsuperimposable mirror images of one another.

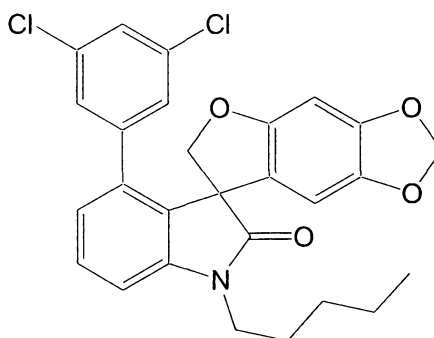
A "tautomer" refers to a proton shift from one atom of a molecule to another atom of the same molecule. The present invention includes tautomers of any said compounds.

Also within the scope of the invention are intermediate compounds of formula (I) and all polymorphs of the aforementioned species and crystal habits thereof.

The chemical naming protocol and structure diagrams used herein are a modified form of the I.U.P.A.C. nomenclature system, using the ACD/Name Version 9.07 software program, wherein the compounds of the invention are named herein as derivatives of the central core structure, *i.e.*, the 2-oxindole structure. For complex chemical names employed herein, a substituent group is named before the group to which it attaches. For example, cyclopropylethyl comprises an ethyl backbone with cyclopropyl substituent. In chemical structure diagrams, all bonds are identified, except for some carbon atoms, which are assumed to be bonded to sufficient hydrogen atoms to complete the valency.

Thus, for example, a compound of formula (I) wherein *j* is 0, *k* is 1, *Q* is -O-, *R*¹ is pentyl, *R*^{2a} is 3,5-dichlorophenyl, *R*^{2b}, *R*^{2c} and *R*^{2d} are each hydrogen, *R*^{3a} and *R*^{3d} are each hydrogen, and *R*^{3b} and *R*^{3c}, together with the carbon ring atoms to which they

are attached, form a fused dioxolyl ring; *i.e.*, a compound of the following formula:



is named herein as 4'-(3,5-dichlorophenyl)-1'-pentylspiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-2'(1'H)-one.

5 EMBODIMENTS OF THE INVENTION

Of the various aspects of the invention set forth above in the Summary of the Invention, certain embodiments are preferred.

One embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention wherein:

10 at least one of *j* and *k* is 1 and the other is 0 or 1;

Q is -O-;

*R*¹ is hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, -*R*⁸-C(O)*R*⁵, -*R*⁸-C(O)OR⁵, -C(O)N(*R*⁴)*R*⁵, -S(O)₂-*R*⁵, -*R*⁹-S(O)_{*m*}-*R*⁵ (where *m* is 0, 1 or 2), -*R*⁸-OR⁵, -*R*⁸-CN, -*R*⁹-P(O)(OR⁵)₂, or
15 -*R*⁹-O-*R*⁹-OR⁵;

R^{2a}, *R*^{2b}, *R*^{2c} and *R*^{2d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, -*R*⁸-CN, -*R*⁸-NO₂, -*R*⁸-OR⁵,
20 -*R*⁸-N(*R*⁴)*R*⁵, -N=C(*R*⁴)*R*⁵, -S(O)_{*m*}*R*⁴, -OS(O)₂CF₃, -*R*⁸-C(O)*R*⁴, -C(S)*R*⁴, -C(*R*⁴)₂C(O)*R*⁵, -*R*⁸-C(O)OR⁴, -C(S)OR⁴, -*R*⁸-C(O)N(*R*⁴)*R*⁵, -C(S)N(*R*⁴)*R*⁵, -N(*R*⁵)C(O)*R*⁴, -N(*R*⁵)C(S)*R*⁴, -N(*R*⁵)C(O)OR⁴, -N(*R*⁵)C(S)OR⁴, -N(*R*⁵)C(O)N(*R*⁴)*R*⁵, -N(*R*⁵)C(S)N(*R*⁴)*R*⁵, -N(*R*⁵)S(O)_{*n*}*R*⁴, -N(*R*⁵)S(O)_{*n*}N(*R*⁴)*R*⁵, -*R*⁸-S(O)_{*n*}N(*R*⁴)*R*⁵, -N(*R*⁵)C(=NR⁵)N(*R*⁴)*R*⁵, and -N(*R*⁵)C(=N-CN)N(*R*⁴)*R*⁵,
25 wherein each *m* is independently 0, 1, or 2 and each *n* is independently 1 or 2; and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for

- R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$, $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;
- or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;
- or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2d} are as defined above;
- or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;
- R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;
- or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;
- or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3d} are as defined above;
- or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl,

and R^{3a} and R^{3b} are as defined above;

each R^4 and R^5 is independently selected from group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;

5 or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl; and

each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and

10 each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain.

Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention wherein:

j is 0 and k is 1;

15 Q is -O-;

R^1 is hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$, $-R^9-S(O)_m-R^5$ (where m is 0, 1 or 2), $-R^8-OR^5$, $-R^8-CN$, $-R^9-P(O)(OR^5)_2$, or $-R^9-O-R^9-OR^5$;

20 R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from hydrogen, halo or alkyl;

R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of

hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$,

25 wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

30 or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3c} are as defined above;

each R^4 and R^5 is independently selected from group consisting of hydrogen, alkyl,

35 alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl,

heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;
 or when R⁴ and R⁵ are each attached to the same nitrogen atom, then R⁴ and R⁵,
 together with the nitrogen atom to which they are attached, may form a
 heterocyclyl or heteroaryl; and

- 5 each R⁸ is a direct bond or a straight or branched alkylene chain, a straight or
 branched alkenylene chain or a straight or branched alkynylene chain; and
 each R⁹ is a straight or branched alkylene chain, a straight or branched alkenylene
 chain or a straight or branched alkynylene chain.

Another embodiment of the invention are the compounds of formula (I) as set
 10 forth above in the Summary of the invention wherein:

R¹ is hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, cycloalkyl, cycloalkylalkyl, -R⁸-OR⁵,
 -R⁸-C(O)R⁵, -R⁸-C(O)OR⁵, -R⁸-C(O)N(R⁴)R⁵, -S(O)₂-R⁵, -R⁸-CN,
 -R⁹-P(O)(OR⁵)₂, or -R⁹-O-R⁹-OR⁵;

R^{2a}, R^{2b}, R^{2c} and R^{2d} are each independently selected from hydrogen, halo or alkyl;

- 15 R^{3a} and R^{3d} are both hydrogen;

R^{3b} and R^{3c}, together with the carbon ring atoms to which they are directly attached,
 form a fused dioxolyl ring;

each R⁴ and R⁵ is independently selected from group consisting of hydrogen, alkyl,
 alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl,
 20 heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;

or when R⁴ and R⁵ are each attached to the same nitrogen atom, then R⁴ and R⁵,
 together with the nitrogen atom to which they are attached, may form a
 heterocyclyl or heteroaryl;

- each R⁸ is a direct bond or a straight or branched alkylene chain, a straight or
 25 branched alkenylene chain or a straight or branched alkynylene chain; and
 each R⁹ is a straight or branched alkylene chain, a straight or branched alkenylene
 chain or a straight or branched alkynylene chain.

Another embodiment of the invention are the compounds of formula (I) as set
 forth above in the Summary of the invention, selected from the group consisting of:

- 30 1'-(2-cyclopropylethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 4'-bromo-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 ethyl (2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetate;
 spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 35 1'-[3-(benzyloxy)propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;

- 4',7'-dichloro-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 4'-bromospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 4'-bromo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one;
 5'-methylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 5 ethyl (4'-bromo-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-
 yl)acetate;
 ethyl (4'-chloro-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-
 yl)acetate;
 ethyl (5'-chloro-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-
 10 yl)acetate;
 7'-fluorospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 (2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetic acid;
N-(4-chlorobenzyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-
 yl)acetamide;
 15 *N*-(3-fluorophenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-
 yl)acetamide;
N-butyl-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
 1'-(2-oxo-2-piperidin-1-ylethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
N-butyl-*N*-methyl-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-
 20 yl)acetamide;
 2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)-*N*-phenylacetamide;
N-(4-fluorophenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-
 yl)acetamide;
N-(3-fluorobenzyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-
 25 yl)acetamide;
N-(3-chlorophenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-
 yl)acetamide;
N-(2-fluorophenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-
 yl)acetamide;
 30 *N*-(2-ethylphenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-
 yl)acetamide;
N-(4-ethylphenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-
 yl)acetamide;
N-(3-methylphenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-
 35 yl)acetamide;

- N*-(2,3-dimethylphenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- N*-(3,5-dimethylphenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- 5 2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)-*N*-pentylacetamide;
2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)-*N*-propylacetamide;
N-isopropyl-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
N-(3-methylbutyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- 10 *N*-isobutyl-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
N-hexyl-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
N-cyclohexyl-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- 15 *N*-cyclopentyl-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
N-heptyl-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
N-(2-chlorobenzyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- 20 *N*-(2,6-dimethylphenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
N-(2-methoxyphenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- 25 *N*-[(5-methyl-2-furyl)methyl]-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
N-ethyl-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
N-methyl-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- 30 *N*-(2-fluorobenzyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
N-[2-(3-methoxyphenyl)ethyl]-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- 35 *N*-(2-ethoxyethyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
N-(4-methoxybenzyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- 35 *N*-(2,4-dimethylphenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;

- yl)acetamide;
N-(3-isopropoxypropyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
N-(2-furylmethyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
5 *N*-(cyclohexylmethyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
N-(3-fluoro-2-methylphenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
10 *N*-(4-methoxyphenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
N-cyclobutyl-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
N-(2,5-difluorophenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
15 *N*-benzyl-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
N-(cyclopropylmethyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
N-butyl-*N*-ethyl-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
20 *N*-octyl-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
N-(3,3-dimethylbutyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
N-(4-chloro-2-methylphenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
25 *N*-(3-methoxyphenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
N-(2-fluoro-4-methylphenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
N-(3,4-dimethylphenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
30 *N*-(3-chlorobenzyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
N-(3-methoxybenzyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
35 *N*-(3,4-difluorophenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-

- yl)acetamide;
- N*-(3-methylbenzyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- N*-(2-methoxybenzyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- 5 *N*-(4-isopropylphenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- N*-(2,3-difluorophenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- 10 2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)-*N*-(tetrahydrofuran-2-ylmethyl)acetamide;
- N*-[2-(4-methylphenyl)ethyl]-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- N*-[2-(3-chlorophenyl)ethyl]-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- 15 *N*-(4-cyanophenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- N*-(2,3-dihydro-1*H*-inden-1-yl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- 20 *N*-(2-methoxyethyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- N*-[2-(4-methoxyphenyl)ethyl]-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- N*-(2-cyanoethyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- 25 *N*-(2,4-dichlorobenzyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- N*-(3,5-difluorobenzyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- 30 *N*-(2,4-difluorobenzyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- N*-(2-methylbenzyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- 35 *N*-(3,4-difluorobenzyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;

- N*-(2,5-difluorobenzyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- 2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)-*N,N*-dipropylacetamide;
- N,N*-dibutyl-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- 5 *N*-(2,6-difluorobenzyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- N*-(2-(methylthio)phenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- N*-(2-isopropylphenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- 10 *N*-(4-bromophenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- N*-(4-chlorophenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- 15 *N*-(2,4-dichlorophenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- N*-(3,5-dichlorophenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- N,N*-diethyl-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- 20 *N*-methyl-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)-*N*-phenylacetamide;
- N*-(4-hydroxybutyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- N*-allyl-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- 25 *N*-(2-fluoro-5-methylphenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- N*-(1,3-benzodioxol-5-ylmethyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- N*-cyclopropyl-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- 30 *N*-(2-cyclopropylethyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- N*-(3,4-dichlorobenzyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
- 35 *N*-(2,3-dichlorobenzyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;

- yl)acetamide;
N-(2,5-dimethylphenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
N-(3,4-dichlorophenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
5 *N,N*-dimethyl-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
N-methyl-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)-*N*-(2-phenylethyl)acetamide;
10 2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)-*N*-(2-phenylpropyl)acetamide;
N-[(1*R*)-1-cyclohexylethyl]-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
N-[(1*S*)-1-cyclohexylethyl]-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
15 2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)-*N*-(2-piperidin-1-ylethyl)acetamide;
2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)-*N*-[3-(trifluoromethyl)phenyl]acetamide;
20 *N*-(3-cyanophenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
1'-(2-morpholin-4-yl-2-oxoethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)-*N*-(2-phenylethyl)acetamide;
25 *N*-(4-bromo-2-chlorophenyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
N-(2-biphenyl-4-ylethyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide;
30 1'-prop-2-yn-1-ylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
1'-(2-ethoxyethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
1'-[(2*E*)-pent-2-en-1-yl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
1'-hex-5-en-1-ylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
1'-(cyclobutylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
35 1'-pent-2-yn-1-ylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;

- 1'-(5-chloropentyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-(4-fluorobutyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-(5-methylhexyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-[(3*Z*)-4-methylhex-3-en-1-yl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 5 1'-(2-bromoethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 5-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)pentanenitrile;
 1'-[2-(2-methoxyethoxy)ethyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-(cyclopropylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-(4,4,4-trifluorobutyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 10 diethyl [2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-
 yl)ethyl]phosphonate;
 1'-[(2,2,3,3-tetrafluorocyclobutyl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
 2'(1'*H*)-one;
 1'-[(benzyloxy)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 15 1'-allylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-(2-ethylbutyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-(4-methylpentyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-(3-methylbut-2-en-1-yl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-pent-4-en-1-ylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 20 4-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)butanenitrile;
 1'-[(2-methylcyclopropyl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-
 one;
 1'-(3-cyclopropylpropyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-hexylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 25 1'-[(2-cyclopropyl-6-hydroxypyrimidin-4-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-
 7,3'-indol]-2'(1'*H*)-one;
 1'-[(2-methylcyclopropyl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-
 one;
 1'-(3-cyclopropylpropyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 30 1'-butylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-[4-(trifluoromethoxy)benzyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-Propylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 4'-bromo-1'-methylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
tert-butyl 4-[(4'-bromo-2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-
 35 yl)methyl]piperidine-1-carboxylate;

ethyl 5-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)pentanoate;
 ethyl 4-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)butanoate;
 1'-(3-chloropropyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-(cyclohexylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 5 1'-(methylsulfonyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-(3-hydroxypropyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propanal; and
 2'-oxo-1'-pentyl-1',2'-dihydrospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indole]-4'-
 carbonitrile.

10 Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the Invention wherein:

R^1 is hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, cycloalkyl, cycloalkylalkyl, $-R^8-OR^5$,
 $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$, $-R^8-CN$,
 $-R^9-P(O)(OR^5)_2$, or $-R^9-O-R^9-OR^5$;

15 R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from hydrogen, halo or alkyl;

R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of

hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl,
 haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl,
 heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$,
 20 $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$,
 $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$,
 $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$,
 $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$,
 $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$,

25 wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

each R^4 and R^5 is independently selected from group consisting of hydrogen, alkyl,
 alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl,
 heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;

or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 ,

30 together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl;

each R^8 is a direct bond or a straight or branched alkylene chain, a straight or
 branched alkenylene chain or a straight or branched alkynylene chain; and

each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene

35 chain or a straight or branched alkynylene chain.

- Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention, selected from the group consisting of:
- 5,6-difluoro-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one;
 - 5-fluoro-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one;
 - 5 5-bromo-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one;
 - 5-chloro-6-fluoro-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one;
 - 6-methoxy-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one;
 - 6-chloro-5-fluoro-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one;
 - 1'-pentyl-5-(trifluoromethyl)spiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one;
 - 10 5,6-dichloro-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one;
 - 6-bromo-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one;
 - 5-bromospiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one;
 - 6-(trifluoromethoxy)spiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one;
 - ethyl (4'-bromo-5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2' *H*)-yl)acetate;
 - 15 methyl (6-chloro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2'*H*)-yl)acetate;
 - ethyl (5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2'*H*)-yl)acetate;
 - 2-(4'-bromo-5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2'*H*)-yl)-*N*-(2-fluorophenyl)acetamide;
 - 2-(6-chloro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2'*H*)-yl)-*N*-(2-
 - 20 fluorophenyl)acetamide;
 - 2-(5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2'*H*)-yl)-*N*-(2-fluorophenyl)acetamide;
 - 2-(5-bromo-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2'*H*)-yl)-*N*-(2-fluorophenyl)acetamide;
 - 25 1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one;
 - 6-anilino-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one;
 - 6-morpholin-4-yl-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one;
 - 6-amino-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one;
 - 1'-pentyl-6-phenoxy spiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one;
 - 30 1'-pentyl-6-phenoxy spiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one;
 - 1'-pentyl-6-pyridin-4-yl spiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one;
 - 6-(methylsulfonyl)-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one;
 - 1'-pentyl-6-(phenylsulfonyl)spiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one;
 - 1'-pentyl-5-phenoxy spiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one;
 - 35 5-hydroxy spiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one;

- 2'-oxo-1',2'-dihydrospiro[1-benzofuran-3,3'-indol]-5-yl trifluoromethanesulfonate;
 1'-pentyl-5-pyridin-3-ylspiro[1-benzofuran-3,3'-indol]-2'(1'H)-one;
 1'-pentyl-5-pyrimidin-5-ylspiro[1-benzofuran-3,3'-indol]-2'(1'H)-one;
 1'-pentyl-5-pyridin-4-ylspiro[1-benzofuran-3,3'-indol]-2'(1'H)-one;
 5 2'-oxo-1'-pentyl-1',2'-dihydrospiro[1-benzofuran-3,3'-indole]-5-carbonitrile;
N-(2-fluorophenyl)-2-(2'-oxo-5-pyridin-3-ylspiro[1-benzofuran-3,3'-indol]-1'(2'H)-
 yl)acetamide;
tert-butyl 3-(2'-oxo-1',2'-dihydrospiro[1-benzofuran-3,3'-indol]-5-yl)piperidine-1-
 carboxylate;
 10 5-methoxy-1'-methylspiro [1-benzofuran-3,3'-indol]-2'(1'H)-one.
- Another embodiment of the invention are the compounds of formula (I) as set
 forth above in the Summary of the Invention wherein:
- R^1 is hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, cycloalkyl, cycloalkylalkyl, $-R^8-OR^5$,
 $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$, $-R^8-CN$,
 15 $-R^9-P(O)(OR^5)_2$, or $-R^9-O-R^9-OR^5$;
- R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from hydrogen, halo or alkyl;
 R^{3a} and R^{3d} are both hydrogen;
 R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached,
 form a fused optionally substituted heterocyclyl ring or a fused optionally
 20 substituted cycloalkyl ring;
- each R^4 and R^5 is independently selected from group consisting of hydrogen, alkyl,
 alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl,
 heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;
 or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 ,
 25 together with the nitrogen atom to which they are attached, may form a
 heterocyclyl or heteroaryl;
- each R^8 is a direct bond or a straight or branched alkylene chain, a straight or
 branched alkenylene chain or a straight or branched alkynylene chain; and
 each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene
 30 chain or a straight or branched alkynylene chain.
- Another embodiment of the invention are the compounds of formula (I) as set
 forth above in the Summary of the invention, selected from the group consisting of:
 5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'H)-one;
 ethyl (4'-bromo-6,6-dimethyl-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-
 35 indol]-1'(2'H)-yl)acetate;

- ethyl (2'-oxo-6,7-dihydro-5*H*-spiro[indeno[5,6-*b*]furan-3,3'-indol]-1'(2'*H*)-yl)acetate;
 ethyl (2-oxo-5',6',7',8'-tetrahydrospiro[indole-3,3'-naphtho[2,3-*b*]furan]-1(2*H*)-yl)acetate;
 6,7-dihydrospiro[benzo[1,2-*b*:4,5-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one;
 5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one;
 5 ethyl (2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)acetate;
 (2'-oxo-6,7-dihydro-5*H*-spiro[indeno[5,6-*b*]furan-3,3'-indol]-1'(2'*H*)-yl)acetic acid;
 (4'-chloro-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)acetic
 acid;
 (4'-bromo-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)acetic
 10 acid;
 (5'-chloro-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)acetic
 acid;
 (2-oxo-5',6',7',8'-tetrahydrospiro[indole-3,3'-naphtho[2,3-*b*]furan]-1(2*H*)-yl)acetic acid;
 (2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)acetic acid;
 15 *N*-(2-fluorophenyl)-2-(2'-oxo-6,7-dihydro-5*H*-spiro[indeno[5,6-*b*]furan-3,3'-indol]-1'(2'*H*)-
 yl)acetamide;
N-(2-fluorophenyl)-2-(2-oxo-5',6',7',8'-tetrahydrospiro[indole-3,3'-naphtho[2,3-*b*]furan]-
 1(2*H*)-yl)acetamide;
 2-(4'-bromo-6,6-dimethyl-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-
 20 1'(2'*H*)-yl)-*N*-(2-fluorophenyl)acetamide;
 2-(4'-chloro-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)-*N*-
 (2-fluorophenyl)acetamide;
 2-(5'-chloro-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)-*N*-
 (2-fluorophenyl)acetamide;
 25 2-(4'-fluoro-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)-*N*-
 (2-fluorophenyl)acetamide;
 2-(4'-bromo-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)-*N*-
 (2-fluorophenyl)acetamide;
N-(2-fluorophenyl)-2-(2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-
 30 1'(2'*H*)-yl)acetamide; and
 2-(4'-fluoro-7'-methyl-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-
 1'(2'*H*)-yl)-*N*-(2-fluorophenyl)acetamide.

Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the Invention wherein:

- 35 R¹ is aryl, heteroaryl or heterocyclyl;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each hydrogen; and

R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, form a fused dioxolyl ring.

Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention wherein:

at least one of j and k is 1 and the other is 0 or 1;

Q is -O-;

R^1 is hydrogen, alkyl, $-R^8-C(O)OR^5$ or $-R^8-C(O)N(R^4)R^5$;

R^{2a} is selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2; and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl and heteroarylalkyl groups for R^{2a} is optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$, $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

R^{2b} , R^{2c} and R^{2d} are each hydrogen;

R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from hydrogen or halo; or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl and R^{3a} and R^{3d} are as defined above;

each R^4 and R^5 is independently selected from group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl,

heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;
 or when R⁴ and R⁵ are each attached to the same nitrogen atom, then R⁴ and R⁵,
 together with the nitrogen atom to which they are attached, may form a
 heterocyclyl or heteroaryl; and

- 5 each R⁸ is a direct bond or a straight or branched alkylene chain, a straight or
 branched alkenylene chain or a straight or branched alkynylene chain; and
 each R⁹ is a straight or branched alkylene chain, a straight or branched alkenylene
 chain or a straight or branched alkynylene chain.

Another embodiment of the invention are the compounds of formula (I) as set
 forth above in the Summary of the invention wherein:

j is 0 and k is 1 or j is 1 and k is 0;

Q is -O-;

R¹ is hydrogen or alkyl;

- R^{2a} is selected from the group consisting of alkyl, haloalkenyl, aryl, aralkyl, aralkenyl,
 15 heterocyclyl, heteroaryl, -R⁸-C(O)N(R⁴)R⁵, and -R⁸-N(R⁴)R⁵;
 wherein each of the aryl, aralkyl, aralkenyl, heterocyclyl and heteroaryl groups
 for R^{2a} is optionally substituted by one or more substituents selected
 from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo,
 haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl,
 20 aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl,
 heteroarylalkyl, -R⁸-CN, -R⁸-NO₂, -R⁸-OR⁵, -R⁸-N(R⁴)R⁵, -S(O)_mR⁴,
 -R⁸-S(O)_nN(R⁴)R⁵, -R⁸-C(O)R⁴, -R⁸-C(O)OR⁴, -R⁸-C(O)N(R⁴)R⁵,
 -N(R⁵)C(O)R⁴, and -N(R⁵)S(O)_nR⁴, wherein each m is independently 0,
 1, or 2 and each n is independently 1 or 2;

- 25 R^{2b}, R^{2c} and R^{2d} are each hydrogen;
 R^{3a}, R^{3b}, R^{3c} and R^{3d} are each independently selected from hydrogen or halo;
 or R^{3b} and R^{3c}, together with the carbon ring atoms to which they are directly attached,
 form a fused dioxolyl ring or a fused optionally substituted tetrahydrofuranyl
 ring, and R^{3a} and R^{3d} are as defined above;
 30 each R⁴ and R⁵ is independently selected from group consisting of hydrogen, alkyl,
 alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl,
 heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;
 or when R⁴ and R⁵ are each attached to the same nitrogen atom, then R⁴ and R⁵,
 together with the nitrogen atom to which they are attached, may form a
 35 heterocyclyl or heteroaryl; and

each R⁸ is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain.

Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention, selected from the group consisting of:

- 5 4'-[6-(dimethylamino)pyridin-3-yl]-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-(3,5-dimethoxyphenyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-(4-fluorophenyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 10 4'-(3,5-dichlorophenyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-[4-(dimethylamino)phenyl]-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-pentyl-4'-(3,4,5-trimethoxyphenyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 15 4-(2'-oxo-1'-pentyl-1',2'-dihydrospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-4'-yl)benzonitrile;
- 4'-dibenzo[*b,d*]furan-4-yl-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 20 4'-(1-benzyl-1*H*-pyrazol-4-yl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-(2-methoxypyrimidin-5-yl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-(2,4-dimethoxypyrimidin-5-yl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 25 4-(2'-oxo-1'-pentyl-1',2'-dihydrospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-4'-yl)benzamide;
- 4'-{4-[(dimethylamino)methyl]phenyl}-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 30 4'-(1-benzofuran-2-yl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-(6-methoxypyridin-3-yl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- N,N*-dimethyl-4-(2'-oxo-1'-pentyl-1',2'-dihydrospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-4'-yl)benzamide;
- 35 4'-dibenzo[*b,d*]thien-4-yl-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-

- one;
- 3-(2'-oxo-1'-pentyl-1',2'-dihydrospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-4'-yl)benzonitrile;
- 1'-pentyl-4'-pyridin-3-ylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 5 4'-(3-fluoro-4-methoxyphenyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-pentyl-4'-[2-(trifluoromethoxy)phenyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 10 4'-[3,5-bis(trifluoromethyl)phenyl]-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-pentyl-4'-[4-(trifluoromethyl)pyridin-3-yl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-(2-fluoro-5-methoxyphenyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 15 4'-(4-ethoxy-3-fluorophenyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-(1-benzothien-2-yl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-isobutyl-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-pentyl-4'-[4-(trifluoromethoxy)phenyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 20 4'-(5-fluoro-2-methoxyphenyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-(1,3-benzodioxol-5-yl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 25 1'-pentyl-4'-phenylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-pentyl-4'-[2-(trifluoromethyl)phenyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-(4-chlorophenyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-(2,3-dihydro-1,4-benzodioxin-6-yl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 30 1'-pentyl-4'-quinolin-3-ylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-(3,5-difluorophenyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-isoquinolin-4-yl-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-(6-methoxypyridin-2-yl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 35 one;

- 4'-(1*H*-indol-5-yl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one;
N-[2-(2'-oxo-1'-pentyl-1',2'-dihydrospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-4'-yl)phenyl]acetamide;
- 4'-(4-fluoro-2-methylphenyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
5 2'-(1'*H*)-one;
1'-pentyl-4'-quinolin-6-ylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one;
N-[4-(2'-oxo-1'-pentyl-1',2'-dihydrospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-4'-yl)phenyl]methanesulfonamide;
- 4'-(5-chloro-2-methoxyphenyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
10 2'-(1'*H*)-one;
1'-pentyl-4'-[3-(trifluoromethoxy)phenyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'-(1'*H*)-one;
1'-pentyl-4'-(4-phenoxyphenyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one;
4'-(2,4-dimethoxyphenyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-
15 one;
4'-(3-furyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one;
4'-(3,4-dimethoxyphenyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-
one;
N-[4-(2'-oxo-1'-pentyl-1',2'-dihydrospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-4'-
20 yl)phenyl]acetamide;
1'-pentyl-4'-[(*E*)-2-phenylvinyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one;
4'-(4-methoxyphenyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one;
4'-(6-fluoropyridin-3-yl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-
one;
- 25 4'-(3-chloro-4-fluorophenyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'-(1'*H*)-one;
4'-(3-chlorophenyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one;
4'-(1-benzothien-3-yl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one;
1'-pentyl-4'-(2-phenoxyphenyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one;
30 4'-(4-isopropoxyphenyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-
one;
4'-[(*E*)-2-(4-fluorophenyl)vinyl]-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'-(1'*H*)-one;
4'-(6-fluoropyridin-2-yl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-
35 one;

- 1'-pentyl-4'-[1-(phenylsulfonyl)-1*H*-indol-3-yl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-(3-fluorophenyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-(3-acetylphenyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 5 4'-(2-furyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-(4-methylphenyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-(1-methyl-1*H*-pyrrol-3-yl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-(2,5-difluorophenyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 10 4'-(2-fluorophenyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-(2-chlorophenyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-(2,4-difluorophenyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-(4-morpholin-4-ylphenyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 15 *tert*-butyl 5-methoxy-3-(2'-oxo-1'-pentyl-1',2'-dihydrospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-4'-yl)-1*H*-indole-1-carboxylate;
- 1'-pentyl-4'-pyrimidin-5-ylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- tert*-butyl 4-[2-(2'-oxo-1'-pentyl-1',2'-dihydrospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-4'-yl)phenyl]piperazine-1-carboxylate;
- 20 4'-(2-methoxypyridin-3-yl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-(5-methoxypyridin-3-yl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-(4-butoxy-3-fluorophenyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 25 1'-pentyl-4'-pyridin-4-ylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-pentyl-4'-phenoxathiin-4-ylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-[(1*Z*)-3-chloroprop-1-en-1-yl]-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 30 1'-pentyl-4'-(3-thienyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-(2,3-dimethoxyphenyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-(4-butylphenyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-(3-fluoro-5-methoxyphenyl)-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 35

- 4'-[3-fluoro-4-(pentyloxy)phenyl]-1'-pentyldispiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'(1'*H*)-one;
- 4'-(2-butoxy-5-fluorophenyl)-1'-pentyldispiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'(1'*H*)-one;
- 5 4'-(3-butoxyphenyl)-1'-pentyldispiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
4'-(4-butoxyphenyl)-1'-pentyldispiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
4'-(4-isobutoxyphenyl)-1'-pentyldispiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-
one;
- 4'-{2-chloro-4-[(3,5-dimethoxybenzyl)oxy]phenyl}-1'-pentyldispiro[furo[2,3-
10 *f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-[4-(benzyloxy)-3-chlorophenyl]-1'-pentyldispiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'(1'*H*)-one;
- 4'-(1-methyl-1*H*-indol-5-yl)-1'-pentyldispiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-
one;
- 15 4'-(4-methoxypyridin-3-yl)-1'-pentyldispiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-
one;
- 4'-[(6-methoxypyridin-3-yl)amino]-1'-pentyldispiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'(1'*H*)-one;
- 4'-(3-furyl)dispiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 20 4'-dibenzo[*b,d*]furan-4-ylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-pyrimidin-5-ylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-methyl-4'-pyrimidin-5-ylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-(3-furyl)-1'-methylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-(6-fluoropyridin-3-yl)-1'-methylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-
25 one;
- 1'-(2-cyclopropylethyl)-4'-quinolin-3-ylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'(1'*H*)-one;
- 4'-[(6-methoxypyridin-3-yl)amino]-1'-pentyldispiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'(1'*H*)-one;
- 30 4'-[(3,5-difluorophenyl)amino]-1'-pentyldispiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'(1'*H*)-one;
- 4'-[(4,6-dimethylpyridin-2-yl)amino]-1'-pentyldispiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-
indol]-2'(1'*H*)-one;
- 4'-[(4-methyl-1,3-thiazol-2-yl)amino]-1'-pentyldispiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-
35 indol]-2'(1'*H*)-one;

- 4'-bromo-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 4'-morpholino-1'-pentyl-6*H*-spiro[benzofuro[6,5-*d*][1,3]dioxole-7,3'-indolin]-2'-one;
 4'-(4-methylpiperazin-1-yl)-1'-pentyl-6*H*-spiro[benzofuro[6,5-*d*][1,3]dioxole-7,3'-indolin]-
 2'-one;
 5 1'-pentyl-4'-(pyrimidin-4-ylamino)-6*H*-spiro[benzofuro[6,5-*d*][1,3]dioxole-7,3'-indolin]-2'-
 one;
 1'-pentyl-4'-(pyridin-3-ylamino)-6*H*-spiro[benzofuro[6,5-*d*][1,3]dioxole-7,3'-indolin]-2'-
 one;
 4'-(4-chloro-2-(trifluoromethyl)phenylamino)-1'-pentyl-6*H*-spiro[benzofuro[6,5-
 10 *d*][1,3]dioxole-7,3'-indolin]-2'-one;
 1'-pentyl-4'-(pyrimidin-2-ylamino)-6*H*-spiro[benzofuro[6,5-*d*][1,3]dioxole-7,3'-indolin]-2'-
 one;
 4'-(benzo[*d*][1,3]dioxol-5-ylamino)-1'-pentyl-6*H*-spiro[benzofuro[6,5-*d*][1,3]dioxole-7,3'-
 indolin]-2'-one;
 15 4'-(3-fluorophenylamino)-1'-pentyl-6*H*-spiro[benzofuro[6,5-*d*][1,3]dioxole-7,3'-indolin]-2'-
 one;
 4'-(naphthalen-2-ylamino)-1'-pentyl-6*H*-spiro[benzofuro[6,5-*d*][1,3]dioxole-7,3'-indolin]-
 2'-one;
 4'-(2-methoxyphenylamino)-1'-pentyl-6*H*-spiro[benzofuro[6,5-*d*][1,3]dioxole-7,3'-
 20 indolin]-2'-one;
 4'-(4-methylthiazol-2-ylamino)-1'-pentyl-6*H*-spiro[benzofuro[6,5-*d*][1,3]dioxole-7,3'-
 indolin]-2'-one;
 4'-(4,6-dimethylpyridin-2-ylamino)-1'-pentyl-6*H*-spiro[benzofuro[6,5-*d*][1,3]dioxole-7,3'-
 indolin]-2'-one;
 25 4'-(3,5-difluorophenylamino)-1'-pentyl-6*H*-spiro[benzofuro[6,5-*d*][1,3]dioxole-7,3'-
 indolin]-2'-one;
 4'-(6-methoxypyridin-3-ylamino)-1'-pentyl-6*H*-spiro[benzofuro[6,5-*d*][1,3]dioxole-7,3'-
 indolin]-2'-one;
 1'-pentyl-7*H*-spiro[furo[3,4-*f*][1,3]benzodioxole-5,3'-indol]-2'(1'*H*)-one;
 30 2'-oxo-1'-pentyl-*N*-pyridin-2-yl-1',2'-dihydrospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-
 indole]-4'-carboxamide;
N-(3-methoxyphenyl)-2'-oxo-1'-pentyl-1',2'-dihydrospiro[furo[2,3-*f*][1,3]benzodioxole-
 7,3'-indole]-4'-carboxamide;
 2-(5,6-difluoro-2'-oxo-4'-pyrimidin-5-yl)spiro[1-benzofuran-3,3'-indol]-1'(2' *H*)-yl)-*N*-(2-
 35 fluorophenyl)acetamide;

2-(6,6-dimethyl-2'-oxo-4'-pyrimidin-5-yl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'-(2'*H*)-yl)-*N*-(2-fluorophenyl)acetamide; and
N-(2-fluorophenyl)-2-(2'-oxo-4'-pyrimidin-5-yl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'-(2'*H*)-yl)acetamide.

5 Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention wherein:

at least one of *j* and *k* is 1 and the other is 0 or 1;

Q is -O-;

*R*¹ is aralkyl substituted by -C(O)N(*R*⁶)*R*⁷ where:

10 *R*⁶ is hydrogen, alkyl, aryl or aralkyl; and

*R*⁷ is hydrogen, alkyl, haloalkyl, -*R*⁹-CN, -*R*⁹-OR⁵, -*R*⁹-N(*R*⁴)*R*⁵, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl;

or *R*⁶ and *R*⁷, together with the nitrogen to which they are attached, form a

15 heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroaryl groups for *R*⁶ and *R*⁷ may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, -*R*⁸-CN, -*R*⁸-OR⁵, heterocyclyl and heteroaryl;

20 *R*^{2a}, *R*^{2b}, *R*^{2c} and *R*^{2d} are each independently selected from the group consisting of

hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, -*R*⁸-CN, -*R*⁸-NO₂, -*R*⁸-OR⁵, -*R*⁸-N(*R*⁴)*R*⁵, -N=C(*R*⁴)*R*⁵, -S(O)_{*m*}*R*⁴, -OS(O)₂CF₃, -*R*⁸-C(O)*R*⁴, -C(S)*R*⁴, -C(*R*⁴)₂C(O)*R*⁵, -*R*⁸-C(O)OR⁴, -C(S)OR⁴, -*R*⁸-C(O)N(*R*⁴)*R*⁵, -C(S)N(*R*⁴)*R*⁵, -N(*R*⁵)C(O)*R*⁴, -N(*R*⁵)C(S)*R*⁴, -N(*R*⁵)C(O)OR⁴, -N(*R*⁵)C(S)OR⁴, -N(*R*⁵)C(O)N(*R*⁴)*R*⁵, -N(*R*⁵)C(S)N(*R*⁴)*R*⁵, -N(*R*⁵)S(O)_{*n*}*R*⁴, -N(*R*⁵)S(O)_{*n*}N(*R*⁴)*R*⁵, -*R*⁸-S(O)_{*n*}N(*R*⁴)*R*⁵, -N(*R*⁵)C(=NR⁵)N(*R*⁴)*R*⁵, and -N(*R*⁵)C(=N-CN)N(*R*⁴)*R*⁵,

25 wherein each *m* is independently 0, 1, or 2 and each *n* is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl,

heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for *R*^{2a}, *R*^{2b}, *R*^{2c} and *R*^{2d} may be optionally substituted by one or more

substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl,

35

- cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$, $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is
- 5 independently 0, 1, or 2 and each n is independently 1 or 2;
- or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;
- or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached,
- 10 may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2d} are as defined above;
- or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;
- 15 R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$,
- 20 $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;
- 25 or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;
- or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl,
- 30 and R^{3a} and R^{3d} are as defined above;
- or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3b} are as defined above;
- each R^4 and R^5 is independently selected from group consisting of hydrogen, alkyl,
- 35 alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl,

- heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;
or when R⁴ and R⁵ are each attached to the same nitrogen atom, then R⁴ and R⁵,
together with the nitrogen atom to which they are attached, may form a
heterocyclyl or heteroaryl; and
- 5 each R⁸ is a direct bond or a straight or branched alkylene chain, a straight or
branched alkenylene chain or a straight or branched alkynylene chain; and
each R⁹ is a straight or branched alkylene chain, a straight or branched alkenylene
chain or a straight or branched alkynylene chain.
- Another embodiment of the invention are the compounds of formula (I) as set
10 forth above in the Summary of the invention wherein:
j is 0 and k is 1;
Q is -O-;
R¹ is aralkyl substituted by -C(O)N(R⁶)R⁷ where:
R⁶ is hydrogen, alkyl, aryl or aralkyl; and
15 R⁷ is hydrogen, alkyl, haloalkyl, -R⁹-CN, -R⁹-OR⁵, -R⁹-N(R⁴)R⁵, aryl, aralkyl,
cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl,
heteroarylalkyl;
or R⁶ and R⁷, together with the nitrogen to which they are attached, form a
heterocyclyl or heteroaryl;
20 and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl,
heterocyclylalkyl, heteroaryl and heteroaryl groups for R⁶ and R⁷ may be
optionally substituted by one or more substituents selected from the
group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl,
-R⁸-CN, -R⁸-OR⁵, heterocyclyl and heteroaryl;
- 25 R^{2a}, R^{2b}, R^{2c} and R^{2d} are each hydrogen;
R^{3a} and R^{3d} are each hydrogen;
R^{3b} and R^{3c}, together with the carbon ring atoms to which they are directly attached,
form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl;
each R⁴ and R⁵ is independently selected from group consisting of hydrogen, alkyl,
30 alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl,
heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;
or when R⁴ and R⁵ are each attached to the same nitrogen atom, then R⁴ and R⁵,
together with the nitrogen atom to which they are attached, may form a
heterocyclyl or heteroaryl; and
35 each R⁸ is a direct bond or a straight or branched alkylene chain, a straight or

branched alkenylene chain or a straight or branched alkynylene chain; and each R⁹ is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain.

Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention wherein:

j is 0 and k is 1;

Q is -O-;

R¹ is aralkyl substituted by -C(O)N(R⁶)R⁷ where:

R⁶ is hydrogen, alkyl, aryl or aralkyl; and

R⁷ is hydrogen, alkyl, haloalkyl, -R⁹-CN, -R⁹-OR⁵ or -R⁹-N(R⁴)R⁵;

or R⁶ and R⁷, together with the nitrogen to which they are attached, form a heterocyclyl or heteroaryl;

wherein each aryl, aralkyl, heterocyclyl and heteroaryl groups for R⁶ and R⁷ is optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, -R⁸-CN, -R⁸-OR⁵, heterocyclyl and heteroaryl;

R^{2a}, R^{2b}, R^{2c} and R^{2d} are each hydrogen;

R^{3a} and R^{3d} are each hydrogen;

R^{3b} and R^{3c}, together with the carbon ring atoms to which they are directly attached, form a fused dioxolyl ring;

each R⁴ and R⁵ is independently selected from group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;

or when R⁴ and R⁵ are each attached to the same nitrogen atom, then R⁴ and R⁵, together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl; and

each R⁸ is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and each R⁹ is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain.

Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention, selected from the group consisting of:

N-(3-methylbutyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;

N,N-diisopropyl-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-

- yl)methyl]benzamide;
- N*-butyl-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-
- 5 pentylbenzamide;
- N*-hexyl-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-
- propylbenzamide;
- 10 *N*-isopropyl-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-heptyl-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 1'-[2-(piperidin-1-ylcarbonyl)benzyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-
- 15 one;
- N*-isobutyl-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(3-methoxypropyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 20 *N*-(3-ethoxypropyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-hexyl-*N*-methyl-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(3-isopropoxypropyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 25 *N*-(2-ethoxyethyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-methyl-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 30 *N*-ethyl-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-(2,2,2-trifluoroethyl)benzamide;
- N*-[2-(diethylamino)ethyl]-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 35

- N*-(3,3-dimethylbutyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(2-ethylbutyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 5 *N*-(2-methoxyethyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(2-cyanoethyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 10 1'-[2-[(4-pyrimidin-2-ylpiperazin-1-yl)carbonyl]benzyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-[2-[[4-(1,3-benzodioxol-5-ylmethyl)piperazin-1-yl]carbonyl]benzyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-[2-(morpholin-4-ylcarbonyl)benzyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 15 *N*-[3-(dimethylamino)propyl]-*N*-methyl-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(3-methylbutyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N,N*-diisopropyl-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 20 *N*-butyl-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-pentylbenzamide;
- 25 3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-propylbenzamide;
- N*-isopropyl-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 1'-[3-(piperidin-1-ylcarbonyl)benzyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 30 *N*-isobutyl-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-hexyl-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 35 *N*-heptyl-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-

- yl)methyl]benzamide;
- N*-(3-methoxypropyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-[2-(diethylamino)ethyl]-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 5 *N*-methyl-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-ethyl-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 10 *N*-(3-ethoxypropyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-hexyl-*N*-methyl-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(3-isopropoxypropyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 15 *N*-(2-ethoxyethyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(2-ethylbutyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 20 *N*-(2-methoxyethyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 1'-[3-(morpholin-4-ylcarbonyl)benzyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-{3-[(4-pyrimidin-2-ylpiperazin-1-yl)carbonyl]benzyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 25 1'-{3-[(4-methylpiperazin-1-yl)carbonyl]benzyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- N*-(3,3-dimethylbutyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 30 *N*-(2-cyanoethyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-butyl-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 1'-[4-(piperidin-1-ylcarbonyl)benzyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 35

- N,N*-diisopropyl-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-pentylbenzamide;
- 5 4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-propylbenzamide;
- N*-isopropyl-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-isobutyl-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 10 *N*-hexyl-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-heptyl-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 15 *N*-(3-methoxypropyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-[2-(diethylamino)ethyl]-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-methyl-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 20 *N*-ethyl-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(3-ethoxypropyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 25 *N*-(4-methylpentyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-(2,2,2-trifluoroethyl)benzamide;
- N*-hexyl-*N*-methyl-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 30 *N*-(3-isopropoxypropyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(2-ethoxyethyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 35 *N*-(2-ethylbutyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-

yl)methyl]benzamide;
N-(2-methoxyethyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-
 yl)methyl]benzamide;
N-(2-cyanoethyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-
 5 yl)methyl]benzamide; and
N-[3-(dimethylamino)propyl]-*N*-methyl-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-
 indol]-1'(2'*H*)-yl)methyl]benzamide.

Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention wherein:

10 j is 0 and k is 1;

Q is -O-;

R¹ is aralkyl substituted by -C(O)N(R⁶)R⁷ where:

R⁶ is hydrogen, alkyl, aryl or aralkyl; and

R⁷ is aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclalkyl,
 15 heteroaryl, heteroarylalkyl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclalkyl, heteroaryl and heteroaryl groups for R⁶ and R⁷ may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl,
 20 -R⁸-CN, -R⁸-OR⁵, heterocyclyl and heteroaryl;

R^{2a}, R^{2b}, R^{2c} and R^{2d} are each hydrogen;

R^{3a} and R^{3d} are each hydrogen;

R^{3b} and R^{3c}, together with the carbon ring atoms to which they are directly attached, form a fused dioxolyl ring;

25 each R⁴ and R⁵ is independently selected from group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl, and heteroarylalkyl;

or when R⁴ and R⁵ are each attached to the same nitrogen atom, then R⁴ and R⁵, together with the nitrogen atom to which they are attached, may form a
 30 heterocyclyl or heteroaryl; and

each R⁸ is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and

each R⁹ is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain.

35 Another embodiment of the invention are the compounds of formula (I) as set

forth above in the Summary of the invention, selected from the group consisting of:

N-[2-(4-chlorophenyl)ethyl]-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;

2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-

5 phenylbenzamide;

N-(3-fluorophenyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;

N-(4-chlorobenzyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;

10 *N*-cyclohexyl-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;

N-cyclopentyl-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;

N-(4-fluorophenyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;

15

N-(3-fluorobenzyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;

N-(3-chlorophenyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;

20 *N*-(2-fluorophenyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;

N-(2-ethylphenyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;

N-(4-ethylphenyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;

25

N-(3-methylphenyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;

N-(2,3-dimethylphenyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;

30 *N*-(3,5-dimethylphenyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;

N-(2-chlorobenzyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;

N-(2,6-dimethylphenyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;

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- N*-(2-methoxyphenyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-[2-(4-methylphenyl)ethyl]-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 5 2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-(tetrahydrofuran-2-ylmethyl)benzamide;
- N,N*-dibenzyl-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-(3-phenylpropyl)benzamide;
- 10 *N*-[2-(3-chlorophenyl)ethyl]-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-[2-(4-fluorophenyl)ethyl]-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 15 *N*-(4-fluorobenzyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(4-methoxybenzyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(cyclopropylmethyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 20 *N*-(cyclohexylmethyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(2-furylmethyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 25 *N*-(2,4-dimethylphenyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(4-cyanophenyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(3,5-dichlorophenyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 30 *N*-(3-fluoro-2-methylphenyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(4-methoxyphenyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 35 *N*-(5-chloro-2-methylphenyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-

- 1'(2'H)-yl)methyl]benzamide;
2-[(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]-N-[3-(trifluoromethyl)phenyl]benzamide;
2-[(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]-N-(pyridin-4-ylmethyl)benzamide;
5 N-cyclobutyl-2-[(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]benzamide;
N-(2,2-diphenylethyl)-2-[(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]benzamide;
10 2-[(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]-N-(2-pyrrolidin-1-ylethyl)benzamide;
N-[(1-ethylpyrrolidin-2-yl)methyl]-2-[(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]benzamide;
2-[(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]-N-(2-piperidin-1-ylethyl)benzamide;
15 N-(2-morpholin-4-ylethyl)-2-[(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]benzamide;
N-[(1S)-1-cyclohexylethyl]-2-[(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]benzamide;
20 N-(2-fluoro-5-methylphenyl)-2-[(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]benzamide;
N-(2,4-difluorophenyl)-2-[(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]benzamide;
2-[(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]-N-(4-propylphenyl)benzamide;
25 N-(3,3-diphenylpropyl)-2-[(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]benzamide;
N-(2,5-difluorobenzyl)-2-[(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]benzamide;
30 2-[(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]-N-(2-thienylmethyl)benzamide;
N-[4-chloro-2-(trifluoromethyl)phenyl]-2-[(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]benzamide;
N-[2-(4-methoxyphenyl)ethyl]-2-[(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]benzamide;
35

- N*-(3,5-dichlorobenzyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(3-chlorobenzyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 5 2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-[2-(2-thienyl)ethyl]benzamide;
- N*-(2,3-dihydro-1*H*-inden-1-yl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 10 2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-[4-(trifluoromethyl)benzyl]benzamide;
- N*-[4-fluoro-2-(trifluoromethyl)phenyl]-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-(pyridin-3-ylmethyl)benzamide;
- 15 2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-[2-(trifluoromethyl)benzyl]benzamide;
- N*-(3-methylpyridin-2-yl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(1-benzylpiperidin-4-yl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 20 2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-[2-(trifluoromethyl)phenyl]benzamide;
- N*-[(1*R*)-1-cyclohexylethyl]-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 25 *N*-(6-methoxypyridin-3-yl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-1,3-thiazol-2-ylbenzamide;
- 2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-1,3,4-
- 30 thiadiazol-2-ylbenzamide;
- N*-(4,6-dimethylpyridin-2-yl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(2,3-dihydro-1*H*-inden-5-yl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 35 *N*-2-adamantyl-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-

- yl)methyl]benzamide;
N-1-adamantyl-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
N-1-naphthyl-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
5 *N*-(3,5-difluorophenyl)-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
N-[2-(3-chlorophenyl)ethyl]-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
10 3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-phenylbenzamide;
N-(3-fluorophenyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
N-(4-chlorobenzyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
15 *N*-(3-fluorobenzyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
N-(3-chlorophenyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
20 *N*-(2-fluorophenyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
N-(2-ethylphenyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
N-(4-ethylphenyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
25 *N*-(3-methylphenyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
N-(2,3-dimethylphenyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
30 *N*-(3,5-dimethylphenyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
N-cyclohexyl-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
N-cyclopentyl-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
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- N*-(2-methoxybenzyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(2-methoxyphenyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 5 *N*-cyclopropyl-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(2,4-dimethylphenyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 10 3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-(tetrahydrofuran-2-ylmethyl)benzamide;
- N,N*-dibenzyl-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-[3-(trifluoromethyl)phenyl]benzamide;
- 15 *N*-(4-methoxybenzyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(3,5-dichlorophenyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 20 3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-pyridin-3-ylbenzamide;
- 3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-(pyridin-4-ylmethyl)benzamide;
- N*-(2-furylmethyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 25 *N*-(3-fluoro-2-methylphenyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(cyclopropylmethyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(4-methoxyphenyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 30 *N*-cyclobutyl-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-[2-(4-fluorophenyl)ethyl]-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 35 *N*-(cyclohexylmethyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-

- yl)methyl]benzamide;
N-[2-(4-methylphenyl)ethyl]-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
N-benzyl-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
5 yl)methyl]benzamide;
N-(1-benzylpiperidin-4-yl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
N-[2-(4-methoxyphenyl)ethyl]-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
10 3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-(2-piperidin-1-ylethyl)benzamide;
N-(1-cyclohexylethyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-(2-
15 thienylmethyl)benzamide;
3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-(4-propylphenyl)benzamide;
N-(2,4-difluorobenzyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
20 *N*-(3,5-difluorophenyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
N-(2,3-dihydro-1*H*-inden-5-yl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-[4-
25 (trifluoromethyl)benzyl]benzamide;
3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-[2-(2-thienyl)ethyl]benzamide;
3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-(pyridin-3-ylmethyl)benzamide;
30 3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-[2-(trifluoromethyl)benzyl]benzamide;
N-[2-(4-chlorophenyl)ethyl]-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-(2-pyrrolidin-
35 1-ylethyl)benzamide;

- N*-(3-methylpyridin-2-yl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-1,3-benzodioxol-5-yl-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 5 *N*-(2-morpholin-4-ylethyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-1,3-thiazol-2-ylbenzamide;
- N*-(6-methoxypyridin-3-yl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 10 *N*-(3,5-dichlorobenzyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-1-naphthyl-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 15 *N*-(4,6-dimethylpyridin-2-yl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-pyrimidin-4-ylbenzamide;
- N*-(5-methyl-1,3-thiazol-2-yl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 20 *N*-(4-methylbenzyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-[3-(1*H*-imidazol-1-yl)propyl]-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 25 *N*-(5-cyclopropyl-1,3,4-thiadiazol-2-yl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-1,3,4-thiadiazol-2-ylbenzamide;
- N*-(4-morpholin-4-ylphenyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 30 *N*-[(1-ethylpyrrolidin-2-yl)methyl]-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(2,2-diphenylethyl)-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 35 *N*-(3-fluorophenyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-

- yl)methyl]benzamide;
- N*-(3-fluorobenzyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(4-chlorobenzyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 5 *N*-(3-chlorophenyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(2-fluorophenyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 10 *N*-(2-ethylphenyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(4-ethylphenyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(4-methylphenyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 15 *N*-(3,5-dimethylphenyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(2,3-dimethylphenyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 20 *N*-cyclohexyl-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-cyclopentyl-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(2-methoxybenzyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 25 *N*-(2,6-dimethylphenyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(2-methoxyphenyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 30 *N*-cyclopropyl-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-phenylbenzamide;
- N*-(2,4-dimethylphenyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 35

- 4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-
(tetrahydrofuran-2-ylmethyl)benzamide;
N,N-dibenzyl-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-
yl)methyl]benzamide;
5 4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-[3-
(trifluoromethyl)phenyl]benzamide;
N-(4-methoxybenzyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-
yl)methyl]benzamide;
N-(3,5-dichlorophenyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-
10 yl)methyl]benzamide;
4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-pyridin-3-
ylbenzamide;
N-(4-cyanophenyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-
yl)methyl]benzamide;
15 4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-(pyridin-4-
ylmethyl)benzamide;
N-[2-(3-chlorophenyl)ethyl]-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
1'(2'*H*)-yl)methyl]benzamide;
N-(2-furylmethyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-
20 yl)methyl]benzamide;
N-(3-fluoro-2-methylphenyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
1'(2'*H*)-yl)methyl]benzamide;
N-(cyclopropylmethyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-
yl)methyl]benzamide;
25 *N*-(4-methoxyphenyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-
yl)methyl]benzamide;
N-cyclobutyl-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-
yl)methyl]benzamide;
N-(2,2-diphenylethyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-
30 yl)methyl]benzamide;
N-[2-(4-fluorophenyl)ethyl]-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
1'(2'*H*)-yl)methyl]benzamide;
N-(cyclohexylmethyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-
yl)methyl]benzamide;
35 *N*-(2-fluoro-4-methylphenyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-

- 1'(2'H)-yl)methyl]benzamide;
N-[2-(4-methylphenyl)ethyl]-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]benzamide;
N-benzyl-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]benzamide;
5 *N*-(2-methoxyethyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]benzamide;
1'-[4-(morpholin-4-ylcarbonyl)benzyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'H)-one;
10 *N*-(1-benzylpiperidin-4-yl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]benzamide;
N-[2-(4-methoxyphenyl)ethyl]-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]benzamide;
4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]-*N*-[2-(trifluoromethyl)phenyl]benzamide;
15 *N*-[4-chloro-2-(trifluoromethyl)phenyl]-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]benzamide;
N-[4-fluoro-2-(trifluoromethyl)phenyl]-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]benzamide;
20 *N*-[(1*S*)-1-cyclohexylethyl]-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]benzamide;
N-[(1*R*)-1-cyclohexylethyl]-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]benzamide;
N-(2,4-difluorophenyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]benzamide;
25 *N*-(2,3-dihydro-1*H*-inden-1-yl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]benzamide;
4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]-*N*-(2-thienylmethyl)benzamide;
30 *N*-[(1-ethylpyrrolidin-2-yl)methyl]-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]benzamide;
4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]-*N*-(4-propylphenyl)benzamide;
N-(2,5-difluorobenzyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]benzamide;
35

- N*-(2,3-dihydro-1*H*-inden-5-yl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(2,5-difluorophenyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 5 4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-[4-(trifluoromethyl)benzyl]benzamide;
- 4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-[2-(2-thienyl)ethyl]benzamide;
- 10 4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-(pyridin-3-ylmethyl)benzamide;
- 4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-[2-(trifluoromethyl)benzyl]benzamide;
- N*-[2-(4-chlorophenyl)ethyl]-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 15 4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-(2-pyrrolidin-1-ylethyl)benzamide;
- N*-(3-methylpyridin-2-yl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-1,3-benzodioxol-5-yl-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 20 *N*-(2-morpholin-4-ylethyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 1'-{4-[(4-pyrimidin-2-yl)piperazin-1-yl]carbonyl}benzyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 25 4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-*N*-1,3-thiazol-2-ylbenzamide;
- N*-(6-methoxypyridin-3-yl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- N*-(3,5-dichlorobenzyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 30 *N*-1-naphthyl-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide;
- 1'-{4-[(4-(1,3-benzodioxol-5-ylmethyl)piperazin-1-yl]carbonyl}benzyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 35 *N*-(4,6-dimethylpyridin-2-yl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-

- 1'(2'H)-yl)methyl]benzamide;
 4-[(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]-N-pyrimidin-4-ylbenzamide;
 N-(5-methyl-1,3-thiazol-2-yl)-4-[(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]benzamide;
 5 N-(2-cyano-6-fluorophenyl)-4-[(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]benzamide;
 N-(4-methylbenzyl)-4-[(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]benzamide;
 10 N-[3-(1H-imidazol-1-yl)propyl]-4-[(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]benzamide;
 N-(4-morpholin-4-ylphenyl)-4-[(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]benzamide;
 1'-{4-[(4-methylpiperazin-1-yl)carbonyl]benzyl}spiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-2'(1'H)-one; and
 15 N-(5-cyclopropyl-1,3,4-thiadiazol-2-yl)-4-[(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)methyl]benzamide.

Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention wherein:

- 20 at least one of j and k is 1 and the other is 0 or 1;
 Q is -O-;
 R¹ is aralkyl optionally substituted by one or more substituents selected from the group consisting of -R⁸-OR⁵, -C(O)OR⁵, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;
 25 R^{2a}, R^{2b}, R^{2c} and R^{2d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, -R⁸-CN, -R⁸-NO₂, -R⁸-OR⁵, -R⁸-N(R⁴)R⁵, -N=C(R⁴)R⁵, -S(O)_mR⁴, -OS(O)₂CF₃, -R⁸-C(O)R⁴, -C(S)R⁴,
 30 -C(R⁴)₂C(O)R⁵, -R⁸-C(O)OR⁴, -C(S)OR⁴, -R⁸-C(O)N(R⁴)R⁵, -C(S)N(R⁴)R⁵, -N(R⁵)C(O)R⁴, -N(R⁵)C(S)R⁴, -N(R⁵)C(O)OR⁴, -N(R⁵)C(S)OR⁴, -N(R⁵)C(O)N(R⁴)R⁵, -N(R⁵)C(S)N(R⁴)R⁵, -N(R⁵)S(O)_nR⁴, -N(R⁵)S(O)_nN(R⁴)R⁵, -R⁸-S(O)_nN(R⁴)R⁵, -N(R⁵)C(=NR⁵)N(R⁴)R⁵, and -N(R⁵)C(=N-CN)N(R⁴)R⁵,
 35 wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2; and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl,

- heterocyclyl, heterocyclalkyl, heteroaryl and heteroarylalkyl groups for R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$, $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;
- 10 or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;
- or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2d} are as defined above;
- 15 or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;
- R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;
- 20 or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;
- or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3d} are as defined above;
- 25 or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached,
- 30
- 35

may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3b} are as defined above;

each R^4 and R^5 is independently selected from group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl, and heteroarylalkyl;

or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl; and

each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain.

Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention wherein:

j is 0 and k is 1;

Q is -O-;

R^1 is aralkyl optionally substituted by one or more substituents selected from the group consisting of $-R^8-OR^5$, $-C(O)OR^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from hydrogen, alkyl or halo;

R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of

hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$,

$-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$,

$-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$,

$-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$,

$-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$,

$-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$,

wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;

or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl,

- and R^{3a} and R^{3d} are as defined above;
 or R^{3c} and R^{3d}, together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl,
 and R^{3a} and R^{3b} are as defined above;
- 5 each R⁵ is independently selected from group consisting of hydrogen, alkyl, alkenyl,
 alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl,
 heterocyclyl and heteroaryl; and
 each R⁸ is a direct bond or a straight or branched alkylene chain, a straight or
 branched alkenylene chain or a straight or branched alkynylene chain.
- 10 Another embodiment of the invention are the compounds of formula (I) as set
 forth above in the Summary of the invention wherein:
 j is 0 and k is 1;
 Q is -O-;
 R¹ is aralkyl optionally substituted by one or more substituents selected from the group
 15 consisting of -R⁸-OR⁵, -C(O)OR⁵, halo, haloalkyl, alkyl, nitro, cyano, aryl,
 aralkyl, heterocyclyl and heteroaryl;
 R^{2a}, R^{2b}, R^{2c} and R^{2d} are each independently selected from hydrogen, alkyl or halo;
 R^{3a}, R^{3b}, R^{3c} and R^{3d} are each independently selected from the group consisting of
 hydrogen, halo, and -R⁸-OR⁵;
 20 or R^{3b} and R^{3c}, together with the carbon ring atoms to which they are directly attached,
 form a fused ring selected from cycloalkyl, dioxolyl, tetrahydrofuranyl, and
 heteroaryl, and R^{3a} and R^{3d} are each hydrogen;
 each R⁵ is independently selected from group consisting of hydrogen, alkyl, alkenyl,
 alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl,
 25 heterocyclyl and heteroaryl; and
 each R⁸ is a direct bond or a straight or branched alkylene chain, a straight or
 branched alkenylene chain or a straight or branched alkynylene chain.
- Another embodiment of the invention are the compounds of formula (I) as set
 forth above in the Summary of the invention, selected from the group consisting of:
- 30 methyl 2-[(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-
 yl)methyl]benzoate;
 methyl 3-[(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-
 yl)methyl]benzoate;
 methyl 4-[(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-
 35 yl)methyl]benzoate;

- 1'-(diphenylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-(diphenylmethyl)-5'-methylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 2'-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzoic acid;
 3'-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzoic acid;
 5 1'-(4-fluorobenzyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-benzylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-(3,5-difluorobenzyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-(3-nitrobenzyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-(3-fluorobenzyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 10 3'-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzonitrile;
 1'-[4-(1*H*-pyrazol-1-yl)benzyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-(biphenyl-4-ylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 4'-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]biphenyl-2-carbonitrile;
 15 1'-(biphenyl-2-ylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-(diphenylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-(4-fluoro-3-methylbenzyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-(5-fluoro-2-methylbenzyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-(2,5-difluorobenzyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 20 1'-[4-(1*H*-pyrrol-1-yl)benzyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-[3-(1*H*-pyrrol-1-yl)benzyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-[(4-chlorophenoxy)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-[2-fluoro-3-(trifluoromethyl)benzyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 25 1'-[2-fluoro-6-(trifluoromethyl)benzyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-[3-fluoro-4-(trifluoromethyl)benzyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-[4-fluoro-3-(trifluoromethyl)benzyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 30 2'(1'*H*)-one;
 1'-[2-fluoro-5-(trifluoromethyl)benzyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 2'(1'*H*)-one;
 1'-[4-fluoro-2-(trifluoromethyl)benzyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 35 1'-[5-fluoro-2-(trifluoromethyl)benzyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-

- 2'(*1H*)-one;
 1'-[2-fluoro-4-(trifluoromethyl)benzyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
 2'(*1H*)-one;
 1'-(2,3-difluorobenzyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1H*)-one;
 5 1'-[(1-bromo-2-naphthyl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1H*)-
 one;
 1'-(1-naphthylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1H*)-one;
 1'-[3-fluoro-5-(trifluoromethyl)benzyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
 2'(*1H*)-one;
 10 1'-(2,4-difluorobenzyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1H*)-one;
 1'-(2,6-difluorobenzyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1H*)-one;
 1'-(3-methoxybenzyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1H*)-one;
 1'-[4-(1*H*-1,2,4-triazol-1-yl)benzyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1H*)-
 one;
 15 1'-[4,4-bis(4-fluorophenyl)butyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1H*)-one;
 1'-(2-chloro-4-fluorobenzyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1H*)-one;
 1'-[2-(trifluoromethoxy)benzyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1H*)-one;
 1'-[3-(trifluoromethoxy)benzyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1H*)-one;
 1'-[4-(trifluoromethoxy)benzyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1H*)-one;
 20 1'-(2,3-difluorobenzyl)-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]2'(*1H*)-
 one;
 1'-(4-methoxybenzyl)-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]2'(*1H*)-one;
 4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(*2H*)-yl)methyl]benzoic acid;
 5-bromo-1'-(diphenylmethyl)spiro[1-benzofuran-3,3'-indol]-2'(*1H*)-one;
 25 1'-(diphenylmethyl)-6-(trifluoromethoxy)spiro[1-benzofuran-3,3'-indol]-2'(*1H*)-one;
 1'-(4-methoxybenzyl)-6-(trifluoromethoxy)spiro[1-benzofuran-3,3'-indol]-2'(*1H*)-one;
 1'-(diphenylmethyl)-5-hydroxyspiro[1-benzofuran-3,3'-indol]-2'(*1H*)-one;
 1'-(diphenylmethyl)-5-pyridin-3-ylspiro[1-benzofuran-3,3'-indol]-2'(*1H*)-one;
 1'-(diphenylmethyl)-5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-
 30 2'(*1H*)-one;
 2-methyl-1'-pentylspiro[furo[2,3-*f*][1,3]benzothiazole-7,3'-indol]-2'(*1H*)-one;
 1'-(diphenylmethyl)-6,7-dihydrospiro[benzo[1,2-*b*:4,5-*b'*]difuran-3,3'-indol]-2'(*1H*)-one;
 and
 1'-(diphenylmethyl)-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(*1H*)-one.
 35 Another embodiment of the invention are the compounds of formula (I) as set

forth above in the Summary of the invention wherein:

at least one of j and k is 1 and the other is 0 or 1;

Q is -O-;

R¹ is -R⁹-N(R¹⁰)R¹¹, -R⁹-N(R¹²)C(O)R¹¹ or -R⁹-N(R¹⁰)C(O)N(R¹⁰)R¹¹ where:

- 5 each R¹⁰ is hydrogen, alkyl, aryl, aralkyl or heteroaryl;
 each R¹¹ is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, -R⁹-OC(O)R⁵, -R⁹-C(O)OR⁵, -R⁹-C(O)N(R⁴)R⁵, -R⁹-C(O)R⁵, -R⁹-N(R⁴)R⁵, -R⁹-OR⁵, or -R⁹-CN;
- 10 R¹² is hydrogen, alkyl, aryl, aralkyl or -C(O)R⁵;
 and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclalkyl, heteroaryl and heteroarylalkyl groups for R¹⁰ and R¹¹ may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, -R⁸-CN, -R⁸-OR⁵, -R⁸-C(O)R⁵, heterocyclyl and heteroaryl;
- 15 R^{2a}, R^{2b}, R^{2c} and R^{2d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, -R⁸-CN, -R⁸-NO₂, -R⁸-OR⁵, -R⁸-N(R⁴)R⁵, -N=C(R⁴)R⁵, -S(O)_mR⁴, -R⁸-C(O)R⁴, -C(S)R⁴, -C(R⁴)₂C(O)R⁵, -R⁸-C(O)OR⁴, -C(S)OR⁴, -R⁸-C(O)N(R⁴)R⁵, -C(S)N(R⁴)R⁵, -N(R⁵)C(O)R⁴, -N(R⁵)C(S)R⁴, -N(R⁵)C(O)OR⁴, -N(R⁵)C(S)OR⁴, -N(R⁵)C(O)N(R⁴)R⁵, -N(R⁵)C(S)N(R⁴)R⁵, -N(R⁵)S(O)_nR⁴, -N(R⁵)S(O)_nN(R⁴)R⁵, -R⁸-S(O)_nN(R⁴)R⁵, -N(R⁵)C(=NR⁵)N(R⁴)R⁵, and -N(R⁵)C(=N-CN)N(R⁴)R⁵, wherein each m is
- 20 independently 0, 1, or 2 and each n is independently 1 or 2;
 and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl and heteroarylalkyl groups for R^{2a}, R^{2b}, R^{2c} and R^{2d} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, -R⁸-CN, -R⁸-NO₂, -R⁸-OR⁵, -R⁸-N(R⁴)R⁵, -S(O)_mR⁴, -R⁸-S(O)_nN(R⁴)R⁵, -R⁸-C(O)R⁴, -R⁸-C(O)OR⁴, -R⁸-C(O)N(R⁴)R⁵, -N(R⁵)C(O)R⁴, and -N(R⁵)S(O)_nR⁴, wherein each m is
- 30 independently 0, 1, or 2 and each n is independently 1 or 2;
- 35

- or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;
- or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2d} are as defined above;
- or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;
- R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;
- or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;
- or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3d} are as defined above;
- or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3b} are as defined above;
- each R^4 and R^5 is independently selected from group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;
- or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl; and
- each R^8 is a direct bond or a straight or branched alkylene chain, a straight or

branched alkenylene chain or a straight or branched alkynylene chain; and each R⁹ is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain.

Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention wherein:

j is 0 and k is 1;

Q is -O-;

R¹ is -R⁹-N(R¹⁰)R¹¹, -R⁹-N(R¹²)C(O)R¹¹ or -R⁹-N(R¹⁰)C(O)N(R¹⁰)R¹¹ where:

each R¹⁰ is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each R¹¹ is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, -R⁹-OC(O)R⁵, -R⁹-C(O)OR⁵, -R⁹-C(O)N(R⁴)R⁵, -R⁹-C(O)R⁵, -R⁹-N(R⁴)R⁵, -R⁹-OR⁵, or -R⁹-CN;

R¹² is hydrogen, alkyl, aryl, aralkyl or -C(O)R⁵;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclalkyl, heteroaryl and heteroarylalkyl groups for R¹⁰ and R¹¹ may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, -R⁸-CN, -R⁸-OR⁵, -R⁸-C(O)R⁵, heterocyclyl and heteroaryl;

R^{2a}, R^{2b}, R^{2c} and R^{2d} are each hydrogen;

R^{3a} and R^{3d} are each hydrogen;

R^{3b} and R^{3c}, together with the carbon ring atoms to which they are directly attached, form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl;

each R⁴ and R⁵ is independently selected from group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl, and heteroarylalkyl;

or when R⁴ and R⁵ are each attached to the same nitrogen atom, then R⁴ and R⁵, together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl; and

each R⁸ is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and each R⁹ is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain.

Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention wherein:

- j is 0 and k is 1;
 Q is -O-;
 R¹ is -R⁹-N(R¹⁰)R¹¹ where:
 each R¹⁰ is hydrogen, alkyl, aryl, aralkyl or heteroaryl;
 5 each R¹¹ is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl,
 heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, -R⁹-OC(O)R⁵,
 -R⁹-C(O)OR⁵, -R⁹-C(O)N(R⁴)R⁵, -R⁹-C(O)R⁵, -R⁹-N(R⁴)R⁵, -R⁹-OR⁵, or
 -R⁹-CN;
 and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl,
 10 heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R¹⁰ and R¹¹
 may be optionally substituted by one or more substituents selected from
 the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl,
 nitro, -R⁸-CN, -R⁸-OR⁵, -R⁸-C(O)R⁵, heterocyclyl and heteroaryl;
 R^{2a}, R^{2b}, R^{2c} and R^{2d} are each hydrogen;
 15 R^{3a} and R^{3d} are each hydrogen;
 R^{3b} and R^{3c}, together with the carbon ring atoms to which they are directly attached,
 form a fused dioxolyl ring;
 each R⁴ and R⁵ is independently selected from group consisting of hydrogen, alkyl,
 alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl,
 20 heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;
 or when R⁴ and R⁵ are each attached to the same nitrogen atom, then R⁴ and R⁵,
 together with the nitrogen atom to which they are attached, may form a
 heterocyclyl or heteroaryl; and
 each R⁸ is a direct bond or a straight or branched alkylene chain, a straight or
 25 branched alkenylene chain or a straight or branched alkynylene chain; and
 each R⁹ is a straight or branched alkylene chain, a straight or branched alkenylene
 chain or a straight or branched alkynylene chain.

- Another embodiment of the invention are the compounds of formula (I) as set
 forth above in the Summary of the invention, selected from the group consisting of:
 30 1'-[2-(diethylamino)ethyl]spiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-2'(1'H)-one;
 1'-[2-(pyridin-2-ylamino)ethyl]spiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-2'(1'H)-one;
 1'-[2-(dipyridin-2-ylamino)ethyl]spiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-2'(1'H)-one;
 1'-[3-[(cyclopropylmethyl)amino]propyl]spiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-
 2'(1'H)-one;
 35 1'-[3-[(4-fluorobenzyl)amino]propyl]spiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-2'(1'H)-

- one;
- 1'-[3-[(4-chlorophenyl)amino]propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-[3-(pentylamino)propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 5 1'-[3-[(2-ethoxyethyl)amino]propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-[3-[(3-methoxypropyl)amino]propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-[3-[(3-methylbutyl)amino]propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 10 one;
- 1'-[3-[(3-ethoxypropyl)amino]propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-[3-[(2,2-dimethylpropyl)amino]propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 15 3-[[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]amino}propanenitrile;
- 1'-[3-[(2,2,2-trifluoroethyl)amino]propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-[3-(cyclopropylamino)propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 20 1'-[3-(cyclobutylamino)propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-[3-[(2-cyclopropylethyl)amino]propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-[3-(isobutylamino)propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-[3-(hexylamino)propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 25 1'-[3-(heptylamino)propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-[3-(isopropylamino)propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-[3-[(tetrahydrofuran-2-ylmethyl)amino]propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-[3-(benzylamino)propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 30 1'-[3-[(2-phenylethyl)amino]propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- one;
- 1'-[3-(dibenzylamino)propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-[3-(propylamino)propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-[3-[[2-(3-fluorophenyl)ethyl]amino]propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 35

- 1'-{3-[(3-phenylpropyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'(1'*H*)-one;
- 1'-{3-[(2,2-diphenylethyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'(1'*H*)-one;
- 5 1'-{3-[(2-(4-methylphenyl)ethyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-
indol]-2'(1'*H*)-one;
- 1'-{3-[(2-(3-chlorophenyl)ethyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-
indol]-2'(1'*H*)-one;
- 1'-{3-[(2-pyridin-4-ylethyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
10 2'(1'*H*)-one;
- 1'-{3-[(pyridin-4-ylmethyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'(1'*H*)-one;
- 1'-{3-[(2-(4-fluorophenyl)ethyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-
indol]-2'(1'*H*)-one;
- 15 1'-{3-[(pyridin-2-ylmethyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'(1'*H*)-one;
- 1'-{3-[(1*R*)-1-cyclohexylethyl]amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-
indol]-2'(1'*H*)-one;
- 1'-{3-[(2-furylmethyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-
20 one;
- 1'-{3-[(4-chlorobenzyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'(1'*H*)-one;
- 1'-{3-[(4-methoxybenzyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'(1'*H*)-one;
- 25 1'-{3-[(3-isopropoxypropyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'(1'*H*)-one;
- 1'-{3-[(2-(2-fluorophenyl)ethyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-
indol]-2'(1'*H*)-one;
- 1'-{3-[(3,3-dimethylbutyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
30 2'(1'*H*)-one;
- 1'-{3-[(cyclohexylmethyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'(1'*H*)-one;
- 1'-{3-[(1*S*)-1-cyclohexylethyl]amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-
indol]-2'(1'*H*)-one;
- 35 1'-{3-[(2-piperidin-1-ylethyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-

- 2'(1'*H*)-one;
 1'-{3-[(2-pyrrolidin-1-ylethyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
 2'(1'*H*)-one;
 1'-{3-[(2-morpholin-4-ylethyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
 5 2'(1'*H*)-one;
 1'-[3-(cyclohexylamino)propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-[3-(cyclopentylamino)propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-{3-[(2-chlorobenzyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
 2'(1'*H*)-one;
 10 1'-[3-(dibutylamino)propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-[3-(dipropylamino)propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-{3-[[2-(dimethylamino)ethyl]amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-
 indol]-2'(1'*H*)-one;
 1'-{3-[[2-(diethylamino)ethyl](methyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-
 15 7,3'-indol]-2'(1'*H*)-one;
 1'-{3-[[2-(diisopropylamino)ethyl]amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-
 indol]-2'(1'*H*)-one;
 1'-[3-(diisopropylamino)propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-[3-(methylamino)propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 20 1'-[3-(ethylamino)propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-{3-[bis(2-methoxyethyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
 2'(1'*H*)-one;
 1'-{3-[(2-fluorobenzyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-
 one;
 25 1'-{3-[(3,5-difluorobenzyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
 2'(1'*H*)-one;
 1'-{3-[[3-(dimethylamino)propyl]amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-
 indol]-2'(1'*H*)-one;
 1'-[3-(diethylamino)propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 30 1'-[3-(octylamino)propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
 1'-{3-[(1-methylbutyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-
 one;
 1'-{3-[butyl(methyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-
 one;
 35 1'-{3-[(2-isopropoxyethyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-

- 2'(*1H*)-one;
 1'-{3-[(2,4-difluorobenzyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
 2'(*1H*)-one;
 1'-{3-[(2-methylbenzyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
 5 2'(*1H*)-one;
 1'-{3-[(3-fluorobenzyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1H*)-
 one;
 1'-{3-[(2,6-difluorobenzyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
 2'(*1H*)-one;
 10 1'-{3-[(1,2-dimethylpropyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
 2'(*1H*)-one;
 1'-{3-[(2-(1-methylpyrrolidin-2-yl)ethyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-
 7,3'-indol]-2'(*1H*)-one;
 1'-{3-[(2-pyridin-3-ylethyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
 15 2'(*1H*)-one;
 1'-{3-[(1-methyl-2-phenylethyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-
 indol]-2'(*1H*)-one;
 1'-{3-[(2-(2-chlorophenyl)ethyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-
 indol]-2'(*1H*)-one;
 20 1'-{3-[(2-cyclohexylethyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
 2'(*1H*)-one;
 1'-{3-[(2-pyridin-2-ylethyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
 2'(*1H*)-one;
 1'-{3-[(2-biphenyl-4-ylethyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
 25 2'(*1H*)-one;
 1'-{3-[(3-morpholin-4-ylpropyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-
 indol]-2'(*1H*)-one;
 1'-{3-[(5-methyl-2-furyl)methyl]amino}propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-
 indol]-2'(*1H*)-one;
 30 1'-{3-[(3-methylbenzyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
 2'(*1H*)-one;
 1'-(3-aminopropyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1H*)-one; and
 1'-(2-aminoethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1H*)-one.

Another embodiment of the invention are the compounds of formula (I) as set
 35 forth above in the Summary of the invention wherein:

j is 0 and k is 1;

Q is -O-;

R¹ is -R⁹-N(R¹²)C(O)R¹¹ where:

each R¹⁰ is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

5 each R¹¹ is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, -R⁹-OC(O)R⁵, -R⁹-C(O)OR⁵, -R⁹-C(O)N(R⁴)R⁵, -R⁹-C(O)R⁵, -R⁹-N(R⁴)R⁵, -R⁹-OR⁵, or -R⁹-CN;

R¹² is hydrogen, alkyl, aryl, aralkyl or -C(O)R⁵;

10 and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R¹⁰ and R¹¹ may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, -R⁸-CN, -R⁸-OR⁵, -R⁸-C(O)R⁵, heterocyclyl and heteroaryl;

15 R^{2a}, R^{2b}, R^{2c} and R^{2d} are each hydrogen;

R^{3a} and R^{3d} are each hydrogen;

R^{3b} and R^{3c}, together with the carbon ring atoms to which they are directly attached, form a fused dioxolyl ring;

each R⁴ and R⁵ is independently selected from group consisting of hydrogen, alkyl,

20 alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;

or when R⁴ and R⁵ are each attached to the same nitrogen atom, then R⁴ and R⁵, together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl; and

25 each R⁸ is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and each R⁹ is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain.

Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention, selected from the group consisting of:

1'-(3-aminopropyl)spiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-2'-(1'H)-one;

3-chloro-N-[3-(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'-(2'H)-yl)propyl]thiophene-2-carboxamide;

N-[3-(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'-(2'H)-

35 yl)propyl]cyclopropanecarboxamide;

- N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]cyclobutanecarboxamide;
- 2-chloro-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]nicotinamide;
- 5 *N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]cyclopentanecarboxamide;
- 2,2-dimethyl-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]propanamide;
- 2-(4-methoxyphenyl)-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]acetamide;
- 10 4-*tert*-butyl-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]benzamide;
- 3,3-dimethyl-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]butanamide;
- 15 *N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]biphenyl-4-carboxamide;
- 3-methyl-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]-1-benzofuran-2-carboxamide;
- 2-(benzyloxy)-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]acetamide;
- 20 *N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]-2-furamide;
- N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]-1,3-benzodioxole-5-carboxamide;
- N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]quinoline-2-carboxamide;
- 25 *N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]-2-phenylacetamide;
- N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]piperidine-1-carboxamide;
- 30 2-methoxy-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]acetamide;
- 4-(dimethylamino)-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]benzamide;
- 4-ethoxy-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]benzamide;
- 35

- 2-methyl-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]butanamide;
N-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]-2-phenoxyacetamide;
5 *N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]quinoxaline-2-carboxamide;
N-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]cyclohexanecarboxamide;
4-fluoro-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]benzamide;
10 2-ethyl-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]butanamide;
2-(4-fluorophenyl)-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]acetamide;
15 6-chloro-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]nicotinamide;
2-fluoro-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]benzamide;
N-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]-2-phenylcyclopropanecarboxamide;
20 4-methyl-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]benzamide;
1-(4-fluorophenyl)-5-methyl-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]-1*H*-pyrazole-4-carboxamide;
25 *N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]-1-benzofuran-5-carboxamide;
N-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]-2,1,3-benzoxadiazole-5-carboxamide;
2,4-dichloro-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]benzamide;
30 1-methyl-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]-1*H*-1,2,3-benzotriazole-5-carboxamide;
5-fluoro-2-methyl-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]benzamide;
35 2-chloro-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-

- yl)propyl]isonicotinamide;
- N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]-2,3-dihydro-1,4-benzodioxine-6-carboxamide;
- 5-methyl-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]isoxazole-3-carboxamide;
- 5 *N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]-1-benzofuran-2-carboxamide;
- N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]-1-benzothiophene-2-carboxamide;
- 10 *N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]-2,3-dihydro-1,4-benzodioxine-2-carboxamide;
- N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]-4-(1*H*-pyrazol-1-yl)benzamide;
- 1,3-dimethyl-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]-1*H*-pyrazole-5-carboxamide;
- 15 4-methyl-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]-3,4-dihydro-2*H*-1,4-benzoxazine-7-carboxamide;
- N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]quinoxaline-6-carboxamide;
- 20 *N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]-2,3-dihydro-1-benzofuran-2-carboxamide;
- N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]-2,3-dihydro-1-benzothiophene-5-carboxamide;
- N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]-2-
- 25 (trifluoromethoxy)benzamide;
- N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]pentanamide;
- N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]heptanamide;
- 3-cyclopentyl-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]propanamide;
- 30 9-oxo-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]-9*H*-fluorene-4-carboxamide;
- N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]-4-(trifluoromethyl)benzamide;
- 2,5-difluoro-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]benzamide;
- 35

- 2,5-dimethyl-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)propyl]-3-furamide;
- N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)propyl]-4-phenoxybutanamide;
- 5 4-fluoro-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)propyl]-2-(trifluoromethyl)benzamide;
- N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)propyl]-2-(2-thienyl)acetamide;
- 2-chloro-5-fluoro-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)propyl]benzamide;
- 10 *N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)propyl]-2-naphthamide;
- 2-(4-chlorophenoxy)-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)propyl]acetamide;
- 15 2,4-dimethoxy-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)propyl]benzamide;
- 2-nitro-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)propyl]benzamide;
- 2-(4-chlorophenyl)-3-methyl-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)propyl]butanamide;
- 20 4-amino-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)propyl]benzamide;
- 3,4-dimethoxy-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)propyl]benzamide;
- 25 *N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)propyl]-5*H*-dibenzo[*b,f*]azepine-5-carboxamide;
- N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)propyl]adamantane-1-carboxamide;
- 2-[(2-isopropyl-5-methylcyclohexyl)oxy]-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)propyl]acetamide;
- 30 *N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)propyl]-3,5-bis(trifluoromethyl)benzamide;
- 2-(2,5-dimethoxyphenyl)-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)propyl]acetamide;
- 35 2-chloro-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-

- yl)propyl]benzamide;
3-chloro-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]benzamide;
4-chloro-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]benzamide;
5 *N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]hexanamide;
2,6-difluoro-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]benzamide;
2-chloro-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]acetamide;
10 *N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]-2,5-bis(trifluoromethyl)benzamide;
N-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]pyrrolidine-1-carboxamide;
15 2-bromo-2,2-difluoro-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]acetamide;
2,3,5-trifluoro-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]benzamide;
5-fluoro-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]-2-(trifluoromethyl)benzamide;
20 5-chloro-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]-2-(trifluoromethyl)benzamide;
N-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]thiophene-2-carboxamide;
25 *N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]morpholine-4-carboxamide;
2-(1-naphthyl)-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]acetamide;
2-methyl-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]propanamide;
30 *N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]-*N*-propionylpropanamide;
N-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]-4-pentylbenzamide;
35 4,7,7-trimethyl-3-oxo-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-

yl)propyl]-2-oxabicyclo[2.2.1]heptane-1-carboxamide;
 2-bromo-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-
 yl)propyl]benzamide;
 3-cyano-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-
 5 yl)propyl]benzamide;
 4-cyano-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-
 yl)propyl]benzamide; and
N-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]-2-
 (trifluoromethoxy)benzamide.

10 Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention wherein:

j is 0 and *k* is 1;

Q is -O-;

*R*¹ is -*R*⁹-*N*(*R*¹⁰)*C*(*O*)*N*(*R*¹⁰)*R*¹¹ where:

15 each *R*¹⁰ is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each *R*¹¹ is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, -*R*⁹-*OC*(*O*)*R*⁵, -*R*⁹-*C*(*O*)*OR*⁵, -*R*⁹-*C*(*O*)*N*(*R*⁴)*R*⁵, -*R*⁹-*C*(*O*)*R*⁵, -*R*⁹-*N*(*R*⁴)*R*⁵, -*R*⁹-*OR*⁵, or -*R*⁹-*CN*;

20 and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for *R*¹⁰ and *R*¹¹ may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, -*R*⁸-*CN*, -*R*⁸-*OR*⁵, -*R*⁸-*C*(*O*)*R*⁵, heterocyclyl and heteroaryl;

25 *R*^{2a}, *R*^{2b}, *R*^{2c} and *R*^{2d} are each hydrogen;

R^{3a} and *R*^{3d} are each hydrogen;

R^{3b} and *R*^{3c}, together with the carbon ring atoms to which they are directly attached, form a fused dioxolyl ring;

each *R*⁴ and *R*⁵ is independently selected from group consisting of hydrogen, alkyl,

30 alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;

or when *R*⁴ and *R*⁵ are each attached to the same nitrogen atom, then *R*⁴ and *R*⁵, together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl; and

35 each *R*⁸ is a direct bond or a straight or branched alkylene chain, a straight or

branched alkenylene chain or a straight or branched alkynylene chain; and each R⁹ is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain.

- Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention, selected from the group consisting of:
- 1-(4-fluorophenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
 - 1-benzyl-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
 - 1-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]-3-(4-phenoxyphenyl)urea;
 - 1-butyl-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
 - 1-cyclohexyl-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
 - 1-ethyl-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
 - 1-isopropyl-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
 - 1-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]-3-propylurea;
 - 1-*tert*-butyl-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
 - 1-cyclopentyl-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
 - 1-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]-3-pentylurea;
 - 1-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]-3-phenylurea;
 - 1-(2-furylmethyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
 - 1-hexyl-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
 - ethyl *N*-({[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]amino}carbonyl)glycinate;
 - 1-(3-methylphenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
 - 1-(4-methylphenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
 - ethyl *N*-({[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]amino}carbonyl)-beta-alaninate;
 - 1-(4-cyanophenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-

- yl)ethyl]urea;
- N*-({[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]amino}carbonyl)benzamide;
- 1-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]-3-(2-phenylethyl)urea;
- 5 1-(4-methylbenzyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 1-(2-methylbenzyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 10 1-(4-ethylphenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 1-(3-methoxyphenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 1-(2-fluoro-5-methylphenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 15 1-(3-fluoro-4-methylphenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 1-(4-chlorophenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 20 2-({[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]amino}carbonyl)amino]ethyl 2-methylacrylate;
- 1-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]-3-(1,1,3,3-tetramethylbutyl)urea;
- ethyl 4-({[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]amino}carbonyl)amino]butanoate;
- 25 1-[4-(cyanomethyl)phenyl]-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 1-(2,3-dihydro-1*H*-inden-5-yl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 30 1-(3-acetylphenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 1-(4-acetylphenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 1-(4-isopropylphenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 35

- 1-(2-methoxybenzyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)ethyl]urea;
- 1-(4-methoxybenzyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)ethyl]urea;
- 5 1-(4-methoxy-2-methylphenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)ethyl]urea;
- 1-(4-chloro-2-methylphenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)ethyl]urea;
- 1-(3-chloro-4-methylphenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)ethyl]urea;
- 10 1-(3-chloro-2-methylphenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)ethyl]urea;
- 1-(5-chloro-2-methylphenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)ethyl]urea;
- 15 1-(2-chlorobenzyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)ethyl]urea;
- 1-(1-naphthyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)ethyl]urea;
- 1-(2-naphthyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)ethyl]urea;
- 20 1-(3-chloro-2-fluorophenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)ethyl]urea;
- 1-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)ethyl]-3-(5,6,7,8-tetrahydronaphthalen-1-yl)urea;
- 25 1-(4-*tert*-butylphenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)ethyl]urea;
- 1-(4-butylphenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)ethyl]urea;
- 1-[2-(4-ethylphenyl)ethyl]-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)ethyl]urea;
- 30 1-(2,3-dihydro-1,4-benzodioxin-6-yl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)ethyl]urea;
- methyl 4-[[[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)ethyl]amino]carbonyl]amino]benzoate;
- 35 1-(2-ethoxybenzyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-

- yl)ethyl]urea;
- 1-(3,4-dimethoxyphenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 1-(3,5-dimethoxyphenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 5 1-(3-chloro-4-methoxyphenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 1-[4-(difluoromethoxy)phenyl]-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 10 1-[2-(difluoromethoxy)phenyl]-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 1-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]-3-[3-(trifluoromethyl)phenyl]urea;
- 1-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]-3-[2-(trifluoromethyl)phenyl]urea;
- 15 1-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]-3-[4-(trifluoromethyl)phenyl]urea;
- 1-(3,4-dichlorophenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 20 1-(2,3-dichlorophenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 1-(3,5-dichlorophenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- ethyl 4-[[[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]amino]carbonyl]amino]benzoate;
- 25 ethyl 2-[[[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]amino]carbonyl]amino]benzoate;
- 1-[2-(1,3-benzodioxol-5-yl)ethyl]-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 30 methyl 2-methyl-3-[[[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]amino]carbonyl]amino]benzoate;
- 1-(4-butoxyphenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 1-(2-methoxy-4-nitrophenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 35 1-(2'*H*)-yl)ethyl]urea;

- 1-biphenyl-2-yl-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 1-[4-methyl-3-(trifluoromethyl)phenyl]-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 5 1-(2,4-dichlorobenzyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 1-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]-3-[2-(trifluoromethoxy)phenyl]urea;
- 1-[4-fluoro-2-(trifluoromethyl)phenyl]-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 10 1-(5-*tert*-butyl-2-methoxyphenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 1-[2-(3,5-dimethoxyphenyl)ethyl]-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 15 1-(9*H*-fluoren-2-yl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 1-(9*H*-fluoren-9-yl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 1-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]-3-(3,4,5-trimethoxyphenyl)urea;
- 20 1-(diphenylmethyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 1-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]-3-(2-phenoxyphenyl)urea;
- 25 1-(2-biphenyl-4-ylethyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 1-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]-3-(3,4,5-trimethoxybenzyl)urea;
- 1-(2-nitrophenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 30 1-(1,3-benzodioxol-5-yl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 1-[4-(dimethylamino)phenyl]-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea;
- 35 1-(2-fluorobenzyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-

- yl)ethyl]urea;
 1-(4-fluoro-3-methylphenyl)-3-[2-(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)ethyl]urea;
 1-(3-fluorobenzyl)-3-[2-(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)ethyl]urea;
 5 1-(cyclohexylmethyl)-3-[2-(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)ethyl]urea;
 1-(2-methylphenyl)-3-[2-(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)ethyl]urea; and
 10 1-[4-(6-methyl-1,3-benzothiazol-2-yl)phenyl]-3-[2-(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)ethyl]urea.

Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention wherein:

at least one of j and k is 1 and the other is 0 or 1;

- 15 Q is -O-;

R¹ is heterocyclalkyl or heteroarylalkyl where the heterocyclalkyl or the heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclalkyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, -R⁸-OR⁵, -R⁸-C(O)OR⁵, -R⁸-N(R⁴)R⁵, -R⁸-C(O)N(R⁴)R⁵, -R⁸-N(R⁵)C(O)R⁴, -R⁸-S(O)_mR⁴ (where m is 0, 1 or 2), -R⁸-CN, or -R⁸-NO₂;

R^{2a}, R^{2b}, R^{2c} and R^{2d} are each independently selected from the group consisting of

- hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclalkyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, -R⁸-CN, -R⁸-NO₂, -R⁸-OR⁵, -R⁸-N(R⁴)R⁵, -N=C(R⁴)R⁵, -S(O)_mR⁴, -OS(O)₂CF₃, -R⁸-C(O)R⁴, -C(S)R⁴, -C(R⁴)₂C(O)R⁵, -R⁸-C(O)OR⁴, -C(S)OR⁴, -R⁸-C(O)N(R⁴)R⁵, -C(S)N(R⁴)R⁵, -N(R⁵)C(O)R⁴, -N(R⁵)C(S)R⁴, -N(R⁵)C(O)OR⁴, -N(R⁵)C(S)OR⁴, -N(R⁵)C(O)N(R⁴)R⁵, -N(R⁵)C(S)N(R⁴)R⁵, -N(R⁵)S(O)_nR⁴, -N(R⁵)S(O)_nN(R⁴)R⁵, -R⁸-S(O)_nN(R⁴)R⁵, -N(R⁵)C(=NR⁵)N(R⁴)R⁵, and -N(R⁵)C(=N-CN)N(R⁴)R⁵,
 25 wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;
 and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclalkyl, heterocyclalkyl, heteroaryl and heteroarylalkyl groups for R^{2a}, R^{2b}, R^{2c} and R^{2d} may be optionally substituted by one or more
 30 substituents selected from the group consisting of alkyl, alkenyl, alkynyl,

- alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$, $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;
- or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;
- or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2d} are as defined above;
- or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;
- R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;
- or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;
- or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3d} are as defined above;
- or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3b} are as defined above;
- each R^4 and R^5 is independently selected from group consisting of hydrogen, alkyl,

alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl, and heteroarylalkyl;

or when R⁴ and R⁵ are each attached to the same nitrogen atom, then R⁴ and R⁵, together with the nitrogen atom to which they are attached, may form a

5 heterocyclyl or heteroaryl; and

each R⁸ is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and each R⁹ is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain.

10 Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention wherein:

j is 0 and k is 1;

Q is -O-;

R¹ is heterocyclalkyl or heteroarylalkyl where the heterocyclalkyl or the

15 heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, -R⁸-OR⁵, -R⁸-C(O)OR⁵, -R⁸-N(R⁴)R⁵, -R⁸-C(O)N(R⁴)R⁵, -R⁸-N(R⁵)C(O)R⁴, -R⁸-S(O)_mR⁴ (where m is 0, 1 or 2), -R⁸-CN, or -R⁸-NO₂;

20 R^{2a}, R^{2b}, R^{2c} and R^{2d} are each independently selected from hydrogen, halo, alkyl or -R⁸-OR⁵;

R^{3a}, R^{3b}, R^{3c} and R^{3d} are each independently selected from hydrogen, halo, alkyl or -R⁸-OR⁵;

or R^{3b} and R^{3c}, together with the carbon ring atoms to which they are directly attached,

25 form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3d} are each hydrogen;

each R⁵ is independently selected from group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl and heteroaryl; and

30 each R⁸ is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain.

Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention wherein:

j is 0 and k is 1;

35 Q is -O-;

- R¹ is heterocyclalkyl or heteroarylalkyl where the heterocyclalkyl or the heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocycl, heterocyclalkyl, heteroaryl, heteroarylalkyl, -R⁸-OR⁵, -R⁸-C(O)OR⁵, -R⁸-N(R⁴)R⁵, -R⁸-C(O)N(R⁴)R⁵, -R⁸-N(R⁵)C(O)R⁴, -R⁸-S(O)_mR⁴ (where m is 0, 1 or 2), -R⁸-CN, or -R⁸-NO₂;
- R^{2a}, R^{2b}, R^{2c} and R^{2d} are each independently selected from hydrogen, halo, alkyl or -R⁸-OR⁵;
- R^{3a}, R^{3b}, R^{3c} and R^{3d} are each independently selected from hydrogen, halo, alkyl or -R⁸-OR⁵;
- or R^{3b} and R^{3c}, together with the carbon ring atoms to which they are directly attached, form a fused ring selected from dioxolyl or tetrahydrofuranyl, and R^{3a} and R^{3d} are each hydrogen;
- each R⁵ is independently selected from group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocycl and heteroaryl; and
- each R⁸ is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain.
- Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention, selected from the group consisting of:
- 2-[3-(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)propyl]-1H-isoindole-1,3(2H)-dione;
- 2-[2-(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-1'(2'H)-yl)ethyl]-1H-isoindole-1,3(2H)-dione;
- 4'-bromo-1'-(pyridin-2-ylmethyl)-5,6-dihydrospiro[benzo[1,2-b:5,4-b']difuran-3,3'-indol]-2'(1'H)-one;
- 5'-fluoro-1'-{[5-(trifluoromethyl)-2-furyl]methyl}spiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-2'(1'H)-one;
- 5'-methyl-1'-{[5-(trifluoromethyl)-2-furyl]methyl}spiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-2'(1'H)-one;
- 5-bromo-1'-{[5-(trifluoromethyl)-2-furyl]methyl}spiro[1-benzofuran-3,3'-indol]-2'(1'H)-one;
- 4'-Methoxy-1'-{[5-(trifluoromethyl)-2-furyl]methyl}spiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-2'(1'H)-one;
- 7'-fluoro-1'-{[5-(trifluoromethyl)-2-furyl]methyl}spiro[furo[2,3-f][1,3]benzodioxole-7,3'-

- indol]-2'(1*H*)-one;
- 1'-[[1-(2,6-difluorobenzyl)-1*H*-1,2,3-triazol-4-yl]methyl]spiro[furo[2,3-
f][1,3]benzodioxole-7,3'-indol]-2'(1*H*)-one;
- 1'-[[6-(trifluoromethyl)pyridin-3-yl]methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
5 2'(1*H*)-one;
- 1'-[(6-chloropyridin-3-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1*H*)-one;
- 1'-(tetrahydro-2*H*-pyran-2-ylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1*H*)-
one;
- 1'-(tetrahydrofuran-2-ylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1*H*)-one;
- 10 1'-(2,3-dihydro-1,4-benzodioxin-2-ylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-
indol]-2'(1*H*)-one;
- 1'-[(7-methoxy-2-oxo-2*H*-1,4-benzoxazin-3-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-
7,3'-indol]-2'(1*H*)-one;
- 1'-[(5-methyl-2-phenyl-2*H*-1,2,3-triazol-4-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-
15 7,3'-indol]-2'(1*H*)-one;
- 1'-[[5-(trifluoromethyl)-2-furyl]methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'(1*H*)-one;
- 1'-(3,4-dihydro-2*H*-1,5-benzodioxepin-7-ylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-
7,3'-indol]-2'(1*H*)-one;
- 20 1'-(1*H*-1,2,3-triazol-4-ylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1*H*)-one;
- ethyl 1-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]-1*H*-1,2,3-
triazole-5-carboxylate;
- ethyl 1-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]-1*H*-1,2,3-
triazole-4-carboxylate;
- 25 1'-(1,3-thiazol-4-ylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1*H*)-one;
- 1'-[(5-chloro-1-benzothien-3-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'(1*H*)-one;
- 1'-(pyridin-2-ylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1*H*)-one;
- 1'-(pyridin-4-ylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1*H*)-one;
- 30 1'-(pyridin-3-ylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1*H*)-one;
- 1'-[2-(1*H*-pyrrol-1-yl)ethyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1*H*)-one;
- 1'-[[4-chloro-2-(trifluoromethyl)quinolin-6-yl]methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-
7,3'-indol]-2'(1*H*)-one;
- 1'-[(2-methyl-1,3-thiazol-4-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
35 2'(1*H*)-one;

- 1'-(1,3-benzothiazol-2-ylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one;
- 1'-(2,1,3-benzothiadiazol-4-ylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one;
- 5 1'-(2,1,3-benzothiadiazol-5-ylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one;
- 1'-[(1-methyl-1*H*-1,2,3-benzotriazol-5-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one;
- 1'-[3-(1*H*-pyrrol-1-yl)propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one;
- 10 1'-[(3-methyl-5-phenylisoxazol-4-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one;
- 1'-[(7-methoxy-2-oxo-2*H*-chromen-4-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one;
- 1'-[2-(2,5,5-trimethyl-1,3-dioxan-2-yl)ethyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one;
- 15 1'-[(6-fluoro-4*H*-1,3-benzodioxin-8-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one;
- 1'-[(5-phenyl-1,3-oxazol-4-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one;
- 20 1'-(1,3-benzodioxol-5-ylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one;
- 1'-(piperidin-4-ylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one;
- 1'-[(1-methylpiperidin-4-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one hydrochloride;
- 1'-[(1-ethylpiperidin-4-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one hydrochloride;
- 25 1'-[(1-cyclohexylpiperidin-4-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one hydrochloride;
- 1'-[(1-cyclopropylmethyl)piperidin-4-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one hydrochloride;
- 30 1'-[(1-cyclopentylpiperidin-4-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one hydrochloride;
- 1'-[(1-(pyridine-3-ylmethyl)piperidin-4-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one hydrochloride;
- 1'-[(1-(3-methylbutyl)piperidin-4-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one hydrochloride;
- 35

- 1'[{1-(1-ethylpropyl)piperidin-4-yl)methyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'(1'*H*)-one hydrochloride;
- 1'[{1-(1-cyclobutylpiperidin-4-yl)methyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'(1'*H*)-one hydrochloride;
- 5 1'[{1-(1-isopropylpiperidin-4-yl)methyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'(1'*H*)-one hydrochloride;
- 1'[{1-(pyridin-2-ylmethyl)piperidin-4-yl)methyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-
indol]-2'(1'*H*)-one hydrochloride;
- 10 1'[{1-(2-thienylmethyl)piperidin-4-yl)methyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'(1'*H*)-one hydrochloride;
- 1'-[{1-[3-(methylthio)propyl]piperidin-4-yl)methyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-
indol]-2'(1'*H*)-one hydrochloride;
- 1'[{1-(tetrahydro-2*H*-pyran-4-yl)piperidin-4-yl)methyl}spiro[furo[2,3-*f*][1,3]benzodioxole-
7,3'-indol]-2'(1'*H*)-one hydrochloride;
- 15 1'-[{1-(3,3-dimethylbutyl)piperidin-4-yl)methyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-
indol]-2'(1'*H*)-one hydrochloride;
- 7'-fluoro-1'-[{1-(1-isopropylpiperidin-4-yl)methyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-
indol]-2'(1'*H*)-one hydrochloride;
- 1'-[(6-methylpyridin-3-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one
20 hydrochloride;
- 1'-[(6-methoxypyridin-3-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-
one;
- 1'-[(6-chloropyridin-3-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-[(6-(dimethylamino)pyridin-3-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
25 2'(1'*H*)-one hydrochloride;
- 1'-[(6-morpholin-4-ylpyridin-3-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'(1'*H*)-one hydrochloride;
- 1'-[(6-pyrrolidin-1-ylpyridin-3-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'(1'*H*)-one hydrochloride;
- 30 1'-[(5-methylisoxazol-4-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-
one;
- 1'-[(tetrahydro-2*H*-pyran-4-ylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-
one;
- 1'(2,1,3-benzoxadiazol-5-ylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-
35 one;

- 1'[(1-methyl-1*H*-benzotriazol-6-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'(1'*H*)-one;
tert-butyl 4-[(2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-
yl)methyl]piperidine 1-carboxylate;
- 5 1'-(pyridin-2-ylmethyl)-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]2'(1'*H*)-one
hydrochloride;
- 4'-bromo-1'-[[5-(trifluoromethyl)-2-furyl]methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-
indol]-2'(1'*H*)-one;
- 4'-bromo-1'-[[5-(trifluoromethyl)-2-furyl]methyl]-5,6-dihydrospiro[benzo[1,2-*b*:5,4-
10 *b'*]difuran-3,3'-indol]-2'(1'*H*)-one;
- 1'-[(3,5-dimethylisoxazol-4-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'(1'*H*)-one;
- 1'-(2-furylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-(1,2,4-oxadiazol-3-ylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 15 1'-[[5-(3-chlorophenyl)-2-furyl]methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'(1'*H*)-one;
- 1'-[(2-isopropyl-1,3-oxazol-4-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'(1'*H*)-one;
- 1'-[(1-methyl-1*H*-benzimidazol-2-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
20 2'(1'*H*)-one;
- 1'-[(2-oxo-1,3-benzothiazol-3(2*H*)-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-
indol]-2'(1'*H*)-one;
- 1'-[(5-chloro-2-thienyl)methyl]-5'-fluorospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'(1'*H*)-one;
- 25 1'-[(5-chloro-2-furyl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-[(4-hydroxy-1,2,2,6,6-pentamethylpiperidin-4-yl)methyl]spiro[furo[2,3-
f][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-[[5-(2-chlorophenyl)-2-furyl]methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
2'(1'*H*)-one;
- 30 1'-[(5-methyl-2-furyl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-[(5-bromo-2-furyl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-[(5-chloro-2-thienyl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-[[3-hydroxy-5-(trifluoromethyl)-2-thienyl]methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-
7,3'-indol]-2'(1'*H*)-one;
- 35 1'-[[5-(2-trifluoromethylphenyl)-2-furyl]methyl]-4*H*-spiro[furo[2,3-*g*][1,3]benzodioxine-

- 8,3'-indol]-2'(1'*H*)-one;
- 1'-[(2-chloro-1,3-thiazol-5-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-[[5-(trifluoromethyl)-2-thienyl]methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 5 2'(1'*H*)-one;
- 1'-[[3-methoxy-5-(trifluoromethyl)-2-thienyl]methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 4'-methyl-1'-[[5-(trifluoromethyl)-2-furyl]methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 10 5'-methyl-1'-[[5-(trifluoromethyl)-2-furyl]methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-([5-[4-(trifluoromethyl)phenyl]-1,2,4-oxadiazol-3-yl]methyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-(2-thienylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 15 5-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]thiophene-2-carbonitrile;
- 5-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-2-furonitrile;
- 1'-[[5-(methylsulfonyl)-2-furyl]methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 20 1'-[(6-oxo-1,6-dihydropyridin-3-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-[(1-methyl-6-oxo-1,6-dihydropyridin-3-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-[(5-chloro-1,3,4-thiadiazol-2-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 25 2'(1'*H*)-one;
- 1'-[(1-pyridin-2-yl)piperidin-4-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 1'-[(1-phenyl-2-yl)piperidin-4-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;
- 30 1'-(pyridin-2-ylmethyl)-6-(trifluoromethoxy)spiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one hydrochloride;
- 1'-(2-piperidin-1-ylethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one hydrochloride;
- tert*-butyl 4-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]piperidine-1-carboxylate;
- 35

1'-(2-piperidin-4-ylethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one hydrochloride;

1'-[2-(1-cyclopentylpiperidin-4-yl)ethyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one hydrochloride;

5 1'-[2-(1-isopropylpiperidin-4-yl)ethyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one hydrochloride;

1'-[2-(1-cyclobutylpiperidin-4-yl)ethyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one hydrochloride;

10 1'-{2-[1-(tetrahydro-2*H*-pyran-4-yl)piperidin-4-yl]ethyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one hydrochloride;

1'-(3-pyrrolidin-1-ylpropyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one;

1'-(3-piperidin-1-ylpropyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one; and

1'-[(5-fluoro-1*H*-benzimidazol-2-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one.

15 Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention wherein:

at least one of *j* and *k* is 1 and the other is 0 or 1;

Q is -O-;

R¹ is heterocyclalkyl or heteroarylalkyl where the heterocyclalkyl or the

20 heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclalkyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, -R⁸-OR⁵, -R⁸-C(O)OR⁵, -R⁸-N(R⁴)R⁵, -R⁸-C(O)N(R⁴)R⁵, -R⁸-N(R⁵)C(O)R⁴, -R⁸-S(O)_{*m*}R⁴ (where *m* is 0, 1 or 2), -R⁸-CN, or -R⁸-NO₂;

25 R^{2a}, R^{2b}, R^{2c} and R^{2d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclalkyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, -R⁸-CN, -R⁸-NO₂, -R⁸-OR⁵, -R⁸-N(R⁴)R⁵, -N=C(R⁴)R⁵, -S(O)_{*m*}R⁴, -OS(O)₂CF₃, -R⁸-C(O)R⁴, -C(S)R⁴, -C(R⁴)₂C(O)R⁵, -R⁸-C(O)OR⁴, -C(S)OR⁴, -R⁸-C(O)N(R⁴)R⁵, -C(S)N(R⁴)R⁵, -N(R⁵)C(O)R⁴, -N(R⁵)C(S)R⁴, -N(R⁵)C(O)OR⁴, -N(R⁵)C(S)OR⁴, -N(R⁵)C(O)N(R⁴)R⁵, -N(R⁵)C(S)N(R⁴)R⁵, -N(R⁵)S(O)_{*n*}R⁴, -N(R⁵)S(O)_{*n*}N(R⁴)R⁵, -R⁸-S(O)_{*n*}N(R⁴)R⁵, -N(R⁵)C(=NR⁵)N(R⁴)R⁵, and -N(R⁵)C(=N-CN)N(R⁴)R⁵,
30 wherein each *m* is independently 0, 1, or 2 and each *n* is independently 1 or 2;
35 and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl,

- heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$, $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;
- 10 R^{3a} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;
- 15 or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from dioxolyl or tetrahydrofuranyl, and R^{3a} and R^{3d} are as defined above;
- each R^4 and R^5 is independently selected from group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;
- 25 or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl; and
- each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and
- 30 each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain.

Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention, selected from the group consisting of:

- 35 4'-(6-methoxypyridin-3-yl)-1'-[5-(trifluoromethyl)-2-furyl]methyl]spiro[furo[2,3-

- $\text{f}[1,3]\text{benzodioxole-7,3'-indol]-2'(1'H)-one;}$
 4'-[6-(dimethylamino)pyridin-3-yl]-1'-{[5-(trifluoromethyl)-2-furyl]methyl}spiro[furo[2,3-
 $\text{f}[1,3]\text{benzodioxole-7,3'-indol]-2'(1'H)-one;}$
 4'-(3-furyl)-1'-(pyridin-2-ylmethyl)-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-
 5 indol]-2'(1'H)-one;
 1'-(pyridin-2-ylmethyl)-4'-pyrimidin-5-yl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-
 indol]-2'(1'H)-one;
 4'-pyridin-3-yl-1'-(pyridin-2-ylmethyl)-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-
 indol]-2'(1'H)-one;
 10 4'-(3-furyl)-1'-{[5-(trifluoromethyl)-2-furyl]methyl}-5,6-dihydrospiro[benzo[1,2-*b*:5,4-
 $\text{b']difuran-3,3'-indol]-2'(1'H)-one;}$
 4'-quinolin-3-yl-1'-{[5-(trifluoromethyl)-2-furyl]methyl}spiro[furo[2,3- $\text{f}[1,3]\text{benzodioxole-}$
 7,3'-indol]-2'(1'H)-one;
 4'-pyrimidin-5-yl-1'-{[5-(trifluoromethyl)-2-furyl]methyl}-5,6-dihydrospiro[benzo[1,2-
 15 $\text{b:5,4-b']difuran-3,3'-indol]-2'(1'H)-one;}$
tert-butyl 4-[(2'-oxo-4'-pyrimidin-5-ylspiro[furo[2,3- $\text{f}[1,3]\text{benzodioxole-7,3'-indol]-1'(2'H)-}$
 yl)methyl]piperidine-1-carboxylate;
tert-butyl 4-[(5,5-dimethyl-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-
 1'(2'H)-yl)methyl]piperidine-1-carboxylate;
 20 5,5-dimethyl-1'-(piperidin-4-ylmethyl)-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-
 indol]-2'(1'H)-one hydrochloride;
 5,5-dimethyl-1'-{[5-(trifluoromethyl)-2-furyl]methyl}-5,6-dihydrospiro[benzo[1,2-*b*:5,4-
 $\text{b']difuran-3,3'-indol]-2'(1'H)-one;}$
 5,5-dimethyl-1'-(pyridin-3-ylmethyl)-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-
 25 indol]-2'(1'H)-one hydrochloride;
 5,5-dimethyl-1'-(pyridin-2-ylmethyl)-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-
 indol]-2'(1'H)-one hydrochloride;
 1'-[(6-methylpyridin-3-yl)methyl]spiro[furo[2,3- $\text{f}[1,3]\text{benzodioxole-7,3'-indol]-2'(1'H)-one}$
 hydrochloride; and
 30 1'-[(6-methoxypyridin-3-yl)methyl]spiro[furo[2,3- $\text{f}[1,3]\text{benzodioxole-7,3'-indol]-2'(1'H)-}$
 one.

Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention wherein:

at least one of j and k is 1 and the other is 0 or 1;

35 Q is -O-;

R¹ is heterocyclalkyl or heteroarylalkyl where the heterocyclalkyl or the heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocycl, heterocyclalkyl, heteroaryl, heteroarylalkyl, -R⁸-OR⁵, -R⁸-C(O)OR⁵, -R⁸-N(R⁴)R⁵, -R⁸-C(O)N(R⁴)R⁵,
 5 -R⁸-N(R⁵)C(O)R⁴, -R⁸-S(O)_mR⁴ (where m is 0, 1 or 2), -R⁸-CN, or -R⁸-NO₂;

R^{2a}, R^{2b}, R^{2c} and R^{2d} are each independently selected from the group consisting of

hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocycl, heterocyclalkyl, heteroaryl, heteroarylalkyl, -R⁸-CN, -R⁸-NO₂, -R⁸-OR⁵,
 10 -R⁸-N(R⁴)R⁵, -N=C(R⁴)R⁵, -S(O)_mR⁴, -OS(O)₂CF₃, -R⁸-C(O)R⁴, -C(S)R⁴, -C(R⁴)₂C(O)R⁵, -R⁸-C(O)OR⁴, -C(S)OR⁴, -R⁸-C(O)N(R⁴)R⁵, -C(S)N(R⁴)R⁵, -N(R⁵)C(O)R⁴, -N(R⁵)C(S)R⁴, -N(R⁵)C(O)OR⁴, -N(R⁵)C(S)OR⁴, -N(R⁵)C(O)N(R⁴)R⁵, -N(R⁵)C(S)N(R⁴)R⁵, -N(R⁵)S(O)_nR⁴, -N(R⁵)S(O)_nN(R⁴)R⁵,
 15 -R⁸-S(O)_nN(R⁴)R⁵, -N(R⁵)C(=NR⁵)N(R⁴)R⁵, and -N(R⁵)C(=N-CN)N(R⁴)R⁵, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2; and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocycl, heterocyclalkyl, heteroaryl and heteroarylalkyl groups for R^{2a}, R^{2b}, R^{2c} and R^{2d} may be optionally substituted by one or more
 20 substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocycl, heterocyclalkyl, heteroaryl, heteroarylalkyl, -R⁸-CN, -R⁸-NO₂, -R⁸-OR⁵, -R⁸-N(R⁴)R⁵, -S(O)_mR⁴, -R⁸-S(O)_nN(R⁴)R⁵, -R⁸-C(O)R⁴, -R⁸-C(O)OR⁴,
 25 -R⁸-C(O)N(R⁴)R⁵, -N(R⁵)C(O)R⁴, and -N(R⁵)S(O)_nR⁴, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

R^{3a}, R^{3b}, R^{3c} and R^{3d} are each independently selected from the group consisting of

hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocycl, heterocyclalkyl, heteroaryl, heteroarylalkyl, -R⁸-CN, -R⁸-NO₂, -R⁸-OR⁵,
 30 -R⁸-N(R⁴)R⁵, -N=C(R⁴)R⁵, -S(O)_mR⁴, -OS(O)₂CF₃, -R⁸-C(O)R⁴, -C(S)R⁴, -C(R⁴)₂C(O)R⁵, -R⁸-C(O)OR⁴, -C(S)OR⁴, -R⁸-C(O)N(R⁴)R⁵, -C(S)N(R⁴)R⁵, -N(R⁵)C(O)R⁴, -N(R⁵)C(S)R⁴, -N(R⁵)C(O)OR⁴, -N(R⁵)C(S)OR⁴, -N(R⁵)C(O)N(R⁴)R⁵, -N(R⁵)C(S)N(R⁴)R⁵, -N(R⁵)S(O)_nR⁴, -N(R⁵)S(O)_nN(R⁴)R⁵,
 35 -R⁸-S(O)_nN(R⁴)R⁵, -N(R⁵)C(=NR⁵)N(R⁴)R⁵, and -N(R⁵)C(=N=C(R⁴)R⁵)N(R⁴)R⁵,

- wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;
 each R^4 and R^5 is independently selected from group consisting of hydrogen, alkyl,
 alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl,
 heterocyclyl, heterocyclalkyl, heteroaryl, and heteroarylalkyl;
 5 or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 ,
 together with the nitrogen atom to which they are attached, may form a
 heterocyclyl or heteroaryl; and
 each R^8 is a direct bond or a straight or branched alkylene chain, a straight or
 branched alkenylene chain or a straight or branched alkynylene chain; and
 10 each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene
 chain or a straight or branched alkynylene chain.

- Another embodiment of the invention are the compounds of formula (I) as set
 forth above in the Summary of the invention, selected from the group consisting of:
 5-bromo-1'-[(5-chloro-2-thienyl)methyl]spiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one;
 15 1'-(pyridin-3-ylmethyl)-6-(trifluoromethoxy)spiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one
 hydrochloride;
 6-(trifluoromethoxy)-1'-{[5-(trifluoromethyl)-2-furyl]methyl}spiro[1-benzofuran-3,3'-indol]-
 2'(1'*H*)-one;
 2'-oxo-1'-{[5-(trifluoromethyl)-2-furyl]methyl}-1',2'-dihydrospiro[1-benzofuran-3,3'-indol]-
 20 5-yl trifluoromethanesulfonate;
 5-pyridin-3-yl-1'-{[5-(trifluoromethyl)-2-furyl]methyl}spiro[1-benzofuran-3,3'-indol]-
 2'(1'*H*)-one hydrochloride;
tert-butyl 3-(2'-oxo-1'-{[5-(trifluoromethyl)-2-furyl]methyl}-1',2'-dihydrospiro[1-
 benzofuran-3,3'-indol]-5-yl)piperidine-1-carboxylate; and
 25 5-pyridin-4-yl-1'-{[5-(trifluoromethyl)-2-furyl]methyl}spiro[1-benzofuran-3,3'-indol]-
 2'(1'*H*)-one hydrochloride.

- Another embodiment of the invention are the compounds of formula (I) as set
 forth above in the Summary of the invention wherein:
 j is 0 and k is 1 or 2;
 30 Q is -O-;
 R^1 is hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl,
 heteroaryl, heterocyclyl, $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$,
 $-R^9-S(O)_m-R^5$ (where m is 0, 1 or 2), $-R^8-OR^5$, $-R^8-CN$, $-R^9-P(O)(OR^5)_2$, or
 $-R^9-O-R^9-OR^5$;
 35 R^{2a} , R^{2b} , R^{2c} and R^{2d} are each hydrogen;

R^{3a} and R^{3d} are each hydrogen;

R^{3b} and R^{3c}, together with the carbon ring atoms to which they are directly attached, form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl;

each R⁴ and R⁵ is independently selected from group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;

or when R⁴ and R⁵ are each attached to the same nitrogen atom, then R⁴ and R⁵, together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl; and

each R⁸ is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and each R⁹ is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain.

Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention wherein:

j is 0 and k is 1 or 2;

Q is -C(R^{1a})H-, -C(O)-, -CF₂-, -C(O)O- or -N(R⁵)C(O)-;

R^{1a} is hydrogen or -OR⁵;

R¹ is hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, -R⁸-C(O)R⁵, -R⁸-C(O)OR⁵, -R⁸-C(O)N(R⁴)R⁵, -S(O)₂-R⁵, -R⁹-S(O)_m-R⁵ (where m is 0, 1 or 2), -R⁸-OR⁵, -R⁸-CN, -R⁹-P(O)(OR⁵)₂, or -R⁹-O-R⁹-OR⁵;

or R¹ is aralkyl substituted by -C(O)N(R⁶)R⁷ where:

R⁶ is hydrogen, alkyl, aryl or aralkyl; and

R⁷ is hydrogen, alkyl, haloalkyl, -R⁹-CN, -R⁹-OR⁵, -R⁹-N(R⁴)R⁵, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl;

or R⁶ and R⁷, together with the nitrogen to which they are attached, form a heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroaryl groups for R⁶ and R⁷ may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, -R⁸-CN, -R⁸-OR⁵, heterocyclyl and heteroaryl;

or R¹ is aralkyl optionally substituted by one or more substituents selected from the

- group consisting of $-R^8-OR^5$, $-C(O)OR^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;
- or R^1 is $-R^9-N(R^{10})R^{11}$, $-R^9-N(R^{12})C(O)R^{11}$ or $-R^9-N(R^{10})C(O)N(R^{10})R^{11}$ where:
- each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;
- 5 each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$;
- R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;
- 10 and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, $-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;
- 15 or R^1 is heterocyclylalkyl or heteroarylalkyl where the heterocyclylalkyl or the heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$,
- 20 $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$ (where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;
- R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$,
- 25 $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(=N-CN)N(R^4)R^5$,
- 30 wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2; and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl,
- 35 alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl,

- cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$, $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is
- 5 independently 0, 1, or 2 and each n is independently 1 or 2;
- or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;
- or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached,
- 10 may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2d} are as defined above;
- or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;
- 15 R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$,
- 20 $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;
- 25 or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;
- or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl,
- 30 and R^{3a} and R^{3d} are as defined above;
- or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3b} are as defined above;
- each R^4 and R^5 is independently selected from group consisting of hydrogen, alkyl,
- 35 alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl,

heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;
 or when R⁴ and R⁵ are each attached to the same nitrogen atom, then R⁴ and R⁵,
 together with the nitrogen atom to which they are attached, may form a
 heterocyclyl or heteroaryl; and

- 5 each R⁸ is a direct bond or a straight or branched alkylene chain, a straight or
 branched alkenylene chain or a straight or branched alkynylene chain; and
 each R⁹ is a straight or branched alkylene chain, a straight or branched alkenylene
 chain or a straight or branched alkynylene chain.

Another embodiment of the invention are the compounds of formula (I) as set
 forth above in the Summary of the invention wherein:

j is 0 and k is 1 or 2;

Q is -C(R^{1a})H-;

R^{1a} is hydrogen or -OR⁵;

- R¹ is hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl,
 15 heteroaryl, heterocyclyl, -R⁸-C(O)R⁵, -R⁸-C(O)OR⁵, -R⁸-C(O)N(R⁴)R⁵, -S(O)₂-R⁵,
 -R⁹-S(O)_m-R⁵ (where m is 0, 1 or 2), -R⁸-OR⁵, -R⁸-CN, -R⁹-P(O)(OR⁵)₂, or
 -R⁹-O-R⁹-OR⁵;

- R^{2a}, R^{2b}, R^{2c} and R^{2d} are each independently selected from the group consisting of
 hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl,
 20 haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl,
 heterocyclylalkyl, heteroaryl, heteroarylalkyl, -R⁸-CN, -R⁸-NO₂, -R⁸-OR⁵,
 -R⁸-N(R⁴)R⁵, -N=C(R⁴)R⁵, -S(O)_mR⁴, -OS(O)₂CF₃, -R⁸-C(O)R⁴, -C(S)R⁴,
 -C(R⁴)₂C(O)R⁵, -R⁸-C(O)OR⁴, -C(S)OR⁴, -R⁸-C(O)N(R⁴)R⁵, -C(S)N(R⁴)R⁵,
 -N(R⁵)C(O)R⁴, -N(R⁵)C(S)R⁴, -N(R⁵)C(O)OR⁴, -N(R⁵)C(S)OR⁴,
 25 -N(R⁵)C(O)N(R⁴)R⁵, -N(R⁵)C(S)N(R⁴)R⁵, -N(R⁵)S(O)_nR⁴, -N(R⁵)S(O)_nN(R⁴)R⁵,
 -R⁸-S(O)_nN(R⁴)R⁵, -N(R⁵)C(=NR⁵)N(R⁴)R⁵, and -N(R⁵)C(=N-CN)N(R⁴)R⁵,
 wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;
 and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl,

- heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for
 30 R^{2a}, R^{2b}, R^{2c} and R^{2d} may be optionally substituted by one or more
 substituents selected from the group consisting of alkyl, alkenyl, alkynyl,
 alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl,
 cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl,
 heteroaryl, heteroarylalkyl, -R⁸-CN, -R⁸-NO₂, -R⁸-OR⁵, -R⁸-N(R⁴)R⁵,
 35 -S(O)_mR⁴, -R⁸-S(O)_nN(R⁴)R⁵, -R⁸-C(O)R⁴, -R⁸-C(O)OR⁴,

- $-R^8-C(O)N(R^4)R^5$, $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;
- or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;
- or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2d} are as defined above;
- or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;
- R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;
- or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;
- or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3d} are as defined above;
- or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3b} are as defined above;
- each R^4 and R^5 is independently selected from group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;
- or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a

- heterocyclyl or heteroaryl; and
- each R⁸ is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and
- each R⁹ is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain.
- Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention wherein:
- j is 0 and k is 1 or 2;
- Q is -C(R^{1a})H-;
- R^{1a} is hydrogen or -OR⁵;
- R¹ is hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, -R⁸-C(O)R⁵, -R⁸-C(O)OR⁵, -R⁸-C(O)N(R⁴)R⁵, -S(O)₂-R⁵, -R⁹-S(O)_m-R⁵ (where m is 0, 1 or 2), -R⁸-OR⁵, -R⁸-CN, -R⁹-P(O)(OR⁵)₂, or -R⁹-O-R⁹-OR⁵;
- R^{2a}, R^{2b}, R^{2c} and R^{2d} are each hydrogen;
- R^{2a}, R^{2b}, R^{2c} and R^{2d} are each hydrogen;
- R^{3a} and R^{3d} are each hydrogen;
- R^{3b} and R^{3c}, together with the carbon ring atoms to which they are directly attached, form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl;
- each R⁵ is independently selected from group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl and heteroaryl;
- each R⁸ is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and
- each R⁹ is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain.

- Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention wherein:
- j is 0 and k is 1 or 2;
- Q is -C(R^{1a})H-;
- R^{1a} is hydrogen or -OR⁵;
- R¹ is pentyl;
- R^{2a}, R^{2b}, R^{2c} and R^{2d} are each hydrogen;
- R^{3a} and R^{3d} are each hydrogen;
- R^{3b} and R^{3c}, together with the carbon ring atoms to which they are directly attached,

form a fused dioxolyl ring; and
 each R⁵ is independently selected from group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl and heteroaryl.

5 Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention, selected from the group consisting of:
 1'-pentyl-6,7-dihydrospiro[indeno[5,6-*d*][1,3]dioxole-5,3'-indol]-2'(1'*H*)-one;
 1-pentyl-7',8'-dihydro-6'*H*-spiro[indole-3,5'-naphtho[2,3-*d*][1,3]dioxol]-2(1'*H*)-one; and
 7-methoxy-1'-pentyl-6,7-dihydrospiro[indeno[5,6-*d*][1,3]dioxole-5,3'-indol]-2'(1'*H*)-one.

10 Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention wherein:

j is 0 and k is 1 or 2;

Q is -C(O)-, -CF₂-, -C(O)O- or -N(R⁵)C(O)-;

R¹ is hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl,

15 heteroaryl, heterocyclyl, -R⁸-C(O)R⁵, -R⁸-C(O)OR⁵, -R⁸-C(O)N(R⁴)R⁵, -S(O)₂-R⁵,
 -R⁹-S(O)_m-R⁵ (where m is 0, 1 or 2), -R⁸-OR⁵, -R⁸-CN, -R⁹-P(O)(OR⁵)₂, or
 -R⁹-O-R⁹-OR⁵;

or R¹ is aralkyl substituted by -C(O)N(R⁶)R⁷ where:

R⁶ is hydrogen, alkyl, aryl or aralkyl; and

20 R⁷ is hydrogen, alkyl, haloalkyl, -R⁹-CN, -R⁹-OR⁵, -R⁹-N(R⁴)R⁵, aryl, aralkyl,
 cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl,
 heteroarylalkyl;

or R⁶ and R⁷, together with the nitrogen to which they are attached, form a
 heterocyclyl or heteroaryl;

25 and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl,
 heterocyclylalkyl, heteroaryl and heteroaryl groups for R⁶ and R⁷ may be
 optionally substituted by one or more substituents selected from the
 group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl,
 -R⁸-CN, -R⁸-OR⁵, heterocyclyl and heteroaryl;

30 or R¹ is aralkyl optionally substituted by one or more substituents selected from the
 group consisting of -R⁸-OR⁵, -C(O)OR⁵, halo, haloalkyl, alkyl, nitro, cyano, aryl,
 aralkyl, heterocyclyl and heteroaryl;

or R¹ is -R⁹-N(R¹⁰)R¹¹, -R⁹-N(R¹²)C(O)R¹¹ or -R⁹-N(R¹⁰)C(O)N(R¹⁰)R¹¹ where:

each R¹⁰ is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

35 each R¹¹ is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl,

heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$;

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

5 and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, $-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

10 or R^1 is heterocyclylalkyl or heteroarylalkyl where the heterocyclylalkyl or the heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$ (where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

15 R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of

hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(=N-CN)N(R^4)R^5$,
20 wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;
25 and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl,

heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$, $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is
30 independently 0, 1, or 2 and each n is independently 1 or 2;
35

- or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;
- or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached,
 5 may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2d} are as defined above;
- or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;
- 10 R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$,
 15 $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;
- 20 or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;
- or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl,
 25 and R^{3a} and R^{3d} are as defined above;
- or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3b} are as defined above;
- each R^4 and R^5 is independently selected from group consisting of hydrogen, alkyl,
 30 alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;
- or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl; and
- 35 each R^8 is a direct bond or a straight or branched alkylene chain, a straight or

branched alkenylene chain or a straight or branched alkynylene chain; and each R⁹ is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain.

Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention wherein:

j is 0 and k is 1 or 2;

Q is -C(O)-, -CF₂-, -C(O)O- or -N(R⁵)C(O)-;

R¹ is hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, -R⁸-C(O)R⁵, -R⁸-C(O)OR⁵, -R⁸-C(O)N(R⁴)R⁵, -S(O)₂-R⁵,
 10 -R⁹-S(O)_m-R⁵ (where m is 0, 1 or 2), -R⁸-OR⁵, -R⁸-CN, -R⁹-P(O)(OR⁵)₂, or -R⁹-O-R⁹-OR⁵;

R^{2a}, R^{2b}, R^{2c} and R^{2d} are each hydrogen;

R^{2a}, R^{2b}, R^{2c} and R^{2d} are each hydrogen;

R^{3a} and R^{3d} are each hydrogen;

15 R^{3b} and R^{3c}, together with the carbon ring atoms to which they are directly attached, form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl; each R⁵ is independently selected from group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl and heteroaryl;

20 each R⁸ is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and each R⁹ is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain.

Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention wherein:

j is 0 and k is 1 or 2;

Q is -C(O)-, -CF₂-, -C(O)O- or -N(R⁵)C(O)-;

R¹ is pentyl;

R^{2a}, R^{2b}, R^{2c} and R^{2d} are each hydrogen;

30 R^{3a} and R^{3d} are each hydrogen;

R^{3b} and R^{3c}, together with the carbon ring atoms to which they are directly attached, form a fused dioxolyl ring; and

each R⁵ is independently selected from group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl,
 35 heterocyclyl and heteroaryl.

Another embodiment of the invention are the compounds of formula (I) as set forth above in the Summary of the invention, selected from the group consisting of:

1'-pentylspiro[indeno[5,6-*d*][1,3]dioxole-5,3'-indole]-2',7'(1'*H*,6'*H*)-dione;

1-pentyl-6'*H*-spiro[indole-3,5'-naphtho[2,3-*d*][1,3]dioxole]-2,8'(1'*H*,7'*H*)-dione;

5 8',8'-difluoro-1-pentyl-7',8'-dihydro-6'*H*-spiro[indole-3,5'-naphtho[2,3-*d*][1,3]dioxol]-2(1'*H*)-one;

1'-pentyl-6,7-dihydro-5*H*-spiro[1,3-dioxolo[4,5-*g*]isoquinoline-8,3'-indole]-2',5(1'*H*)-dione; and

1'-hexylspiro[1,3-dioxolo[4,5-*g*]chromene-8,3'-indole]-2',6(1'*H*,7'*H*)-dione.

10 One embodiment of the invention is the method of treating or preventing hypercholesterolemia in a mammal, wherein the method comprises administering to the mammal in need thereof a therapeutically effective amount of a compound of formula (I) as set forth above for the embodiments of the compounds of formula (I).

Another embodiment of the invention is the method of treating or preventing
15 benign prostatic hyperplasia in a mammal, wherein the method comprises administering to the mammal in need thereof a therapeutically effective amount of a compound of formula (I) as set forth above for the embodiments of the compounds of formula (I).

Another embodiment of the invention is the method of treating or preventing
20 pruritis in a mammal, wherein the method comprises administering to the mammal in need thereof a therapeutically effective amount of a compound of formula (I) as set forth above for the embodiments of the compounds of formula (I).

Another embodiment of the invention is the method of treating or preventing cancer in a mammal, wherein the method comprises administering to the mammal in
25 need thereof a therapeutically effective amount of a compound of formula (I) as set forth above for the embodiments of the compounds of formula (I).

Specific embodiments of the compounds of formula (I) are described in more detail below in the Preparation of the Compounds of the Invention.

UTILITY AND TESTING OF THE COMPOUNDS OF THE INVENTION

30 The compounds of the invention modulate, preferably inhibit, ion flux through a voltage-dependent sodium channel in a mammal, especially in a human. Any such modulation, whether it be partial or complete inhibition or prevention of ion flux, is sometimes referred to herein as "blocking" and corresponding compounds as "blockers". In general, the compounds of the invention modulates the activity of a

sodium channel downwards, inhibits the voltage-dependent activity of the sodium channel, and/or reduces or prevents sodium ion flux across a cell membrane by preventing sodium channel activity such as ion flux.

The compounds of the invention inhibit the ion flux through a voltage-
5 dependent sodium channel. Preferably, the compounds are state or frequency dependent modifiers of the sodium channels, having a low affinity for the rested/closed state and a high affinity for the inactivated state. These compounds are likely to interact with overlapping sites located in the inner cavity of the sodium conducting pore of the channel similar to that described for other state-dependent sodium channel
10 blockers (Cestèle, S., et al., *op. cit.*). These compounds may also be likely to interact with sites outside of the inner cavity and have allosteric effects on sodium ion conduction through the channel pore.

Any of these consequences may ultimately be responsible for the overall therapeutic benefit provided by these compounds.

15 Accordingly, while not wishing to be bound to any particular mechanism of action, the compounds and pharmaceutical compositions of the invention are useful in the treatment and/or prevention of benign prostatic hyperplasia (BPH), hypercholesterolemia, cancer and/or pruritis (itch) in a mammal, preferably a human.

Benign prostatic hyperplasia (BPH), also known as benign prostatic
20 hypertrophy, is one of the most common diseases affecting aging men. BPH is a progressive condition which is characterized by a nodular enlargement of prostatic tissue resulting in obstruction of the urethra. Consequences of BPH can include hypertrophy of bladder smooth muscle, a decompensated bladder, acute urinary retention and an increased incidence of urinary tract infection.

25 BPH has a high public health impact and is one of the most common reasons for surgical intervention among elderly men. Attempts have been made to clarify the etiology and pathogenesis and, to that end, experimental models have been developed. Spontaneous animal models are limited to the chimpanzee and the dog. BPH in man and the dog share many common features. In both species, the
30 development of BPH occurs spontaneously with advanced age and can be prevented by early/prepubertal castration. A medical alternative to surgery is very desirable for treating BHP and the consequences.

The prostatic epithelial hyperplasia in both man and the dog is androgen sensitive, undergoing involution with androgen deprivation and resuming epithelial
35 hyperplasia when androgen is replaced. Cells originating from the prostate gland have

been shown to express high levels of voltage gated sodium channels. Immunostaining studies clearly demonstrated evidence for voltage gated sodium channels in prostatic tissues (*Prostate Cancer Prostatic Dis.* 2005; 8(3):266-73).

Hypercholesterolemia, *i.e.*, elevated blood cholesterol, is an established risk factor in the development of, *e.g.*, atherosclerosis, coronary artery disease, hyperlipidemia, stroke, hyperinsulinemias, hypertension, obesity, diabetes, cardiovascular diseases (CVD), myocardial ischemia, and heart attack. Thus, lowering the levels of total serum cholesterol in individuals with high levels of cholesterol has been known to reduce the risk of these diseases. The lowering of low density lipoprotein cholesterol in particular is an essential step in the prevention of CVD. Although there are a variety of hypercholesterolemia therapies, there is a continuing need and a continuing search in this field of art for alternative therapies.

The invention provides compounds which are useful as antihypercholesterolemia agents and their related conditions. The present compounds may act in a variety of ways. While not wishing to be bound to any particular mechanism of action, the compounds may be direct or indirect inhibitors of the enzyme acyl CoA: cholesterol acyl transferase (ACAT) that results in inhibition of the esterification and transport of cholesterol across the intestinal wall. Another possibility may be that the compounds of the invention may be direct or indirect inhibitors of cholesterol biosynthesis in the liver. It is possible that some compounds of the invention may act as both direct or indirect inhibitors of ACAT and cholesterol biosynthesis.

Pruritus, commonly known as itch, is a common dermatological condition. While the exact causes of pruritis are complex and poorly understood, there has long been acknowledged to have interactions with pain. In particular, it is believed that sodium channels likely communicate or propagate along the nerve axon the itch signals along the skin. Transmission of the itch impulses results in the unpleasant sensation that elicits the desire or reflex to scratch.

From a neurobiology level, it is believed that there is a shared complexity of specific mediators, related neuronal pathways and the central processes of itch and pain and recent data suggest that there is a broad overlap between pain- and itch-related peripheral mediators and/or receptors (Ikoma *et al.*, *Nature Reviews Neuroscience*, 7:535-547, 2006). Remarkably, pain and itch have similar mechanisms of neuronal sensitization in the peripheral nervous system and the central nervous system but exhibits intriguing differences as well.

For example, the mildly painful stimuli from scratching are effective in abolishing the itch sensation. In contrast, analgesics such as opioids can generate severe pruritus. The antagonistic interaction between pain and itch can be exploited in pruritus therapy, and current research concentrates on the identification of common
5 targets for future analgesic and antipruritic therapy.

Compounds of the present invention have been shown to have analgesic effects in a number of animal models at oral doses ranging from 1 mg/kg to 100 mg/kg. The compounds of the invention can also be useful for treating pruritus.

The types of itch or skin irritation, include, but are not limited to:

- 10 a) psoriatic pruritis, itch due to hemodialysis, aquagenic pruritus, and itching caused by skin disorders (e.g., contact dermatitis), systemic disorders, neuropathy, psychogenic factors or a mixture thereof;
- b) itch caused by allergic reactions, insect bites, hypersensitivity (e.g., dry skin, acne, eczema, psoriasis), inflammatory conditions or injury;
- 15 c) itch associated with vulvar vestibulitis; and
- d) skin irritation or inflammatory effect from administration of another therapeutic such as, for example, antibiotics, antivirals and antihistamines.

The compounds of the invention are also useful in treating or preventing certain hormone sensitive cancers, such as prostate cancer (adenocarcinoma), breast cancer,
20 ovarian cancer, testicular cancer, thyroid neoplasia. The voltage gated sodium channels have been demonstrated to be expressed in prostate and breast cancer cells. Up-regulation of neonatal Na(v)1.5 occurs as an integral part of the metastatic process in human breast cancer and could serve both as a novel marker of the metastatic phenotype and a therapeutic target (*Clin. Cancer Res.*2005, Aug. 1; 11(15): 5381-9).

25 Functional expression of voltage-gated sodium channel alpha-subunits, specifically Na_v1.7, is associated with strong metastatic potential in prostate cancer (CaP) in vitro. Voltage-gated sodium channel alpha-subunits immunostaining, using antibodies specific to the sodium channel alpha subunit was evident in prostatic tissues and markedly stronger in CaP vs non-CaP patients (*Prostate Cancer Prostatic Dis.*
30 2005;8(3):266-73)

The compounds of the invention are also useful in treating or preventing symptoms associated with BPH such as, but not limited to, acute urinary retention and urinary tract infection.

The compounds of the invention are also useful in treating or preventing certain
35 endocrine imbalances or endocrinopathies such as congenital adrenal hyperplasia ,

hyperthyroidism, hypothyroidism, osteoporosis, osteomalacia, rickets, Cushing's Syndrome, Conn's syndrome, hyperaldosteronism, hypogonadism, hypergonadism, infertility, fertility and diabetes.

The present invention readily affords many different means for identification of therapeutic agents, especially as sodium channel modulating agents. Identification of the therapeutic agents can be assessed using a variety of *in vitro* and *in vivo* assays, e.g., measuring current, measuring membrane potential, measuring ion flux, (e.g. sodium or guanidinium), measuring sodium concentration, measuring second messengers and transcription levels, and using e.g., voltage-sensitive dyes, radioactive tracers, and patch-clamp electrophysiology.

One such protocol involves the screening of chemical agents for ability to modulate the activity of a sodium channel thereby identifying it as a modulating agent.

A typical assay described in Bean et al., *J. General Physiology* (1983), 83:613-642, and Leuwer, M., et al., *Br. J. Pharmacol* (2004), 141(1):47-54, uses patch-clamp techniques to study the behaviour of channels. Such techniques are known to those skilled in the art, and may be developed, using current technologies, into low or medium throughput assays for evaluating compounds for their ability to modulate sodium channel behaviour.

A competitive binding assay with known sodium channel toxins such as tetrodotoxin, alpha-scorpion toxins, aconitine, BTX and the like, may be suitable for identifying potential therapeutic agents with high selectivity for a particular sodium channel. The use of BTX in such a binding assay is well known and is described in McNeal, E.T., et al., *J. Med. Chem.* (1985), 28(3):381-8; and Creveling, C.R., et al., *Methods in Neuroscience, Vol.8: Neurotoxins* (Conn PM Ed) (1992), pp. 25-37, Academic Press, New York.

These assays can be carried out in cells, or cell or tissue extracts expressing the channel of interest in a natural endogenous setting or in a recombinant setting. The assays that can be used include plate assays which measure Na⁺ influx through surrogate markers such as ¹⁴C-guanidine influx or determine cell depolarization using fluorescent dyes such as the FRET based and other fluorescent assays or a radiolabelled binding assay employing radiolabelled aconitine, BTX, TTX or STX. More direct measurements can be made with manual or automated electrophysiology systems. The guanidine influx assay is explained in more detail below in the Biological Assays section.

Throughput of test compounds is an important consideration in the choice of

screening assay to be used. In some strategies, where hundreds of thousands of compounds are to be tested, it is not desirable to use low throughput means. In other cases, however, low throughput is satisfactory to identify important differences between a limited number of compounds. Often it will be necessary to combine assay
5 types to identify specific sodium channel modulating compounds.

Electrophysiological assays using patch clamp techniques is accepted as a gold standard for detailed characterization of sodium channel compound interactions, and as described in Bean et al., *op. cit.* and Leuwer, M., et al., *op. cit.* There is a manual low-throughput screening (LTS) method which can compare 2-10 compounds
10 per day; a recently developed system for automated medium-throughput screening (MTS) at 20-50 patches (i.e. compounds) per day; and a technology from Molecular Devices Corporation (Sunnyvale, CA) which permits automated high-throughput screening (HTS) at 1000-3000 patches (i.e. compounds) per day.

One automated patch-clamp system utilizes planar electrode technology to
15 accelerate the rate of drug discovery. Planar electrodes are capable of achieving high-resistance, cells-attached seals followed by stable, low-noise whole-cell recordings that are comparable to conventional recordings. A suitable instrument is the PatchXpress 7000A (Axon Instruments Inc, Union City, CA). A variety of cell lines and culture techniques, which include adherent cells as well as cells growing spontaneously in
20 suspension are ranked for seal success rate and stability. Immortalized cells (e.g. HEK and CHO) stably expressing high levels of the relevant sodium ion channel can be adapted into high-density suspension cultures.

Other assays can be selected which allow the investigator to identify compounds which block specific states of the sodium channel, such as the open state,
25 closed state or the resting state, or which block transition from open to closed, closed to resting or resting to open. Those skilled in the art are generally familiar with such assays.

Binding assays are also available, however these are of only limited functional value and information content. Designs include traditional radioactive filter based
30 binding assays or the confocal based fluorescent system available from Evotec OAI group of companies (Hamburg, Germany), both of which are HTS.

Radioactive flux assays can also be used. In this assay, channels are stimulated to open with veratridine or aconitine and held in a stabilized open state with a toxin, and channel blockers are identified by their ability to prevent ion influx. The
35 assay can use radioactive $^{22}\text{[Na]}$ and $^{14}\text{[C]}$ guanidinium ions as tracers. FlashPlate &

Cytostar-T plates in living cells avoids separation steps and are suitable for HTS. Scintillation plate technology has also advanced this method to HTS suitability. Because of the functional aspects of the assay, the information content is reasonably good.

5 Yet another format measures the redistribution of membrane potential using the FLIPR system membrane potential kit (HTS) available from Molecular Dynamics (a division of Amersham Biosciences, Piscataway, NJ). This method is limited to slow membrane potential changes. Some problems may result from the fluorescent background of compounds. Test compounds may also directly influence the fluidity of
10 the cell membrane and lead to an increase in intracellular dye concentrations. Still, because of the functional aspects of the assay, the information content is reasonably good.

Sodium dyes can be used to measure the rate or amount of sodium ion influx through a channel. This type of assay provides a very high information content
15 regarding potential channel blockers. The assay is functional and would measure Na⁺ influx directly. CoroNa Red, SBFI and/or sodium green (Molecular Probes, Inc. Eugene OR) can be used to measure Na influx; all are Na responsive dyes. They can be used in combination with the FLIPR instrument. The use of these dyes in a screen has not been previously described in the literature. Calcium dyes may also have
20 potential in this format.

In another assay, FRET based voltage sensors are used to measure the ability of a test compound to directly block Na influx. Commercially available HTS systems include the VIPR™ II FRET system (Aurora Biosciences Corporation, San Diego, CA, a division of Vertex Pharmaceuticals, Inc.) which may be used in conjunction with
25 FRET dyes, also available from Aurora Biosciences. This assay measures sub-second responses to voltage changes. There is no requirement for a modifier of channel function. The assay measures depolarization and hyperpolarizations, and provides ratiometric outputs for quantification. A somewhat less expensive MTS version of this assay employs the FLEXstation™ (Molecular Devices Corporation) in conjunction with
30 FRET dyes from Aurora Biosciences. Other methods of testing the compounds disclosed herein are also readily known and available to those skilled in the art.

These results provide the basis for analysis of the structure-activity relationship (SAR) between test compounds and the sodium channel. Certain substituents on the core structure of the test compound tend to provide more potent inhibitory compounds.
35 SAR analysis is one of the tools those skilled in the art may now employ to identify

preferred embodiments of the compounds of the invention for use as therapeutic agents.

Modulating agents so identified are then tested in a variety of *in vivo* models so as to determine if they alleviate the diseases or conditions, especially benign prostatic hyperplasia (BPH), hypercholesterolemia, cancer and pruritis (itch), with minimal
5 adverse events. The assays described below in the Biological Assays Section are useful in assessing the biological activity of the instant compounds.

Typically, a successful therapeutic agent of the present invention will meet some or all of the following criteria. Oral availability should be at or above 20%.
10 Animal model efficacy is less than about 0.1 μg to about 100 mg/Kg body weight and the target human dose is between 0.1 μg to about 100 mg/Kg body weight, although doses outside of this range may be acceptable ("mg/Kg" means milligrams of compound per kilogram of body mass of the subject to whom it is being administered). The therapeutic index (or ratio of toxic dose to therapeutic dose) should be greater
15 than 100. The potency (as expressed by IC_{50} value) should be less than 10 μM , preferably below 1 μM and most preferably below 50 nM. The IC_{50} ("Inhibitory Concentration – 50%") is a measure of the amount of compound required to achieve 50% inhibition of ion flux through a sodium channel, over a specific time period, in an assay of the invention. Compounds of the present invention in the guanidine influx
20 assay have demonstrated IC_{50} 's ranging from less than a nanomolar to less than 10 micromolar.

In an alternative use of the invention, the compounds of the invention can be used in *in vitro* or *in vivo* studies as exemplary agents for comparative purposes to find other compounds also useful in treatment of, or protection from, the various diseases
25 disclosed herein.

Another aspect of the invention relates to inhibiting $\text{Na}_v1.1$, $\text{Na}_v1.2$, $\text{Na}_v1.3$, $\text{Na}_v1.4$, $\text{Na}_v1.5$, $\text{Na}_v1.6$, $\text{Na}_v1.7$, $\text{Na}_v1.8$, or $\text{Na}_v1.9$ activity in a biological sample or a patient, which method comprises administering to the patient, or contacting said biological sample with a compound of formula I or a composition comprising said
30 compound. The term "biological sample", as used herein, includes, without limitation, cell cultures or extracts thereof; biopsied material obtained from a mammal or extracts thereof; and blood, saliva, urine, feces, semen, tears, or other body fluids or extracts thereof.

Inhibition of $\text{Na}_v1.1$, $\text{Na}_v1.2$, $\text{Na}_v1.3$, $\text{Na}_v1.4$, $\text{Na}_v1.5$, $\text{Na}_v1.6$, $\text{Na}_v1.7$, $\text{Na}_v1.8$,
35 or $\text{Na}_v1.9$ activity in a biological sample is useful for a variety of purposes that are

known to one of skill in the art. Examples of such purposes include, but are not limited to, the study of sodium ion channels in biological and pathological phenomena; and the comparative evaluation of new sodium ion channel inhibitors.

A compound of the invention, as set forth above in the Summary of the
5 Invention, as a stereoisomer, enantiomer or tautomer or mixtures thereof, or a pharmaceutically acceptable salt, solvate or prodrug thereof, and/or a pharmaceutical composition of the invention, comprising a pharmaceutically acceptable excipient and one or more compounds of the invention, as set forth above in the Summary of the
10 Invention, as a stereoisomer, enantiomer or tautomer or mixtures thereof, or a pharmaceutically acceptable salt, solvate or prodrug thereof, can also be used in the preparation of a medicament for the treatment and/or prevention of hypercholesterolemia, benign prostatic hyperplasia, pruritis, and/or cancer in a mammal.

PHARMACEUTICAL COMPOSITIONS OF THE INVENTION AND ADMINISTRATION

15 Administration of the compounds of the invention, or their pharmaceutically acceptable salts, in pure form or in an appropriate pharmaceutical composition, can be carried out via any of the accepted modes of administration of agents for serving similar utilities. The pharmaceutical compositions of the invention can be prepared by combining a compound of the invention with an appropriate pharmaceutically
20 acceptable carrier, diluent or excipient, and may be formulated into preparations in solid, semi-solid, liquid or gaseous forms, such as tablets, capsules, powders, granules, ointments, solutions, suppositories, injections, inhalants, gels, microspheres, and aerosols. Typical routes of administering such pharmaceutical compositions include, without limitation, oral, topical, transdermal, inhalation, parenteral, sublingual,
25 rectal, vaginal, and intranasal. The term parenteral as used herein includes subcutaneous injections, intravenous, intramuscular, intrasternal injection or infusion techniques. Pharmaceutical compositions of the invention are formulated so as to allow the active ingredients contained therein to be bioavailable upon administration of the composition to a patient. Compositions that will be administered to a subject or
30 patient take the form of one or more dosage units, where for example, a tablet may be a single dosage unit, and a container of a compound of the invention in aerosol form may hold a plurality of dosage units. Actual methods of preparing such dosage forms are known, or will be apparent, to those skilled in this art; for example, see *The Science and Practice of Pharmacy*, 20th Edition (Philadelphia College of Pharmacy

and Science, 2000). The composition to be administered will, in any event, contain a therapeutically effective amount of a compound of the invention, or a pharmaceutically acceptable salt thereof, for treatment of a disease or condition of interest in accordance with the teachings of this invention.

5 A pharmaceutical composition of the invention may be in the form of a solid or liquid. In one aspect, the carrier(s) are particulate, so that the compositions are, for example, in tablet or powder form. The carrier(s) may be liquid, with the compositions being, for example, an oral syrup, injectable liquid or an aerosol, which is useful in, for example, inhalatory administration.

10 When intended for oral administration, the pharmaceutical composition is preferably in either solid or liquid form, where semi-solid, semi-liquid, suspension and gel forms are included within the forms considered herein as either solid or liquid.

 As a solid composition for oral administration, the pharmaceutical composition may be formulated into a powder, granule, compressed tablet, pill, capsule, chewing
15 gum, wafer or the like form. Such a solid composition will typically contain one or more inert diluents or edible carriers. In addition, one or more of the following may be present: binders such as carboxymethylcellulose, ethyl cellulose, microcrystalline cellulose, gum tragacanth or gelatin; excipients such as starch, lactose or dextrins, disintegrating agents such as alginic acid, sodium alginate, Primogel, corn starch and
20 the like; lubricants such as magnesium stearate or Sterotex; glidants such as colloidal silicon dioxide; sweetening agents such as sucrose or saccharin; a flavoring agent such as peppermint, methyl salicylate or orange flavoring; and a coloring agent.

 When the pharmaceutical composition is in the form of a capsule, for example, a gelatin capsule, it may contain, in addition to materials of the above type, a liquid
25 carrier such as polyethylene glycol or oil.

 The pharmaceutical composition may be in the form of a liquid, for example, an elixir, syrup, solution, emulsion or suspension. The liquid may be for oral administration or for delivery by injection, as two examples. When intended for oral administration, preferred composition contain, in addition to the present compounds,
30 one or more of a sweetening agent, preservatives, dye/colorant and flavor enhancer. In a composition intended to be administered by injection, one or more of a surfactant, preservative, wetting agent, dispersing agent, suspending agent, buffer, stabilizer and isotonic agent may be included.

 The liquid pharmaceutical compositions of the invention, whether they be
35 solutions, suspensions or other like form, may include one or more of the following

adjuvants: sterile diluents such as water for injection, saline solution, preferably physiological saline, Ringer's solution, isotonic sodium chloride, fixed oils such as synthetic mono or diglycerides which may serve as the solvent or suspending medium, polyethylene glycols, glycerin, propylene glycol or other solvents; antibacterial agents
5 such as benzyl alcohol or methyl paraben; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as acetates, citrates or phosphates and agents for the adjustment of tonicity such as sodium chloride or dextrose. The parenteral preparation can be enclosed in ampoules, disposable syringes or multiple dose vials made of glass or plastic.
10 Physiological saline is a preferred adjuvant. An injectable pharmaceutical composition is preferably sterile.

A liquid pharmaceutical composition of the invention intended for either parenteral or oral administration should contain an amount of a compound of the invention such that a suitable dosage will be obtained. Typically, this amount is at
15 least 0.01% of a compound of the invention in the composition. When intended for oral administration, this amount may be varied to be between 0.1 and about 70% of the weight of the composition. Preferred oral pharmaceutical compositions contain between about 4% and about 50% of the compound of the invention. Preferred pharmaceutical compositions and preparations according to the present invention are
20 prepared so that a parenteral dosage unit contains between 0.01 to 10% by weight of the compound prior to dilution of the invention.

The pharmaceutical composition of the invention may be intended for topical administration, in which case the carrier may suitably comprise a solution, emulsion, ointment or gel base. The base, for example, may comprise one or more of the
25 following: petrolatum, lanolin, polyethylene glycols, bee wax, mineral oil, diluents such as water and alcohol, and emulsifiers and stabilizers. Thickening agents may be present in a pharmaceutical composition for topical administration. If intended for transdermal administration, the composition may include a transdermal patch or iontophoresis device. Topical formulations may contain a concentration of the
30 compound of the invention from about 0.1 to about 10% w/v (weight per unit volume).

The pharmaceutical composition of the invention may be intended for rectal administration, in the form, for example, of a suppository, which will melt in the rectum and release the drug. The composition for rectal administration may contain an oleaginous base as a suitable nonirritating excipient. Such bases include, without
35 limitation, lanolin, cocoa butter and polyethylene glycol.

The pharmaceutical composition of the invention may include various materials, which modify the physical form of a solid or liquid dosage unit. For example, the composition may include materials that form a coating shell around the active ingredients. The materials that form the coating shell are typically inert, and may be
5 selected from, for example, sugar, shellac, and other enteric coating agents. Alternatively, the active ingredients may be encased in a gelatin capsule.

The pharmaceutical composition of the invention in solid or liquid form may include an agent that binds to the compound of the invention and thereby assists in the delivery of the compound. Suitable agents that may act in this capacity include a
10 monoclonal or polyclonal antibody, a protein or a liposome.

The pharmaceutical composition of the invention may consist of dosage units that can be administered as an aerosol. The term aerosol is used to denote a variety of systems ranging from those of colloidal nature to systems consisting of pressurized packages. Delivery may be by a liquefied or compressed gas or by a suitable pump
15 system that dispenses the active ingredients. Aerosols of compounds of the invention may be delivered in single phase, bi-phasic, or tri-phasic systems in order to deliver the active ingredient(s). Delivery of the aerosol includes the necessary container, activators, valves, subcontainers, and the like, which together may form a kit. One skilled in the art, without undue experimentation may determine preferred aerosols.

20 The pharmaceutical compositions of the invention may be prepared by methodology well known in the pharmaceutical art. For example, a pharmaceutical composition intended to be administered by injection can be prepared by combining a compound of the invention with sterile, distilled water so as to form a solution. A surfactant may be added to facilitate the formation of a homogeneous solution or
25 suspension. Surfactants are compounds that non-covalently interact with the compound of the invention so as to facilitate dissolution or homogeneous suspension of the compound in the aqueous delivery system.

The compounds of the invention, or their pharmaceutically acceptable salts, are administered in a therapeutically effective amount, which will vary depending upon a
30 variety of factors including the activity of the specific compound employed; the metabolic stability and length of action of the compound; the age, body weight, general health, sex, and diet of the patient; the mode and time of administration; the rate of excretion; the drug combination; the severity of the particular disorder or condition; and the subject undergoing therapy. Generally, a therapeutically effective daily dose is (for
35 a 70 kg mammal) from about 0.001 mg/kg (*i.e.*, 0.07 mg) to about 100 mg/kg (*i.e.*, 7.0

gm); preferably a therapeutically effective dose is (for a 70 kg mammal) from about 0.01 mg/kg (*i.e.*, 0.7 mg) to about 50 mg/kg (*i.e.*, 3.5 gm); more preferably a therapeutically effective dose is (for a 70 kg mammal) from about 1 mg/kg (*i.e.*, 70 mg) to about 25 mg/kg (*i.e.*, 1.75 gm).

- 5 The ranges of effective doses provided herein are not intended to be limiting and represent preferred dose ranges. However, the most preferred dosage will be tailored to the individual subject, as is understood and determinable by one skilled in the relevant arts. (see, e.g., Berkow et al., eds., *The Merck Manual*, 16th edition, Merck and Co., Rahway, N.J., 1992; Goodman et al., eds., *Goodman and Gilman's The*
10 *Pharmacological Basis of Therapeutics*, 10th edition, Pergamon Press, Inc., Elmsford, N.Y., (2001); Avery's *Drug Treatment: Principles and Practice of Clinical Pharmacology and Therapeutics*, 3rd edition, ADIS Press, LTD., Williams and Wilkins, Baltimore, MD. (1987), Ebadi, *Pharmacology*, Little, Brown and Co., Boston, (1985); Osolci et al., eds., *Remington's Pharmaceutical Sciences*, 18th edition, Mack Publishing Co., Easton,
15 PA (1990); Katzung, *Basic and Clinical Pharmacology*, Appleton and Lange, Norwalk, CT (1992)).

 The total dose required for each treatment can be administered by multiple doses or in a single dose over the course of the day, if desired. Generally, treatment is initiated with smaller dosages, which are less than the optimum dose of the compound.

- 20 Thereafter, the dosage is increased by small increments until the optimum effect under the circumstances is reached. The diagnostic pharmaceutical compound or composition can be administered alone or in conjunction with other diagnostics and/or pharmaceuticals directed to the pathology, or directed to other symptoms of the pathology. Effective amounts of a diagnostic pharmaceutical compound or
25 composition of the invention are from about 0.1 µg to about 100 mg/Kg body weight, administered at intervals of 4-72 hours, for a period of 2 hours to 1 year, and/or any range or value therein, such as 0.0001-0.001, 0.001-0.01, 0.01-0.1, 0.1-1.0, 1.0-10, 5-10, 10-20, 20-50 and 50-100 mg/Kg, at intervals of 1-4, 4-10, 10-16, 16-24, 24-36, 24-36, 36-48, 48-72 hours, for a period of 1-14, 14-28, or 30-44 days, or 1-24 weeks, or
30 any range or value therein. The recipients of administration of compounds and/or compositions of the invention can be any vertebrate animal, such as mammals. Among mammals, the preferred recipients are mammals of the Orders Primate (including humans, apes and monkeys), Arteriodactyla (including horses, goats, cows, sheep, pigs), Rodenta (including mice, rats, rabbits, and hamsters), and Carnivora
35 (including cats, and dogs). Among birds, the preferred recipients are turkeys, chickens

and other members of the same order. The most preferred recipients are humans.

For topical applications, it is preferred to administer an effective amount of a pharmaceutical composition according to the invention to target area, e.g., skin surfaces, mucous membranes, and the like, which are adjacent to peripheral neurons which are to be treated. This amount will generally range from about 0.0001 mg to about 1 g of a compound of the invention per application, depending upon the area to be treated, whether the use is diagnostic, prophylactic or therapeutic, the severity of the symptoms, and the nature of the topical vehicle employed. A preferred topical preparation is an ointment, wherein about 0.001 to about 50 mg of active ingredient is used per cc of ointment base. The pharmaceutical composition can be formulated as transdermal compositions or transdermal delivery devices ("patches"). Such compositions include, for example, a backing, active compound reservoir, a control membrane, liner and contact adhesive. Such transdermal patches may be used to provide continuous pulsatile, or on demand delivery of the compounds of the present invention as desired.

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. Controlled release drug delivery systems include osmotic pump systems and dissolutional systems containing polymer-coated reservoirs or drug-polymer matrix formulations. Examples of controlled release systems are given in U.S. Pat. Nos. 3,845,770 and 4,326,525 and in P. J. Kuzma et al, Regional Anesthesia 22 (6): 543-551 (1997), all of which are incorporated herein by reference.

The compositions of the invention can also be delivered through intra-nasal drug delivery systems for local, systemic, and nose-to-brain medical therapies. Controlled Particle Dispersion (CPD)TM technology, traditional nasal spray bottles, inhalers or nebulizers are known by those skilled in the art to provide effective local and systemic delivery of drugs by targeting the olfactory region and paranasal sinuses.

The invention also relates to an intravaginal shell or core drug delivery device suitable for administration to the human or animal female. The device may be comprised of the active pharmaceutical ingredient in a polymer matrix, surrounded by a sheath, and capable of releasing the compound in a substantially zero order pattern on a daily basis similar to devices used to apply testosterone as described in PCT Patent No. WO 98/50016.

Current methods for ocular delivery include topical administration (eye drops),

subconjunctival injections, periocular injections, intravitreal injections, surgical implants and iontophoresis (uses a small electrical current to transport ionized drugs into and through body tissues). Those skilled in the art would combine the best suited excipients with the compound for safe and effective intra-ocular administration.

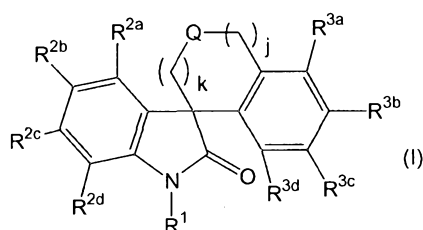
- 5 The most suitable route will depend on the nature and severity of the condition being treated. Those skilled in the art are also familiar with determining administration methods (oral, intravenous, inhalation, sub-cutaneous, rectal etc.), dosage forms, suitable pharmaceutical excipients and other matters relevant to the delivery of the compounds to a subject in need thereof.

10 KITS-OF-PARTS

- The present invention also provides kits that contain a pharmaceutical composition which includes one or more compounds of the above formulae. The kit also includes instructions for the use of the pharmaceutical composition for modulating the activity of ion channels, for the treatment of benign prostatic hyperplasia (BPH),
 15 hypercholesterolemia, cancer and pruritis (itch), as well as other utilities as disclosed herein. Preferably, a commercial package will contain one or more unit doses of the pharmaceutical composition. For example, such a unit dose may be an amount sufficient for the preparation of an intravenous injection. It will be evident to those of ordinary skill in the art that compounds which are light and/or air sensitive may require
 20 special packaging and/or formulation. For example, packaging may be used which is opaque to light, and/or sealed from contact with ambient air, and/or formulated with suitable coatings or excipients.

PREPARATION OF THE COMPOUNDS OF THE INVENTION

- The following Reaction Schemes illustrate methods to make compounds of this
 25 invention, *i.e.*, compounds of formula (I) :



wherein k , j , Q , R^1 , R^{2a} , R^{2b} , R^{2c} , R^{2d} , R^{3a} , R^{3b} , R^{3c} , and R^{3d} are as defined herein, as a stereoisomer, enantiomer, tautomer thereof or mixtures thereof; or a pharmaceutically acceptable salt, solvate or prodrug thereof.

It is understood that in the following description, combinations of substituents and/or variables of the depicted formulae are permissible only if such contributions result in stable compounds.

It will also be appreciated by those skilled in the art that in the process described below the functional groups of intermediate compounds may need to be protected by suitable protecting groups. Such functional groups include hydroxy, amino, mercapto and carboxylic acid. Suitable protecting groups for hydroxy include trialkylsilyl or diarylalkylsilyl (e.g., *t*-butyldimethylsilyl, *t*-butyldiphenylsilyl or trimethylsilyl), tetrahydropyranyl, benzyl, and the like. Suitable protecting groups for amino, amidino and guanidino include *t*-butoxycarbonyl, benzyloxycarbonyl, and the like. Suitable protecting groups for mercapto include -C(O)-R" (where R" is alkyl, aryl or arylalkyl), *p*-methoxybenzyl, trityl and the like. Suitable protecting groups for carboxylic acid include alkyl, aryl or arylalkyl esters.

Protecting groups may be added or removed in accordance with standard techniques, which are known to one skilled in the art and as described herein.

The use of protecting groups is described in detail in Greene, T.W. and P.G.M. Wuts, *Protective Groups in Organic Synthesis* (1999), 3rd Ed., Wiley. The protecting group may also be a polymer resin such as a Wang resin or a 2-chlorotrityl-chloride resin.

It will also be appreciated by those skilled in the art, although such protected derivatives of compounds of this invention may not possess pharmacological activity as such, they may be administered to a mammal and thereafter metabolized in the body to form compounds of the invention which are pharmacologically active. Such derivatives may therefore be described as "prodrugs". All prodrugs of compounds of this invention are included within the scope of the invention.

The following Reaction Schemes illustrate methods to make compounds of this invention. It is understood that one skilled in the art would be able to make these compounds by similar methods or by methods known to one skilled in the art. It is also understood that one skilled in the art would be able to make in a similar manner as described below other compounds of formula (I) not specifically illustrated below by using the appropriate starting components and modifying the parameters of the synthesis as needed. In general, starting components may be obtained from sources such as Sigma Aldrich, Lancaster Synthesis, Inc., Maybridge, Matrix Scientific, TCI, and Fluorochem USA, etc. or synthesized according to sources known to those skilled in the art (see, e.g., Smith, M.B. and J. March, *Advanced Organic Chemistry*:

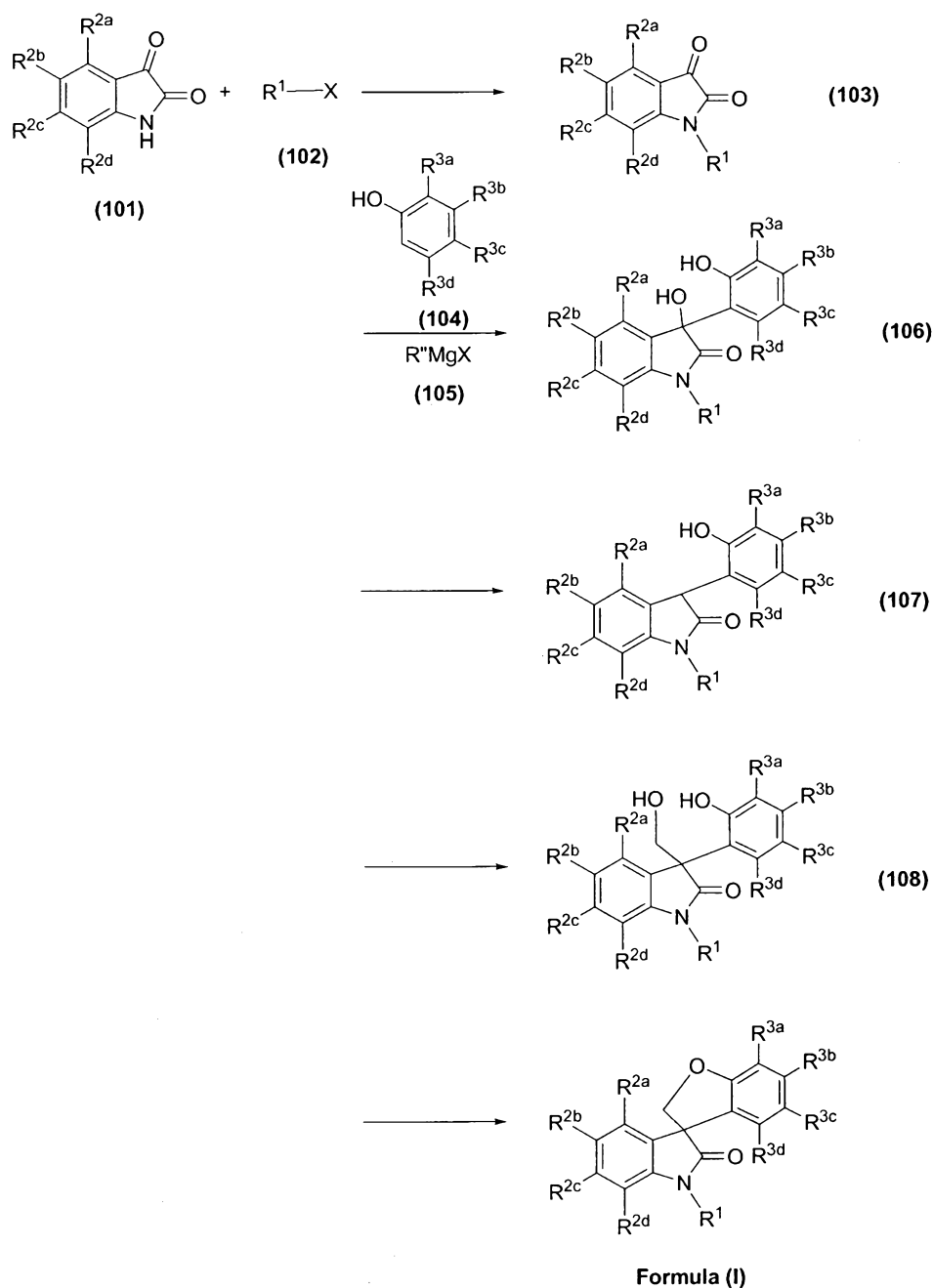
Reactions, Mechanisms, and Structure, 5th edition (Wiley, December 2000)) or prepared as described herein.

In the following Reaction Schemes, R^1 , R^{2a} , R^{2b} , R^{2c} , R^{2d} , R^{3a} , R^{3b} , R^{3c} and R^{3d} are defined as in the Specification unless specifically defined otherwise. X is Cl or Br.

5 R^{11} is an alkyl group.

In general, the compounds of formula (I) of the invention where Q is -O-, j is 0 and k is 1 can be synthesized following the general procedure as described below in REACTION SCHEME 1. As set forth below, an isatin compound of formula (101) is alkylated with the chloro or bromo compound of formula (102) to afford the product of
10 formula (103). The phenol compound of formula (104) is treated with a Grignard reagent of formula (105) at low temperature (0 °C) to form the phenoxymagnesium halide intermediate which reacts with the keto-carbonyl group of the isatin compound of formula (103) in a solvent, such as, but not limited to, methylene chloride or toluene, to afford the oxindole of formula (106). The compound of formula (107) is obtained
15 after the removal of the hydroxyl group at C-3 position of the oxindole by treating the compound of formula (106) with silane such as triethylsilane. The compound of formula (107) can also be achieved by treating the compound of formula (106) with $\text{SOCl}_2/\text{NEt}_3$ then reduction with Zn dust. Compound of formula (107) is treated with a silyl compound, such as, but not limited to, trimethylsilyl chloride, to generate the silyl
20 ether intermediate which is treated with ytterbium (III) trifluoromethanesulfonate and formaldehyde to afford the compound of formula (108). Alternatively, compound of formula (108) can be obtained by treating the compound of formula (107) with a base, such as, but not limited to, LiOH, $i\text{Pr}_2\text{NH}$, LDA, and subsequently reacting with formaldehyde. Intramolecular cyclization via Mitsunobu reaction affords the compound
25 of formula (I) of the invention where Q is -O-, j is 0 and k is 1.

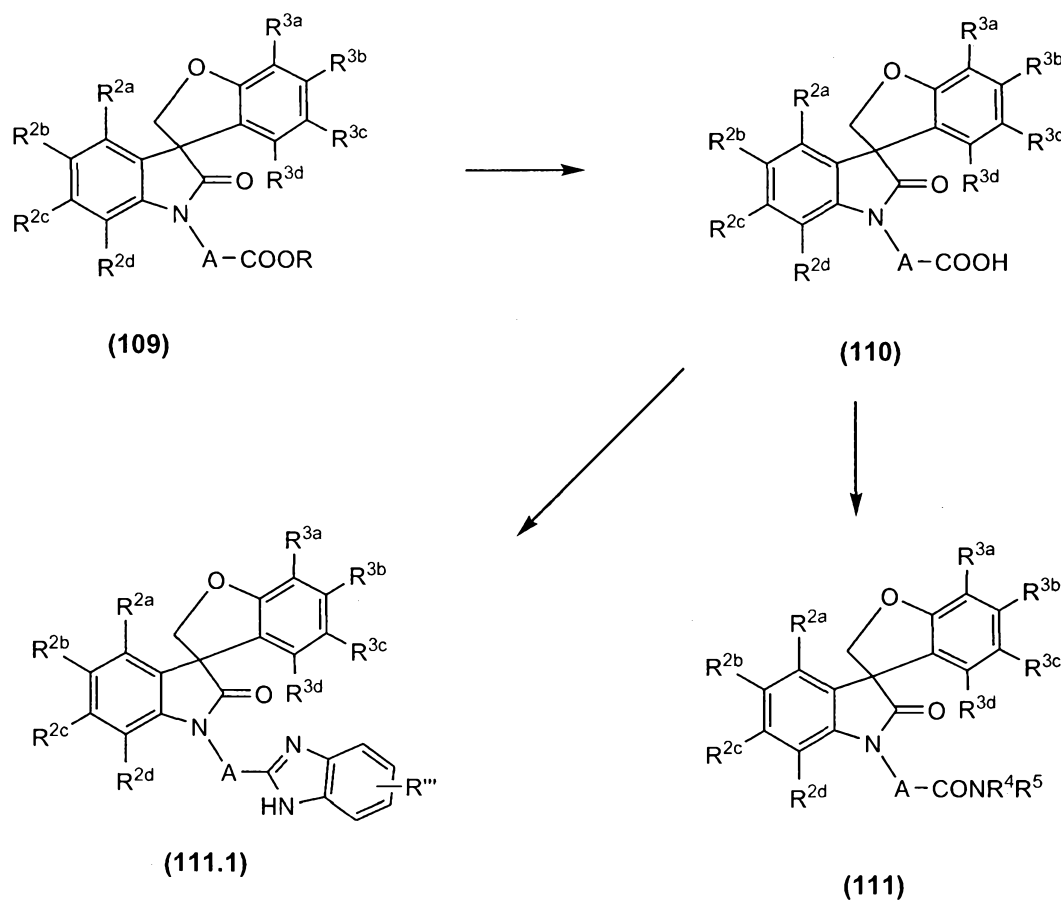
REACTION SCHEME 1



REACTION SCHEME 1.1 below illustrates a schematic synthesis of amide and heterocyclic compounds as compounds of formula (I). When R^1 consists of an ester group, a compound such as a compound of formula (109) (in which A is alkyl or aralkyl) can be converted to the corresponding carboxylic acid compound of formula (110) by treatment of a compound of formula (109) with a base such as, but not limited

to, lithium hydroxide, sodium hydroxide or potassium hydroxide, in a mixed solvent such as, but not limited to, tetrahydrofuran or methanol with water. The acid compound of formula (110) can be converted to a mixed anhydride, by treatment with iso-butyl chloroformate in the presence of a base such as, but not limited to, *N*-methylmorpholine, or to the corresponding acid chloride, by treatment with oxalyl chloride in the presence of catalytic amount of *N,N*-dimethylformamide in a solvent such as, but not limited to, toluene, dichloromethane or chloroform. The mixed anhydride can react directly with, or the acid chloride can react with, in the presence of a base such as, but not limited to, triethylamine or diisopropyl ethylamine, a primary or secondary amine to form the amide compound of formula (111) as a compound of formula (I). The acid compound of formula (110) can react with an aromatic diamine compound in a solvent such as, but not limited to, toluene to form the benzimidazole compound of formula (111.1) as a compound of formula (I).

REACTION SCHEME 1.1

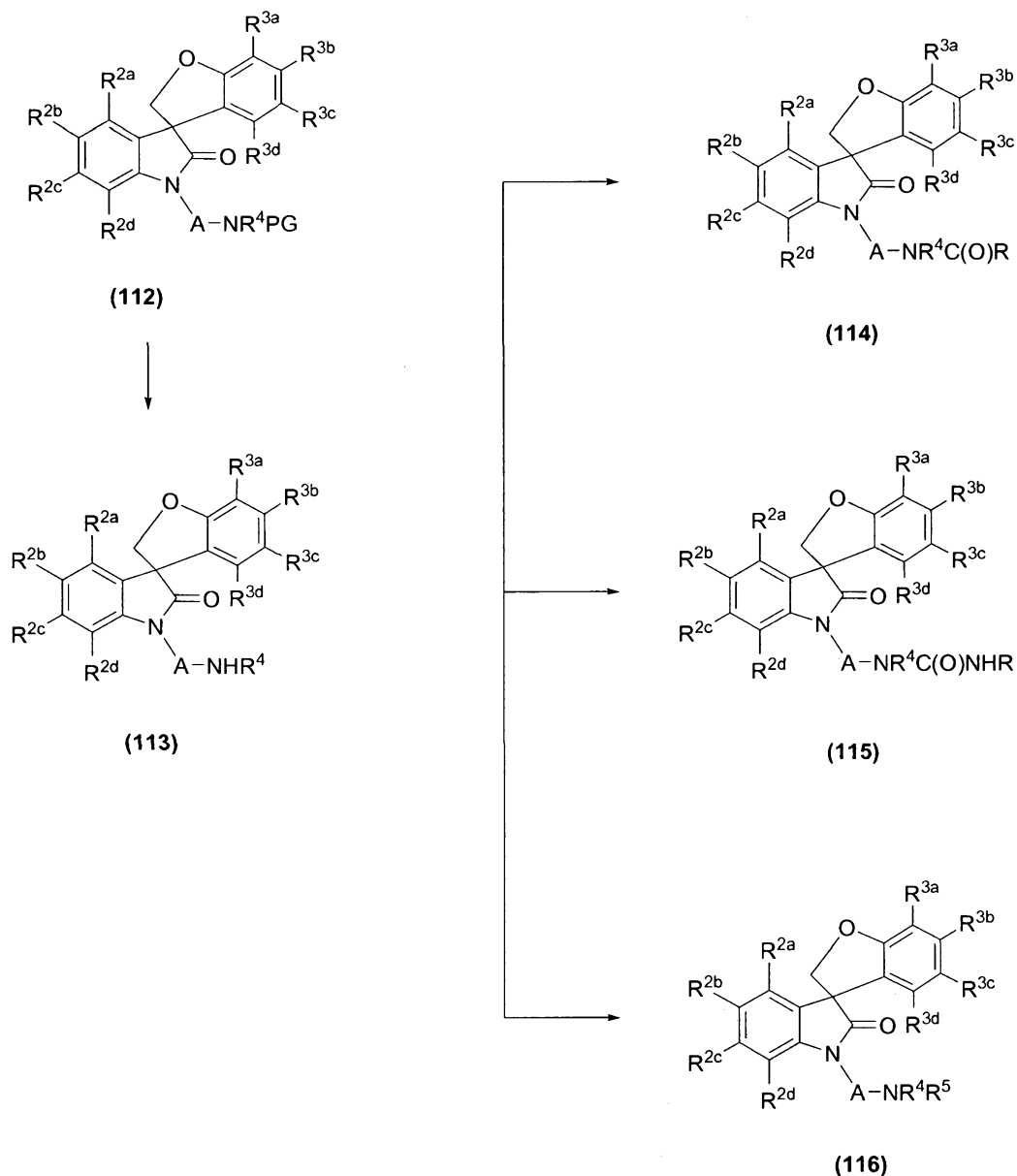


REACTION SCHEME 1.2 below illustrates a schematic synthesis of amine

compounds as compounds of formula (I). From compound (112), after removal of the protecting group (PG) such as, but not limited to, phthalimido or *tert*-butyloxycarbonyl, either the primary or secondary amino compound of formula (113) can be formed.

- Reaction of the amino compound of formula (113) with an acyl chloride in the presence
- 5 of a base such as, but not limited to, triethylamine or diisopropyl ethylamine, in a solvent such as, but not limited to, toluene, dichloromethane or chloroform provides the amide compound of formula (114) as a compound of formula (I). Treatment of amino compound of formula (113) with an isocyanate in the presence of a base such as, but not limited to, triethylamine or diisopropyl ethylamine, in a solvent such as, but not
- 10 limited to, dichloromethane or chloroform leads to the formation of the urea compound of formula (115) as a compound of formula (I). When the primary or secondary amino compound of formula (113) is treated with an aldehyde or a ketone in the presence of a reducing agent such as, but not limited to, sodium cyanoborohydride or sodium triacetoxyborohydride, in a solvent such as, but not limited to, dichloromethane, a high
- 15 order functionalized amine (116) is produced as a compound of formula (I).

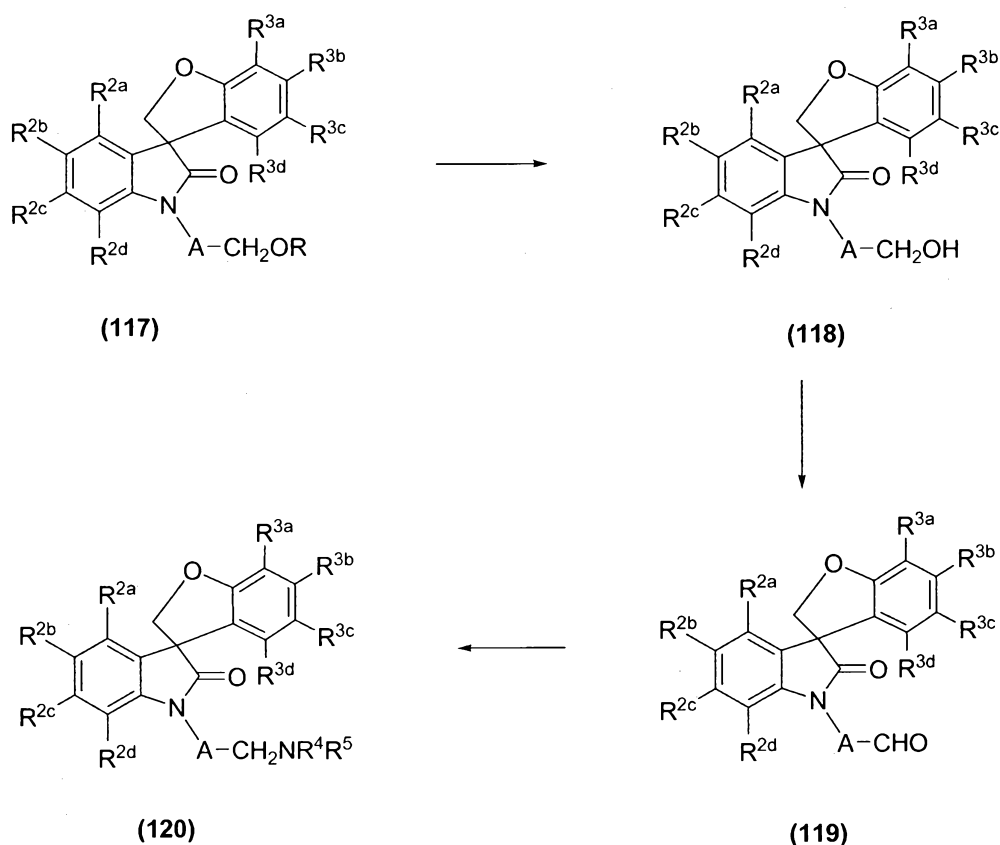
REACTION SCHEME 1.2



REACTION SCHEME 1.3 below illustrates a schematic synthesis of amine compounds as compounds of formula (I). The alcohol compound of formula (118),
 5 upon removal of the protecting group in compound of formula (117), can be oxidized to the aldehyde compound of (119) by using an oxidant such as, but not limited to, pyridinium dichromate or Dess-Martin's reagent. Similarly to the transformation of the compound of formula (113) to the compound of formula (116) as illustrated in REACTION SCHEME 1.2, the amine compound of formula (120) can be obtained as a

compound of formula (I) through the reductive amination of the aldehyde compound of formula (119) with a primary or secondary amine.

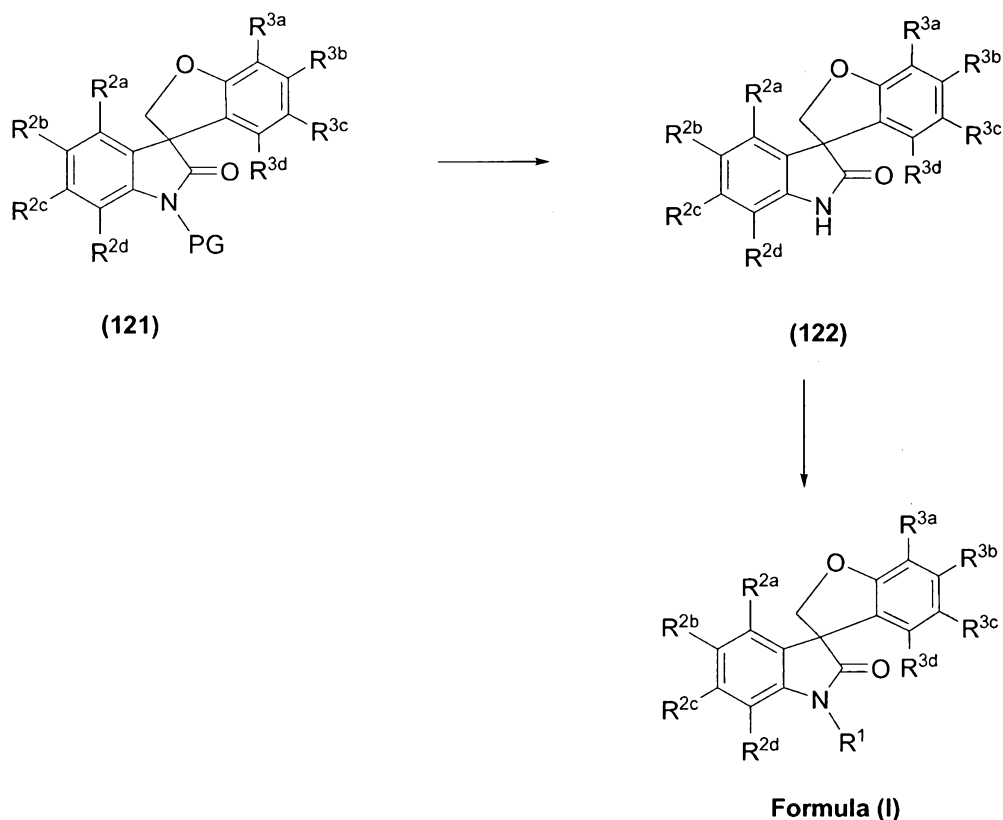
REACTION SCHEME 1.3



- 5 REACTION SCHEME 1.4 below illustrates an alternative synthesis of compounds of formula (I) with the introduction of a variety of R^1 groups. Compound of formula (121) where PG is a protecting group such as, but not limited to, diphenylmethyl, can be synthesized through the sequence as shown in REACTION SCHEME 1 above. The protecting group can be removed under a high pressure of
- 10 hydrogen such as 60 psi to form the oxindole compound of formula (122). The formation of a compound of formula (I) can be achieved by alkylation of the compound of formula (122) with a halide reagent XR^1 (where X is chloro, bromo or iodo) in the presence of a base such as, but not limited to, sodium hydride, sodium
- 15 bis(trimethylsilyl)amide, and lithium hydroxide, in a solvent such as, but not limited to, *N,N*-dimethylformamide, tetrahydrofuran, acetone or acetonitrile. Alternatively, reaction of compound of formula (122) with an alcohol under Mitsunobu reaction conditions in the presence of a phosphine reagent such as, but not limited to,

triphenylphosphine, tributylphosphine or trimethyl phosphine, and azadicarboxylate of diethyl, diisopropyl or di-*tert*-butyl in a solvent such as, but not limited to, tetrahydrofuran, ethyl acetate or dichloromethane, provides the compound of formula (I). Alternatively, treatment of compound of formula (122) with a base such as, but not
 5 limited to, sodium hydride or lithium hydroxide, followed by reacting with an acyl chloride or anhydride, or with a sulfonyl chloride reagent, provides the corresponding acyl or sulfonyl (R^1) compound of formula (I) respectively.

REACTION SCHEME 1.4



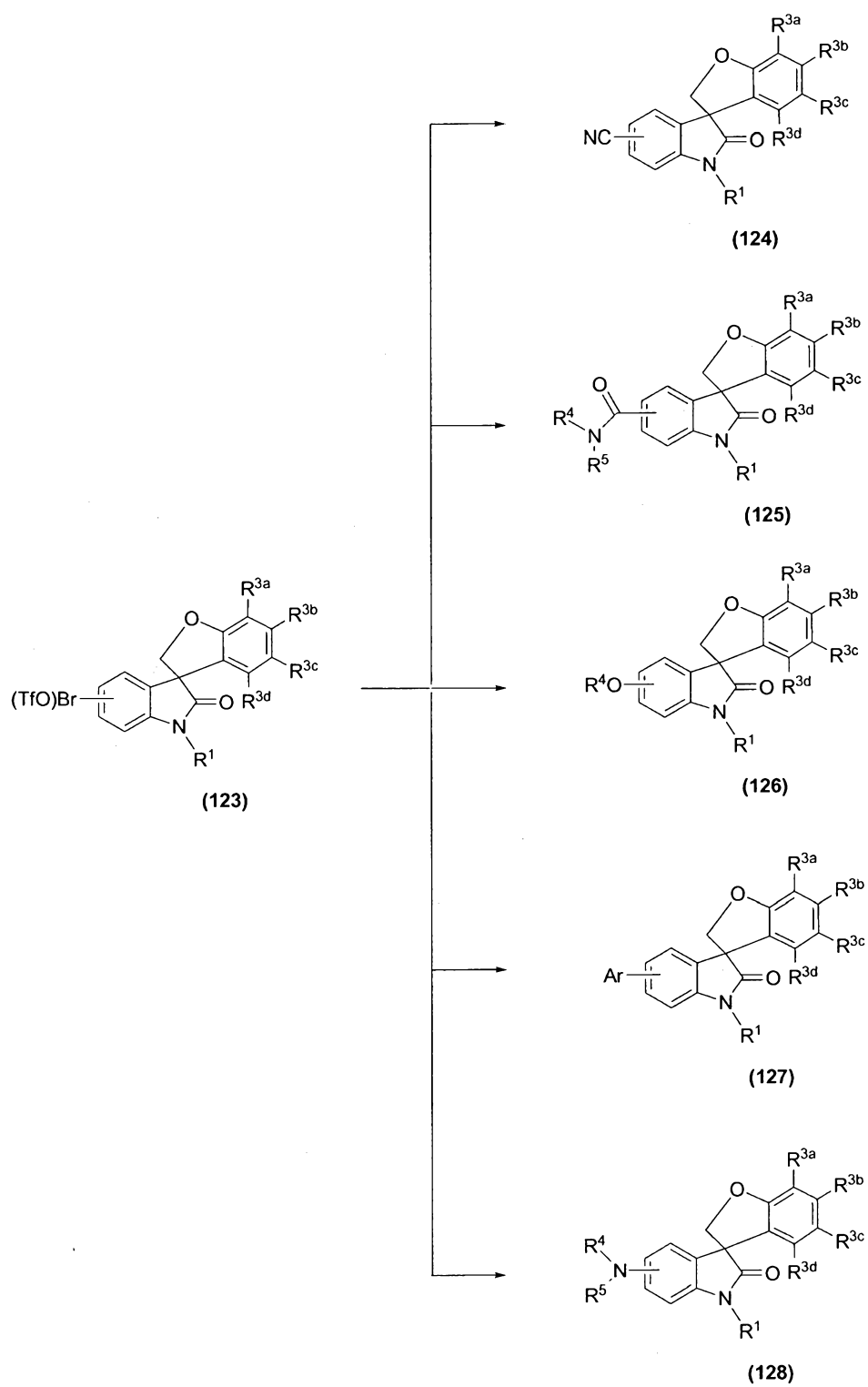
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When R^{2a} , R^{2b} , R^{2c} , R^{2d} , R^{3a} , R^{3b} , R^{3c} or R^{3d} of the compound of formula (I) is a bromo or trifluoromethylsulfonyloxy group, further derivatives can be synthesized as shown in REACTION SCHEME 1.5 and REACTION SCHEME 1.6 below. The triflate
 15 compound can be obtained by treating the bromo compound with diborane in the presence of a palladium catalyst followed by sequential oxidation with hydrogen peroxide/sodium hydroxide and reaction with trifluoromethanesulfonyl anhydride. Compounds of formula (123) or (129) (with either a bromo or a trifluoromethylsulfonyloxy group for R^{2a} , R^{2b} , R^{2c} , R^{2d} , R^{3a} , R^{3b} , R^{3c} or R^{3d}) can react

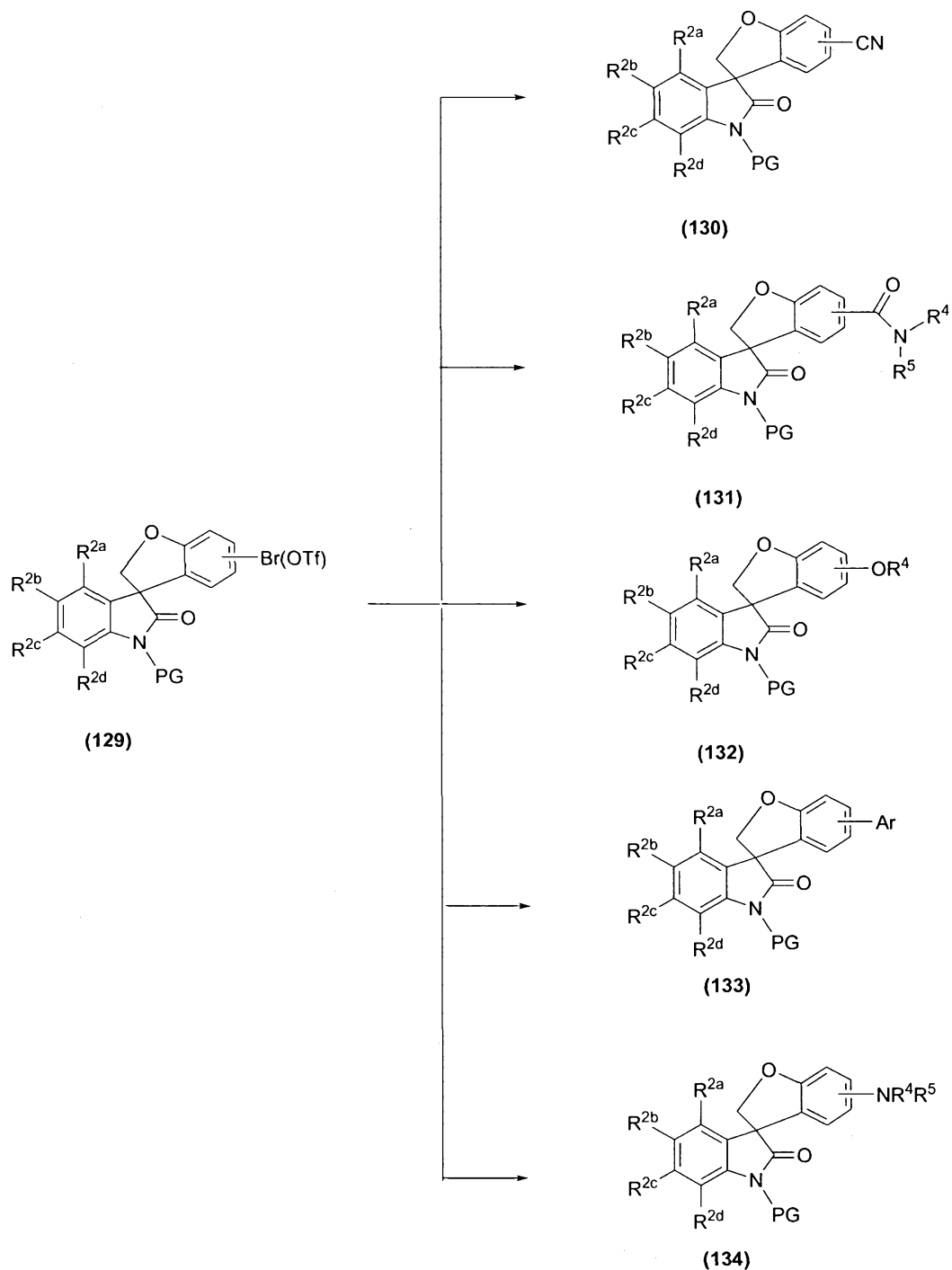
with zinc cyanide or tributyltin cyanide and potassium cyanide in the presence of a palladium catalyst such as, but not limited to, palladium acetate or tris(dibenzylideneacetone)dipalladium(0), and a ligand such as, but not limited to, tri(o-tolyl)phosphine, 1,1'-bis(diphenylphosphino)ferrocene or 2-(di-*tert*-butylphosphino)biphenyl in a solvent such as, but not limited to, *N,N*-dimethylformamide or acetonitrile to provide the cyano compounds of formula (124) or formula (130) as compounds of formula (I) (see Marcantonio, K.M., et al, *Org. Lett.* (2004), 6:3723-5 and Yang, C., et al, *Org. Lett.* (2004), 6:2837-40). Reaction of compounds of formula (123) or formula (129) (with either a bromo or a trifluoromethylsulfonyloxy group for R^{2a} , R^{2b} , R^{2c} , R^{2d} , R^{3a} , R^{3b} , R^{3c} or R^{3d}) with a primary or secondary amine in the presence of a palladium catalyst such as, but not limited to, palladium acetate, tetrakis(triphenylphosphine)palladium(0), or tris(dibenzylideneacetone)dipalladium(0), under a pressure of carbon monoxide in a solvent such as, but not limited to, *N,N*-dimethylformamide or acetonitrile leads to the formation of the amide compound of formula (125) or formula (131) as compounds of formula (I) (See Takahashi, T., et al, *Tetrahedron Lett.* (1999), 40:7843-6 and Schnyder, A., et al, *J. Org. Chem.* (2001), 66:4311-5). Under a typical Ullmann coupling reaction conditions, compounds of formula (123) or formula (129) (with either bromo or trifluoromethylsulfonyloxy group for R^{2a} , R^{2b} , R^{2c} , R^{2d} , R^{3a} , R^{3b} , R^{3c} or R^{3d}) can react with a phenol compound in the presence of a copper reagent such as, but not limited to, copper iodide or copper bromide, a base such as, but not limited to, cesium carbonate or potassium carbonate, an amino acid such as, but not limited to, *N,N*-dimethylglycine, in a solvent such as, but not limited to, dimethyl sulfoxide, dioxane or acetonitrile, to form the diaryl ether compounds of formula (126) or formula (132) as compounds of formula (I) (see Sawyer, J.S. *Tetrahedron* (2000), 56:5045-65 and Ma, D., et al, *Org. Lett.* (2003), 5(21):3799-802). Compounds of formula (123) or formula (129) (with either bromo or trifluoromethylsulfonyloxy group for R^{2a} , R^{2b} , R^{2c} , R^{2d} , R^{3a} , R^{3b} , R^{3c} or R^{3d}) can react with an arylboronic acid in the presence of a palladium catalyst such as, but not limited to, palladium acetate, tetrakis(triphenylphosphine)palladium(0), or tris(dibenzylideneacetone)dipalladium(0), with or without a ligand such as, but not limited to, triphenylphosphine, tri(o-tolyl)phosphine, 1,1'-bis(diphenylphosphino)ferrocene or 2-(di-*tert*-butylphosphino)biphenyl, a base such as, but not limited to, sodium carbonate, cesium carbonate, or sodium bicarbonate, in a solvent such as, but not limited to, dimethoxyethane, dioxane, or tetrahydrofuran to provide the coupled product of

- formula (127) or formula (133) as compounds of formula (I) (see Kotha, S., et al, *Tetrahedron* (2002), 58:9633 and Miyaura, N., et al, *Chem. Rev.* (1995), 95:2457). Compound of formula (123) or formula (129) (with either a bromo or a trifluoromethylsulfonyloxy group for R^{2a} , R^{2b} , R^{2c} , R^{2d} , R^{3a} , R^{3b} , R^{3c} or R^{3d}) can react
- 5 with a primary or secondary amine in the presence of a palladium catalyst such as, but not limited to, tetrakis(triphenylphosphine)palladium(0) or tris(dibenzylideneacetone)dipalladium(0), with or without a ligand such as, but not limited to, triphenylphosphine, tri(o-tolyl)phosphine, 1,1'-bis(diphenylphosphino)ferrocene or 2-(di-*tert*-butylphosphino)biphenyl, a base such as,
- 10 but not limited to, sodium carbonate, cesium carbonate or sodium *tert*-butoxide, in a solvent such as, but not limited to, dioxane or tetrahydrofuran, to provide the amino compound of formula (128) or formula (134) as compounds of formula (I) (see Muci, A. R., et al, *Topics in Current Chemistry* (2002), 219:131).

REACTION SCHEME 1.5



REACTION SCHEME 1.6

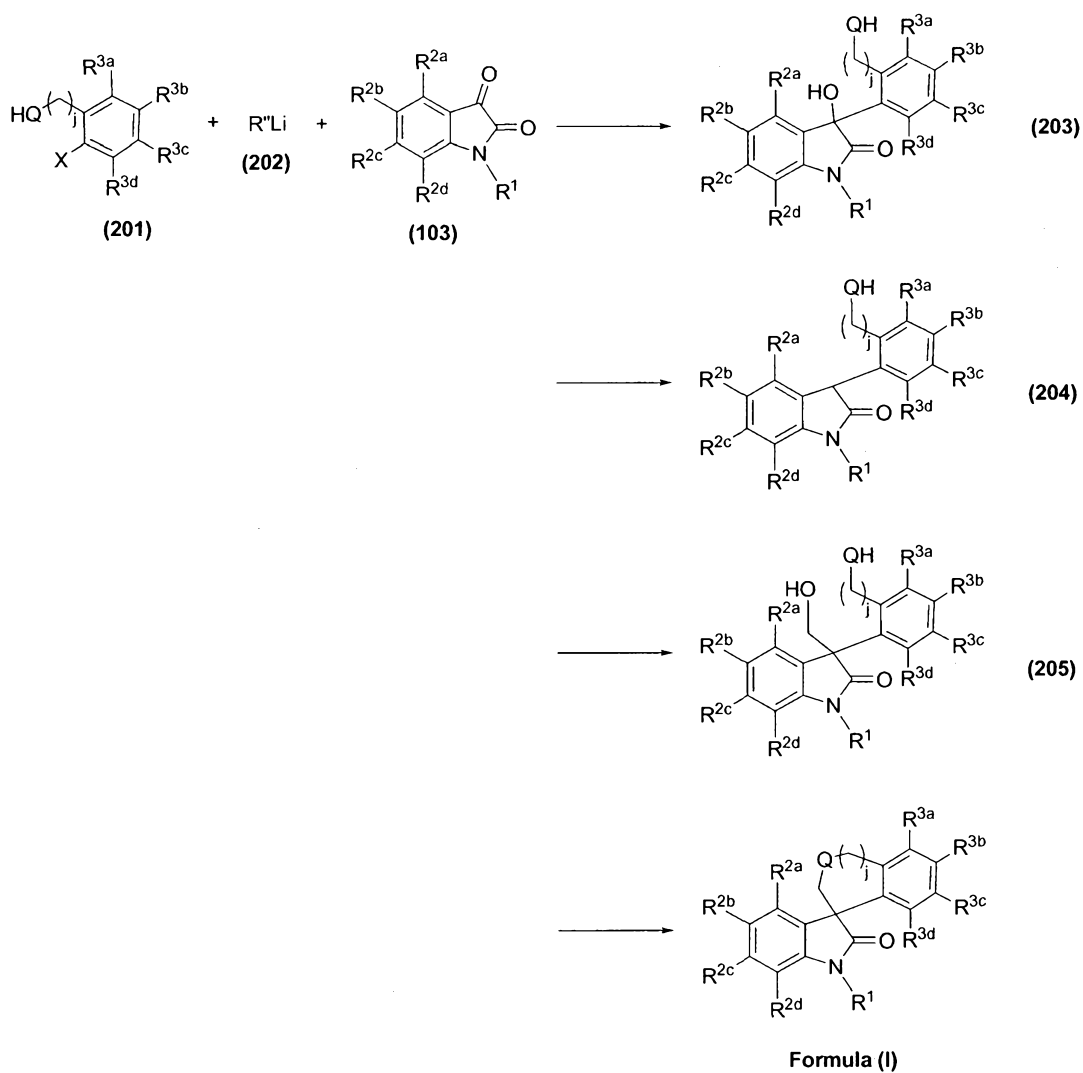


Alternatively, the compound of formula (I) of the invention where Q is -O and k is 1 can be synthesized following the general procedure as described below in

5 REACTION SCHEME 2. As set forth below, a compound of formula (201) is treated

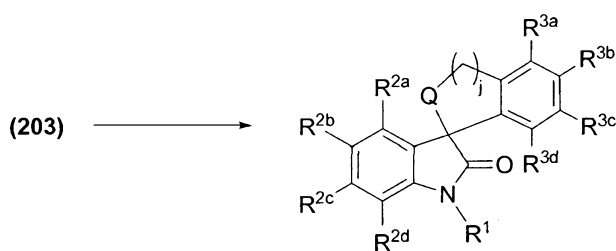
with a lithium reagent of formula (202), such as, but not limited to, *n*-BuLi at low temperature followed by the reaction with keto-carbonyl group of the isatin compound of formula (103) in a solvent, such as, but not limited to, THF to afford the oxindole of formula (203). The compound of formula (204) is obtained after the removal of the hydroxyl group at C-3 position of the oxindole by treating the compound of formula (203) with silane such as triethylsilane. The compound of formula (204) can also be achieved by treating the compound of formula (203) with SOCl₂/NEt₃ then reduction with Zn dust. Compound of formula (204) is treated with a silyl compound, such as, but not limited to, trimethylsilyl chloride to generate the silyl ether intermediate which is treated with ytterbium (III) trifluoromethanesulfonate and formaldehyde to afford the compound of formula (205). Alternatively, a compound of formula (205) can be obtained by treating the compound of formula (204) with a base, such as, but not limited to, LiOH, iPr₂NH, or LDA, and subsequently reacting with formaldehyde. Intramolecular cyclization via Mitsunobu reaction affords the compound of formula (I) of the invention where Q is -O- and k is 1.

REACTION SCHEME 2



- Alternatively, the compound of formula (I) of the invention where Q is -O- or -S- and k is 0 can be synthesized following the general procedure as described below in
- 5 REACTION SCHEME 3 wherein intramolecular cyclization of the compound of formula (203) via Mitsunobu reaction affords the compound of formula (I) of the invention where Q is -O- or -S- and k is 0.

REACTION SCHEME 3

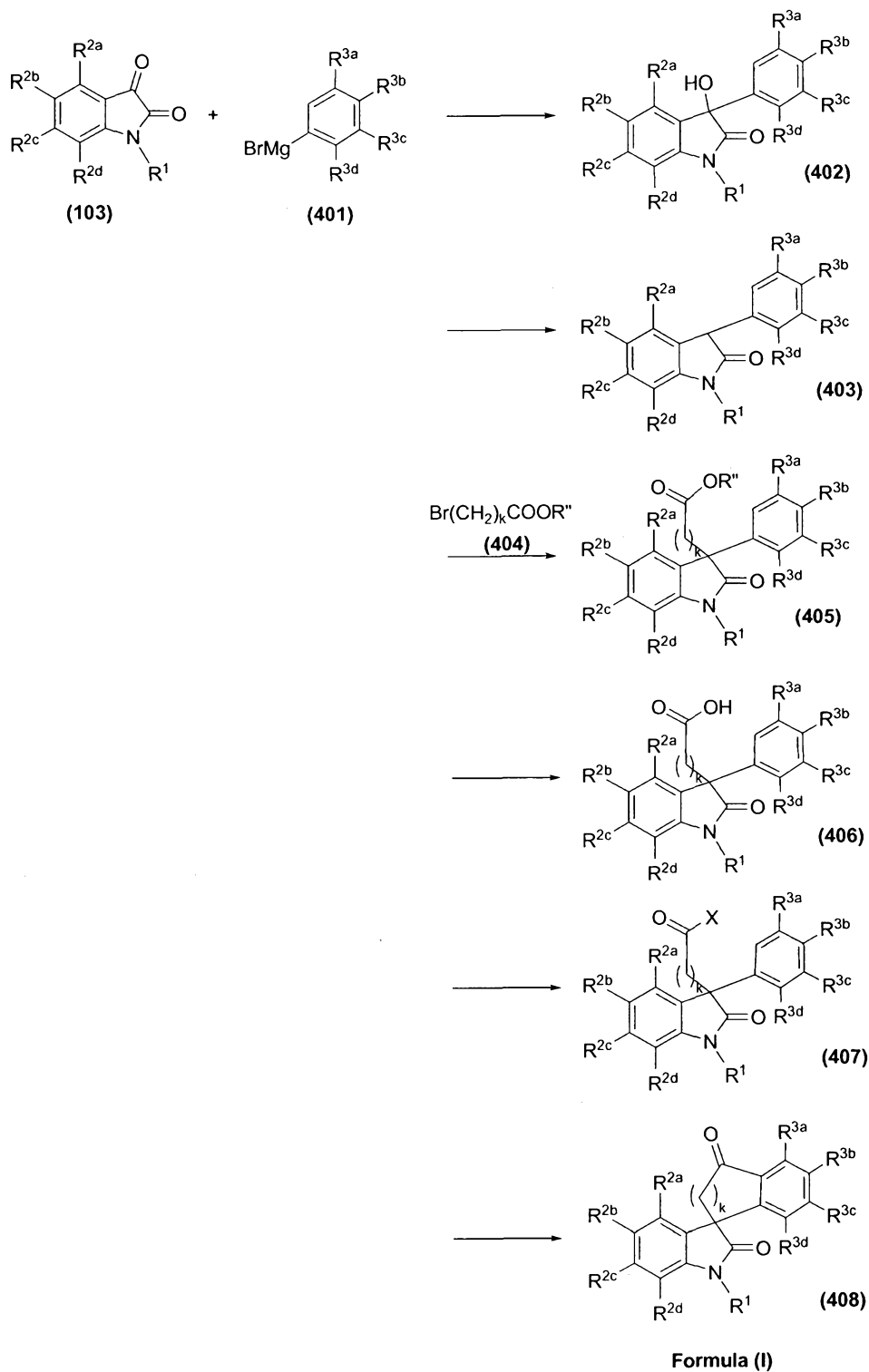


Formula (I)

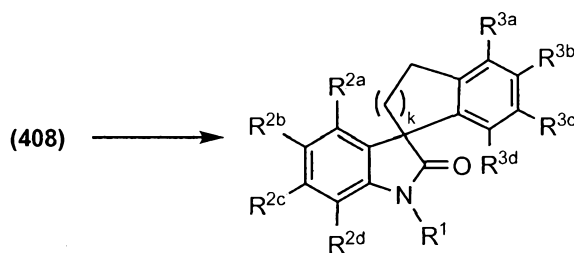
Alternatively, the compound of formula (I) of the invention where Q is -C(O)-, -CH₂- or -CF₂- and j is 0 can be synthesized following the general procedure as described in REACTION SCHEME 4. As set forth below, the Grignard reagent of formula (401) reacts with keto-carbonyl group of the isatin compound of formula (103) in a solvent, such as, but not limited to, methylene chloride or toluene to afford the oxindole of formula (402). The compound of formula (403) is obtained after the removal of the hydroxyl group at C-3 position of the oxindole by treating the compound of formula (402) with silane such as triethylsilane. The compound of formula (403) can also be achieved by treating the compound of formula (402) with SOCl₂/NEt₃, followed by reduction with Zn dust. Compound of formula (403) is alkylated at C-3 position of oxindole ring with a compound of formula (404) to afford the compound of formula (405) which is subjected to saponification to generate the carboxylic acid of formula (406). This carboxylic acid is then converted to an acid chloride of formula (407) following procedures known to one skilled in the art. Intramolecular cyclization in the presence of an Lewis acid, such as, but not limited to, tin(IV) chloride, yields the compound of formula (I) of the invention where Q is -C(O)- and j is 0. The removal of the carbonyl group of the compound of formula (I) using a silane, such as triethylsilane, or other reagents known to the one skilled in the art, yields the compound of formula (I) of the invention where Q is -CH₂- and j is 0. Reaction of the carbonyl group of the compound (408) of formula (I) with a fluorinating reagent such as, but not limited to, bis(2-methoxyethyl)aminosulfur trifluoride leads to the formation of di-fluoro compound of formula (I) of the invention where Q is -CF₂- and j is 0. Reduction of the carbonyl group of the compound (408) of formula (I) with a reducing agent such as, but not limited to, sodium borohydride provides the hydroxy compound of formula (I) of the invention where Q is -CH(OH)- and j is 0. Further alkylation of the hydroxy compound of formula (I) by the method known to one skilled in the art gives the alkylated

compound of formula (I) of the invention where Q is $-\text{CH}(\text{OR}^5)-$ and j is 0.

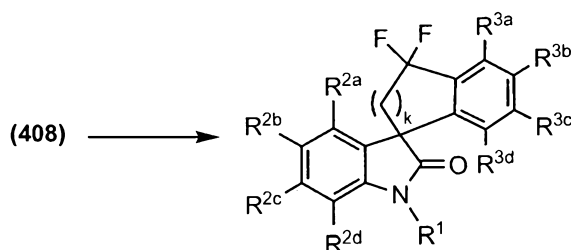
REACTION SCHEME 4



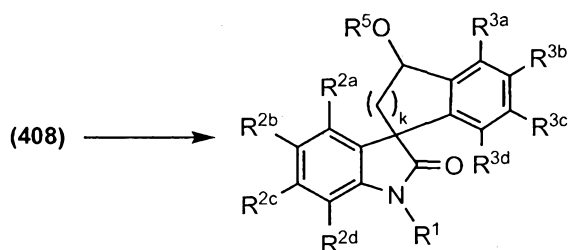
REACTION SCHEME 4 CONTINUED



Formula (I)



Formula (I)

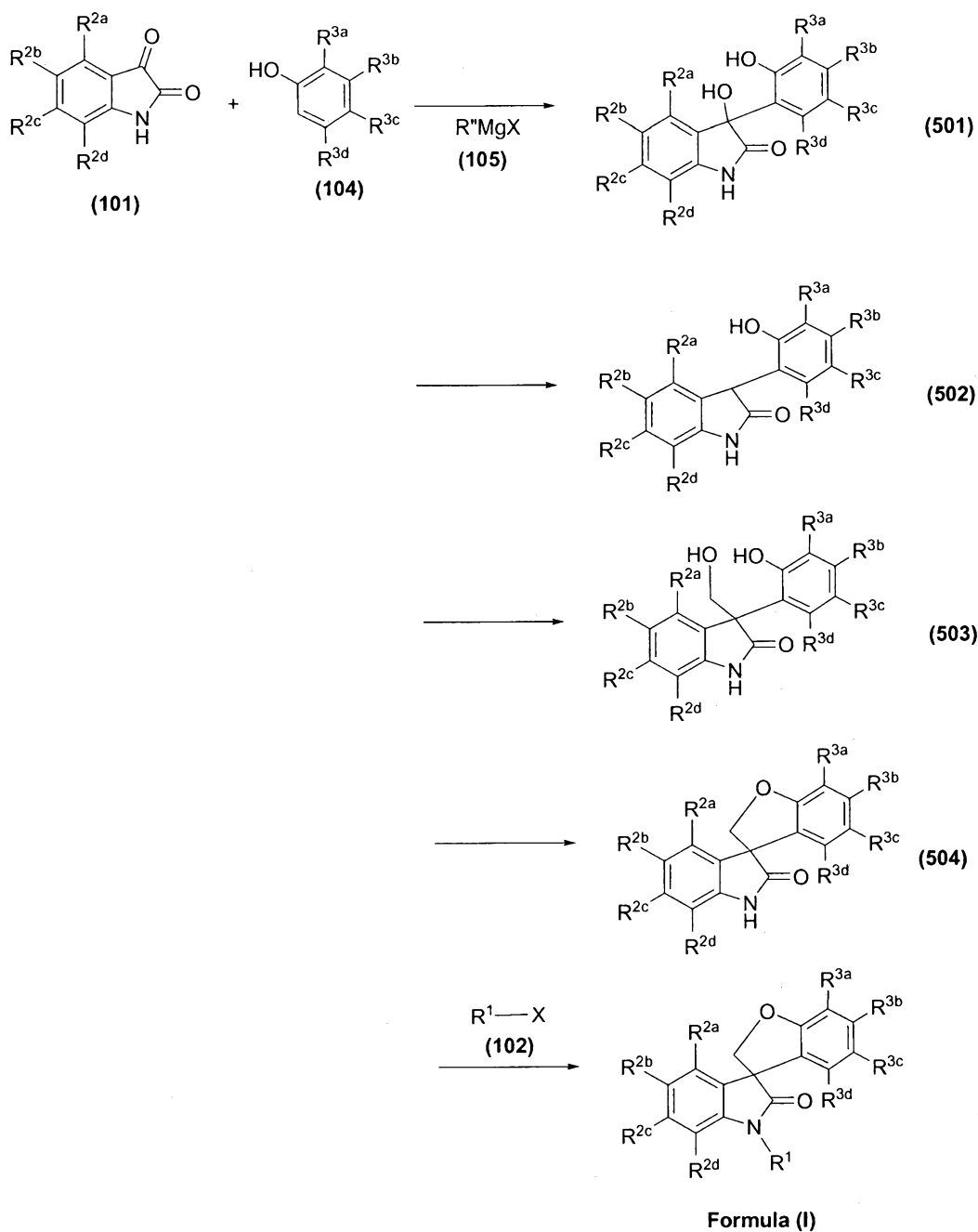


Formula (I)

- Alternatively, the compound of formula (I) of the invention where Q is -O-, j is 0 and k is 1 can be synthesized following the general procedure as described below in
- REACTION SCHEME 5. As set forth below, the phenol compound of formula (104) is
- 5 treated with a Grignard reagent of formula (105) at low temperature (0 °C) to form the phenoxymagnesium halide intermediate which reacts with the keto-carbonyl group of the isatin compound of formula (101) in a solvent, such as, but not limited to, tetrahydrofuran, methylene chloride or toluene, to afford the heterocyclic compound of
- 10 formula (501). The compound of formula (502) can be obtained after the removal of the hydroxyl group of the heterocyclic compound by treating the compound of formula (501) with a silane such as triethylsilane. The compound of formula (502) can also be achieved by treating the compound of formula (501) with SOCl₂/NEt₃ followed by

reduction with Zn dust. Compound of formula (502) is treated with a silyl compound such as, but not limited to, trimethylsilyl chloride, to generate the silyl ether intermediate which is treated with ytterbium (III) trifluoromethanesulfonate and formaldehyde to afford the compound of formula (503). Alternatively, compound of
5 formula (503) can be obtained by treating the compound of formula (502) with a base such as, but not limited to, LiOH, $i\text{Pr}_2\text{NH}$, or LDA, and by subsequently reacting with formaldehyde. Intramolecular cyclization via Mitsunobu reaction affords the compound of formula (504) which can be alkylated with a chloro or bromo compound of formula (102) to afford the compound of formula (I) of the invention where Q is -O-, j is 0 and k
10 is 1.

REACTION SCHEME 5

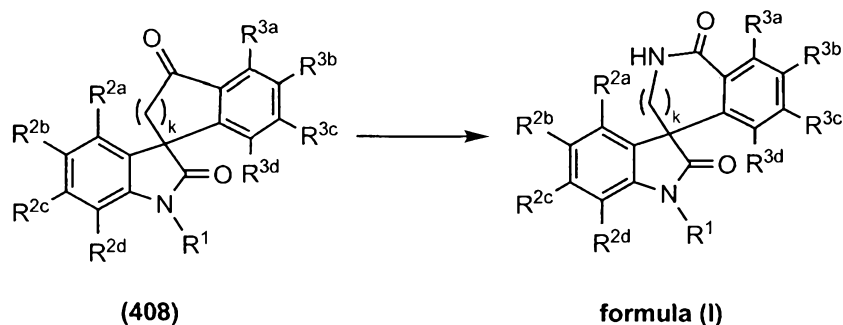


Alternatively, the compound of formula (I) of the invention where Q is $-NHC(O)-$, j is 0 can be synthesized following the general procedure as described below in

5 REACTION SCHEME 6. As set forth below, treatment of the ketone compound (408) with an azide such as, but not limited to, sodium azide in an acid such as, but not limited to, trifluoroacetic acid provides the Schmidt reaction product of formula (I) of the

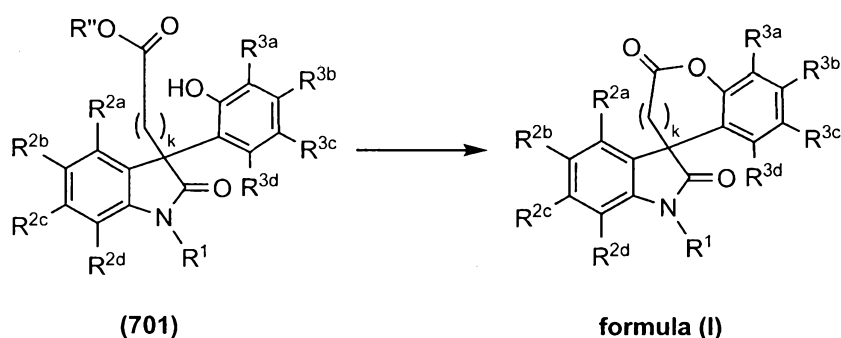
invention where Q is $-\text{NHC(O)}-$, j is 0.

REACTION SCHEME 6



- Alternatively, the compound of formula (I) of the invention where Q is $-\text{C(O)O}-$, j is 0 can be synthesized following the general procedure as described below in
- REACTION SCHEME 7. As set forth below, treatment of the compound of formula (701), which can be obtained following a similar procedure as for the synthesis of compound of formula (405) as described in REACTION SCHEME 4, with a base such as, but not limited to, lithium hydroxide, sodium hydroxide or potassium hydroxide, in a mixed solvent such as, but not limited to, tetrahydrofuran or methanol with water, leads to the formation of the lactone product of formula (I) of the invention where Q is $-\text{C(O)O}-$, j is 0.

REACTION SCHEME 7



- In the following Preparations, which are directed to intermediates used in the preparation of the compounds of formula (I), and in the following Examples, which are directed to compounds of formula (I), the compound numbers presented therein do not correspond to the compound numbers in the above REACTION SCHEMES.

PREPARATION 1

Synthesis of 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one

A. Synthesis of 4-bromo-1-pentyl-1*H*-indole

5 To a mixture of sodium hydride (2.54 g, 66.3 mmol, 60% dispersion in mineral oil) in anhydrous *N,N*-dimethylformamide (50.0 mL) was added 4-bromoindole (10.0 g, 51.0 mmol) at 0 °C. The reaction mixture was stirred for 0.5 h followed by the addition of 1-bromopentane (9.25 g, 61.2 mmol) at 0 °C. The reaction mixture was stirred at ambient temperature for 6 h and quenched with brine solution (20.0 mL). The reaction
10 mixture was diluted with water (100 mL) and extracted with ether (3 x 200 mL). The combined organic layers was washed with brine (100 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography eluting with hexane (100%) to give the title compound (13.3 g, 98%) as a yellow oil: ¹H NMR (300 MHz, CDCl₃) δ 7.30-
15 7.27 (m, 2H), 7.14 (t, 1H), 6.88 (t, 1H), 6.55 (d, 1H), 4.08 (t, 2H), 1.87-1.77 (m, 2H), 1.39-1.22 (m, 4H), 0.89 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 136.3, 129.2, 128.4, 122.2, 122.1, 114.9, 108.7, 101.3, 46.8, 29.9, 29.1, 22.3, 13.9.

B. Synthesis of 4-bromo-1-pentyl-1*H*-indole-2,3-dione

To a solution of 4-bromo-1-pentyl-1*H*-indole (25.0 g, 93.9 mmol) in anhydrous
20 dimethylsulfoxide (350 mL) was added *N*-bromosuccinimide (50.2 g, 282 mmol) in portions over 30 min. The reaction mixture was heated at 60 °C for 3 h, upon which time the internal temperature increased to 120 °C. After cooling down to ambient temperature, the reaction mixture was poured onto ethyl acetate/water (1/1, 600 mL). The organic layer was separated and the aqueous layer was extracted with ethyl
25 acetate (3 x 500 mL). The combined organic layers was washed with water (3 x 500 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness to yield the title compound (25.7 g, 92%) as a yellow solid: ¹H NMR (300 MHz, CDCl₃) δ 7.38 (t, 1H), 7.21 (t, 1H), 6.82 (d, 1H), 3.68 (t, 2H), 1.72-1.59 (m, 2H), 1.39-1.25 (m, 4H), 0.86 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 180.9, 157.2, 152.6,
30 138.4, 128.3, 121.7, 116.3, 108.9, 40.4, 28.9, 26.9, 22.3, 13.9.

C. Synthesis of 4-bromo-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one

To a solution of 1,3-benzodioxol-5-ol (12.8 g, 92.9 mmol) in tetrahydrofuran (200 mL) was added isopropylmagnesium chloride solution (50.7 mL, 101 mmol, 2.0 M

in ether) at 0 °C. The reaction mixture was stirred at 0 °C for 0.5 h, upon which time the colorless precipitate was formed. After the solvent was removed under reduced pressure, the residue was dissolved in methylene chloride (100 mL) and added to a solution of 4-bromo-1-pentyl-1*H*-indole-2,3-dione (25.0 g, 84.5 mmol) in
5 dichloromethane (100 mL) via a canula over 10 min at 0 °C. The reaction mixture was stirred at ambient temperature for 16 h, quenched with saturated ammonium chloride solution (100 mL) and the organic layer was separated. The aqueous layer was extracted with dichloromethane (100 mL). The combined organic layers was washed with brine, dried over anhydrous sodium sulfate and filtered. The filtrate was
10 concentrated *in vacuo* to dryness. The residue was subjected to column chromatography eluting with ethyl acetate-hexane to give the title compound (34.9 g, 97%) as a brown gummy material: ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.95 (s, 1H), 7.29-7.21 (m, 2H), 6.88-6.81 (m, 1H), 6.55, (s, 1H), 6.14 (s, 1H), 5.86 (dd, 2H), 4.24 (s, 1H), 3.70-3.52 (m, 2H), 1.69-1.55 (m, 2H), 1.31-1.24 (m, 4H), 0.83 (t, 3H); ¹³C NMR (75
15 MHz, DMSO-*d*₆) δ 177.6, 152.6, 149.1, 144.8, 141.2, 131.7, 127.7, 127.6, 121.0, 113.8, 108.3, 106.7, 101.7, 101.4, 80.5 40.5, 28.8, 26.7 22.2, 13.9.

D. Synthesis of 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one

To a solution of 4-bromo-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one (34.9 g, 80.4 mmol) in dichloromethane (100 mL)
20 was added trifluoroacetic acid (18.7 g, 161 mmol) and triethylsilane (18.3 g, 161 mmol). The brown solution was stirred at ambient temperature for 3 h and concentrated *in vacuo* to dryness. The residue was diluted with dichloromethane (200 mL), washed with saturated ammonium chloride solution (50.0 mL), brine (3 x 50.0
25 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was crystallized from ether to give the title compound (16.5 g, 49%) as a brown solid: ¹H NMR (300 MHz, CDCl₃) δ 7.29-7.21 (m, 2H), 7.14 (dd, 1H), 6.58 (s, 1H), 6.10 (s, 1H), 5.85 (dd, 2H), 5.01 (s, 1H), 3.75-3.55 (m, 2H), 1.69-1.56 (m, 2H), 1.35-1.21 (m, 4H), 0.86 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 177.9,
30 150.9, 147.6, 145.4, 141.6, 130.3 127.1 126.8, 120.8, 113.3 108.0, 106.7, 101.5, 101.2, 59.9, 48.6, 40.7, 28.9, 26.9, 22.3 13.9; MS (ES+) *m/z* 418.3 (M + 1), 420.3 (M + 1).

E. Synthesis of 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2H-indol-2-one

To a solution of 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one (7.50 g, 17.9 mmol) in dry dichloromethane (150 mL) was added triethylamine (10.9 g, 108 mmol) and chlorotrimethylsilane (7.80 g, 71.8 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 2 h and diluted with dichloromethane (100 mL). The mixture was washed with water (3 x 50.0 mL), dried over anhydrous magnesium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was dissolved in THF (150 mL) followed by the additions of formaldehyde solution (4.90 mL, 179 mmol, 37 wt% in water) and ytterbium (III) trifluoromethanesulfonate (1.11 g, 1.79 mmol). The resulting mixture was stirred at ambient temperature for 36 h. After the solvent was removed under reduced pressure, the residue was diluted with dichloromethane (200 mL), washed with saturated sodium bicarbonate (50.0 mL), saturated ammonium chloride (50.0 mL) and water (100 mL). The organic layer was dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness to yield the title compound (6.32 g, 79%) as a fluffy solid: ¹H NMR (300 MHz, CDCl₃) δ 8.28 (s, 1H), 7.10 (t, 1H), 7.00 (dd, 1H), 6.89 (dd, 1H), 6.83 (s, 1H), 6.27 (s, 1H), 6.85 (dd, 2H), 4.52-4.41 (m, 2H), 3.90 (dd, 1H), 3.70-3.65 (m, 2H), 1.68-1.57 (m, 2H), 1.36-1.29 (m, 4H), 0.83 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 178.1, 150.3, 147.2, 147.2, 140.5, 129.6, 129.2, 125.6, 118.4, 114.8, 109.2, 106.9, 101.0, 98.2, 62.6, 57.6, 39.9, 28.9, 26.7, 22.2, 13.5.

PREPARATION 2

Synthesis of 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2H-indol-2-one

A. Synthesis of 1-(2-cyclopropylethyl)-1H-indole-2,3-dione

To a suspension of sodium hydride (1.61 g, 41.9 mmol, 60% dispersion in mineral oil) in anhydrous *N,N*-dimethylformamide (25.0 mL) was added isatin (6.17 g, 41.9 mmol) at 0 °C. The reaction mixture was stirred for 0.5 h followed by the addition of (2-bromoethyl)cyclopropane (Maercker, A., et al, *Justus Liebigs Ann. Chem.* (1972), 759:132-157) (9.25 g, 61.2 mmol). The resulting mixture was stirred at ambient temperature for 16 h and quenched with water (50.0 mL). The mixture was extracted with ethyl acetate (3 x 100 mL). The combined organic layers was washed with water (3 x 50.0 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness to yield the title compound (6.50 g, 90%) as a

viscous gum: ^1H NMR (300 MHz, CDCl_3) δ 7.57-7.51 (m, 2H), 7.05 (t, 1H), 6.88 (d, 1H), 3.79-3.74 (m, 2H), 1.59-1.52 (m, 2H), 0.70-0.61 (m, 1H), 0.44-0.38 (m, 2H), 0.05-0.02 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 183.7, 158.2, 151.2, 138.4, 125.4, 123.6, 117.5, 110.3, 40.3, 32.2, 8.6, 4.3.

5 B. Synthesis of 1-(2-cyclopropylethyl)-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2H-indol-2-one

To a solution of 1,3-benzodioxol-5-ol (1.25 g, 9.06 mmol) in THF (20.0 mL) was added dropwise a solution of isopropylmagnesium chloride solution (4.53 mL, 9.06 mmol, 2.0 M in THF) at 0 °C over 5 min. The reaction mixture was stirred for 0.5 h
10 upon which time colorless precipitate was formed. After the solvent was removed under reduced pressure, the residue was dissolved in dichloromethane (20.0 mL) and cooled to 0 °C. A solution of 1-(2-cyclopropylethyl)-1H-indole-2,3-dione (1.77 g, 8.23 mmol) in dichloromethane (20.0 mL) was added to the above solution at 0 °C. The resulting mixture was stirred at ambient temperature for 16 h and quenched with
15 saturated ammonium chloride solution (30.0 mL). The organic layer was separated and washed with water (3 x 25.0 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was crystallized from ethyl acetate and ether to give the title compound (2.22 g, 76%) as a colorless solid: ^1H NMR (300 MHz, CDCl_3) δ 9.52 (s, 1H), 7.46 (d, 1H), 7.37 (dt, 1H), 7.18 (dt, 1H), 6.90
20 (d, 1H), 6.56 (s, 1H), 6.23 (s, 1H), 5.84 (dd, 2H), 4.55 (s, 1H), 3.87-3.63 (m, 2H), 1.64-1.44 (m, 2H), 0.68-0.55 (m, 1H), 0.41-0.27 (m, 2H), -0.02-(-0.07) (m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 179.1, 152.4, 148.8, 142.7, 141.3, 130.3, 129.1, 126.3, 123.7, 117.3, 109.5, 106.9, 101.9, 101.4, 79.3, 40.6, 32.2, 8.6, 4.3, 4.2; MS (ES+) *m/z* 337.6 (M - 17).

25 C. Synthesis of 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2H-indol-2-one

To a solution of 1-(2-cyclopropylethyl)-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2H-indol-2-one (2.22 g, 6.27 mmol) in dichloromethane (30.0 mL) was added trifluoroacetic acid (2.12 g, 18.8 mmol) and triethylsilane (2.14 g, 18.8 mmol).
30 The brown solution was stirred at ambient temperature for 0.5 h and concentrated *in vacuo* to dryness. The residue was diluted with dichloromethane (100 mL), washed with water (3 x 50.0 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography eluting with ethyl acetate/hexane (20/80) to give the title compound

(1.69 g, 80%) as a brown solid: ^1H NMR (300 MHz, CDCl_3) δ 9.21-9.10 (br, 1H), 7.38-7.30 (m, 2H), 7.16 (t, 1H), 6.96 (d, 1H), 6.63 (s, 1H), 6.33 (s, 1H), 5.84 (dd, 2H), 5.01 (s, 1H), 3.87-3.72 (m, 2H), 1.66-1.46 (m, 2H), 0.69-0.59 (m, 1H), 0.43-0.30 (m, 2H), 0.09-0.06 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 178.8, 151.3, 147.6, 144.1, 141.5, 128.7, 126.2, 123.1, 115.2, 109.5, 109.4, 106.5, 101.5, 101.2, 47.4, 40.5, 32.2, 8.6, 4.3, 4.2; MS (ES+) m/z 338.3 ($M + 1$).

D. Synthesis of 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 1E, making variations to replace 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one with 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2H-indol-2-one, the title compound was obtained (53%): R_f = 0.28 (EtOAc/Hexanes, 1/1).

PREPARATION 3

Synthesis of ethyl [3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1H-indol-1-yl]acetate

A. Synthesis of ethyl (2,3-dioxo-2,3-dihydro-1H-indol-1-yl)acetate

Following the procedure as described in PREPARATION 2A, and making non-critical variations to replace (2-bromoethyl)cyclopropane with ethyl bromoacetate, the title compound was obtained (79%) as a light yellow powder: ^1H NMR (300 MHz, CDCl_3) δ 7.64-7.54 (m, 2H), 7.16-7.11 (m, 1H), 6.77 (d, 1H), 4.47 (s, 2H), 4.22 (q, 2H), 1.26 (t, 3H); MS(ES+) m/z 256.2 ($M + 23$).

B. Synthesis of ethyl [3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-2-oxo-2,3-dihydro-1H-indol-1-yl]acetate

Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1-(2-cyclopropylethyl)-1H-indole-2,3-dione with ethyl (2,3-dioxo-2,3-dihydro-1H-indol-1-yl)acetate, the title compound was obtained (95%): ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 9.08 (s, 1H), 7.21-7.13 (m, 2H), 6.93-6.86 (m, 3H), 6.57 (s, 1H), 6.19 (s, 1H), 5.88 (m, 2H), 4.47 (m, 2H), 4.13 (q, 2H), 1.19 (t, 3H); MS (ES-) m/z 370.2 ($M - 1$).

C. Synthesis of ethyl [3-(6-hydroxy-1,3-benzodioxol-5-yl)-2-oxo-2,3-dihydro-1H-indol-1-yl]acetate

Following the procedure as described in PREPARATION 1D, and making non-critical variations to replace 4-bromo-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one with ethyl [3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-

5-yl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate, the title compound was obtained (84%) as a white powder: ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.37 (s, 1H), 7.19 (m, 1H), 7.01-6.90 (m, 3H), 6.43 (s, 2H), 5.84 (m, 2H), 4.86 (s, 1H), 4.56 (s, 2H), 4.13 (q, 2H), 1.18 (t, 3H); MS (ES+) *m/z* 378.2 (M + 23).

5 D. Synthesis of ethyl [3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate

Following the procedure as described in PREPARATION 1E, and making non-critical variations to replace 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one with ethyl [3-(6-hydroxy-1,3-benzodioxol-5-yl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate, the title compound was obtained as a white powder: ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.03 (s, 1H), 7.17-6.85 (m, 5H), 6.22 (s, 1H), 5.83 (s, 2H), 5.04 (t, 1H), 4.56-4.08 (m, 5H), 3.69 (m, 1H), 1.18 (t, 3H); MS (ES+) *m/z* 408.1 (M + 23).

PREPARATION 4

15 Synthesis of methyl 3-[[3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]methyl]benzoate

A. Synthesis of methyl 3-[(2,3-dioxo-2,3-dihydro-1*H*-indol-1-yl)methyl]benzoate

Following the procedure as described in PREPARATION 2A, and making non-critical variations to replace (2-bromoethyl)cyclopropane with methyl 3-(bromomethyl)benzoate, the title compound was obtained (84%) as an orange solid: ¹H NMR (300 MHz, CDCl₃) δ 7.99-7.95 (m, 2H), 7.60 (d, 1H), 7.53-7.47 (m, 2H), 7.43 (d, 1H), 7.09 (t, 1H), 6.43 (d, 1H), 4.95 (s, 2H), 3.89 (s, 3H).

B. Synthesis of methyl 3-[[3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]methyl]benzoate

25 Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1-(2-cyclopropylethyl)-1*H*-indole-2,3-dione with methyl 3-[(2,3-dioxo-2,3-dihydro-1*H*-indol-1-yl)methyl]benzoate, the title compound was obtained (96%): ¹H NMR (300 MHz, CDCl₃) δ 8.65 (s, 1H), 7.92 (s, 1H), 7.85 (d, 1H), 7.41-7.38 (m, 1H), 7.32-7.24 (m, 2H), 7.19-7.13 (m, 1H), 7.04-6.9 (m, 1H), 6.63 (d, 1H), 6.44 (s, 1H), 6.39 (s, 1H), 5.79 (s, 2H), 5.05 (s, 1H), 4.83 (dd, 2H), 3.80 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 178.7, 167.0, 151.0, 148.5, 142.1, 141.1, 135.7, 131.6, 130.5, 130.1, 129.1, 129.0, 128.4, 125.5, 123.9, 116.7, 109.7, 106.5, 101.3, 100.5, 78.6, 60.6, 52.4, 43.6; MS (ES+) *m/z* 456.1 (M + 23).

C. Synthesis of methyl 3-[[3-(6-hydroxy-1,3-benzodioxol-5-yl)-2-oxo-2,3-dihydro-1H-indol-1-yl]methyl]benzoate

Following the procedure as described in PREPARATION 2C, and making non-critical variations to replace 1-(2-cyclopropylethyl)-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2H-indol-2-one with methyl 3-[[3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-2-oxo-2,3-dihydro-1H-indol-1-yl]methyl]benzoate, the title compound was obtained (98%): MS (ES+) m/z 418.2 (M + 1).

D. Synthesis of methyl 3-[[3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1H-indol-1-yl]methyl]benzoate

Following the procedure as described in PREPARATION 1E, and making non-critical variations to replace 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one with methyl 3-[[3-(6-hydroxy-1,3-benzodioxol-5-yl)-2-oxo-2,3-dihydro-1H-indol-1-yl]methyl]benzoate, the title compound was obtained (81%) as a white powder: MS (ES+) m/z 470.3 (M + 23), 448.3 (M + 1).

15 Preparation 5

Synthesis of methyl 4-[[3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1H-indol-1-yl]methyl]benzoate

A. Synthesis of methyl 4-[(2,3-dioxo-2,3-dihydro-1H-indol-1-yl)methyl]benzoate

Following the procedure as described in PREPARATION 2A, and making non-critical variations to replace (2-bromoethyl)cyclopropane with methyl 4-(bromomethyl)benzoate, the title compound was obtained (84%) as an orange solid: $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ 8.00 (d, 2H), 7.61 (d, 1H), 7.46 (t, 1H), 7.38 (d, 2H), 7.09 (t, 1H), 6.69 (d, 1H), 4.96 (s, 2H), 3.88 (s, 3H); MS (ES+) m/z 296.1 (M + 1).

25 B. Synthesis of methyl 4-[[3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-2-oxo-2,3-dihydro-1H-indol-1-yl]methyl]benzoate

Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1-(2-cyclopropylethyl)-1H-indole-2,3-dione with methyl 4-[(2,3-dioxo-2,3-dihydro-1H-indol-1-yl)methyl]benzoate, the title compound was obtained (79%): MS (ES+) m/z 416.1 (M - 17).

30 C. Synthesis of methyl 4-[[3-(6-hydroxy-1,3-benzodioxol-5-yl)-2-oxo-2,3-dihydro-1H-indol-1-yl]methyl]benzoate

Following the procedure as described in PREPARATION 2C, and making the variations to replace 1-(2-cyclopropylethyl)-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2H-indol-2-one with methyl 4-[[3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-

5-yl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl)methyl}benzoate, the title compound was obtained (98%) as a solid: MS (ES+) *m/z* 418.1 (*M* + 1).

D. Synthesis of methyl 4-[[3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl)methyl}benzoate

- 5 Following the procedure as described in PREPARATION 1E, and making non-critical variations to replace 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one with methyl 4-[[3-(6-hydroxy-1,3-benzodioxol-5-yl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl)methyl}benzoate, the title compound was obtained (81%): MS (ES+) *m/z* 448.1 (*M* + 1).

10

PREPARATION 6

Synthesis of 2-{3-[3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]propyl}-1*H*-isoindole-1,3(2*H*)-dione

A. Synthesis of 1-[3-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-propyl]-1*H*-indole-2,3-dione

- 15 Following the procedure as described in PREPARATION 2A, and making non-critical variations to replace (2-bromoethyl)cyclopropane with 2-(3-bromopropyl)-1*H*-isoindole-1,3(2*H*)-dione, the title compound was obtained (92%): ¹H NMR (300 MHz, CDCl₃) δ 7.80-7.79 (m, 4H), 7.61-7.56 (m, 1H), 7.49-7.46 (m, 1H), 7.18-7.16 (m, 1H), 7.07-7.05 (m, 1H), 3.72-3.60 (m, 4H), 1.97-1.92 (m, 2H).

- 20 B. Synthesis of 2-{3-[3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]propyl}-1*H*-isoindole-1,3(2*H*)-dione

- Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1-(2-cyclopropylethyl)-1*H*-indole-2,3-dione with 1-[3-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-propyl]-1*H*-indole-2,3-dione, the title compound was obtained (96%): ¹H NMR (300 MHz, CDCl₃) δ 7.86-7.78 (m, 4H), 7.21-7.13 (m, 2H), 7.00-6.97 (m, 1H), 6.87-6.85 (m, 2H), 6.15 (s, 1H), 5.86-5.84 (m, 2H), 3.69-3.65 (m, 4H), 2.46-2.45 (m, 1H), 1.94-1.87 (m, 2H); MS (ES+) *m/z* 473.4 (*M* - 17).

C. Synthesis of 2-{3-[3-(6-hydroxy-1,3-benzodioxol-5-yl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]propyl}-1*H*-isoindole-1,3(2*H*)-dione

- 30 Following the procedure as described in PREPARATION 1D, and making non-critical variations to replace 4-bromo-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one with 2-{3-[3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]propyl}-1*H*-isoindole-1,3(2*H*)-dione, the title compound was obtained (94%): ¹H NMR (300 MHz, CDCl₃) δ 7.81-7.78 (m, 2H), 7.70-

7.67 (m, 2H), 7.32-7.27 (m, 2H), 7.12-7.07 (m, 1H), 6.90-6.87 (m, 1H), 6.54 (s, 1H), 6.45 (s, 1H), 5.86 (dd, 2H), 4.82 (s, 1H), 3.96-3.66 (m, 4H), 2.17-2.04 (m, 2H); MS (ES+) m/z 457.0 ($M + 1$).

D. Synthesis of 2-{3-[3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1H-indol-1-yl]propyl}-1H-isoindole-1,3(2H)-dione

Following the procedure as described in PREPARATION 1E, and making non-critical variations to replace 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one with 2-{3-[3-(6-hydroxy-1,3-benzodioxol-5-yl)-2-oxo-2,3-dihydro-1H-indol-1-yl]propyl}-1H-isoindole-1,3(2H)-dione, the title compound was obtained (94%) as a foam solid: ^1H NMR (300 MHz, CDCl_3) δ 9.20 (s, 1H), 7.81-7.79 (m, 2H), 7.68-7.61 (m, 2H), 7.35-7.25 (m, 2H), 7.16-7.14 (m, 1H), 6.90 (d, 1H), 6.80 (s, 1H), 6.48 (s, 1H), 5.86 (dd, 2H), 4.64 (d, 1H), 3.67-4.13 (m, 5H), 2.18-2.05 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 180.6, 168.6, 151.2, 147.8, 143.2, 141.2, 134.2, 134.2, 131.9, 130.0, 128.7, 125.1, 123.2, 113.9, 108.7, 108.3, 101.3, 100.6, 64.9, 58.0, 37.6, 36.1, 26.5; MS (ES+) m/z 487.3 ($M + 1$).

PREPARATION 7

Synthesis of 2-{2-[3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1H-indol-1-yl]ethyl}-1H-isoindole-1,3(2H)-dione

A. Synthesis of 1-[2-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-ethyl]-1H-indole-2,3-dione

Following the procedure as described in PREPARATION 2A, and making non-critical variations to replace (2-bromoethyl)cyclopropane with 2-(2-bromoethyl)-1H-isoindole-1,3(2H)-dione, the title compound was obtained (75%): ^1H NMR (300 MHz, CDCl_3) δ 7.85-7.78 (m, 4H), 7.65 (td, 1H), 7.55 (dd, 1H), 7.25 (d, 1H), 7.12 (t, 1H), 4.00-3.80 (m, 4H); MS (ES+) m/z 321 ($M + 1$), 343 ($M + 23$).

B. Synthesis of 2-{2-[3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-2-oxo-2,3-dihydro-1H-indol-1-yl]ethyl}-1H-isoindole-1,3(2H)-dione

Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1-(2-cyclopropylethyl)-1H-indole-2,3-dione with 1-[2-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-ethyl]-1H-indole-2,3-dione, the title compound was obtained (99%): ^1H NMR (300 MHz, CD_3OD) δ 7.85-7.68 (m, 4H), 7.29 (td, 1H), 7.18-6.96 (m, 3H), 6.88 (s, 1H), 6.16 (s, 1H), 5.85 (s, 1H), 5.82 (s, 1H), 3.81-4.01 (m, 4H); MS (ES+) m/z 441 ($M - 17$), 458 ($M + 23$).

C. Synthesis of 2-{2-[3-(6-hydroxy-1,3-benzodioxol-5-yl)-2-oxo-2,3-dihydro-1H-indol-1-yl]ethyl}-1H-isoindole-1,3(2H)-dione

Following the procedure as described in PREPARATION 1D, and making non-critical variations to replace 4-bromo-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one with 2-{2-[3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-2-oxo-2,3-dihydro-1H-indol-1-yl]ethyl}-1H-isoindole-1,3(2H)-dione, the title compound was obtained (90%) as a white solid: ¹H NMR (300 MHz, CD₃OD) δ 10.15-10.05 (br, 1H), 8.66-8.58 (m, 4H), 8.07-7.70 (m, 4H), 7.12 (s, 1H), 7.18 (s, 1H), 6.70 (s, 1H), 6.69 (s, 1H), 5.50 (s, 1H), 4.91-4.56 (m, 4H); MS (ES+) *m/z* 443 (M + 1).

10 D. Synthesis of 2-{2-[3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1H-indol-1-yl]ethyl}-1H-isoindole-1,3(2H)-dione

Following the procedure as described in PREPARATION 1E, making variation to replace 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one with 2-{2-[3-(6-hydroxy-1,3-benzodioxol-5-yl)-2-oxo-2,3-dihydro-1H-indol-1-yl]ethyl}-1H-isoindole-1,3(2H)-dione, the title compound was obtained (56%): ¹H NMR (300 MHz, CD₃OD) δ 9.97 (s, 1H), 8.72-8.62 (m, 4H), 8.07-7.67 (m, 5H), 7.01 (s, 1H), 6.71 (s, 1H), 6.70 (s, 1H), 5.79 (t, 1H), 4.88-4.50 (m, 6H); MS (ES+) *m/z* 455 (M - 17), 473 (M + 1), 495 (M + 23).

PREPARATION 8

20 Synthesis of 1-(diphenylmethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2H-indol-2-one

A. Synthesis of 1-(diphenylmethyl)-1H-indole-2,3-dione

Following the procedure as described in PREPARATION 2A, and making non-critical variations to replace (2-bromoethyl)cyclopropane with 1,1'-(bromomethylene)dibenzene, the title compound was obtained (68%) as an orange solid: MS (ES+) *m/z* 336.4 (M + 23).

B. Synthesis of 1-(diphenylmethyl)-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1-(2-cyclopropylethyl)-1H-indole-2,3-dione with 1-(diphenylmethyl)-1H-indole-2,3-dione, the title compound was obtained (99%) as an off-white powder: MS (ES+) *m/z* 474.5 (M + 23).

C. Synthesis of 1-(diphenylmethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 2C, and making the variations to replace 1-(2-cyclopropylethyl)-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2H-indol-2-one with 1-(diphenylmethyl)-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2H-indol-2-one, the title compound was obtained (84%) as an off-white solid: MS (ES+) m/z 458.4 (M + 23).

D. Synthesis of 1-(diphenylmethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 1E, and making non-critical variations using 1-(diphenylmethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2H-indol-2-one to replace 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one, the title compound was obtained (56%): MS (ES+) m/z 488.3 (M + 23).

PREPARATION 9

Synthesis of 1-[3-(benzyloxy)propyl]-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2H-indol-2-one

A. Synthesis of 1-[3-(benzyloxy)propyl]-1H-indole-2,3-dione

Following the procedure as described in PREPARATION 1A, and making non-critical variations to replace 4-bromoindole with isatin, and 1-bromopentane with benzyl 3-bromopropyl ether, the title compound was obtained (95%) as a pale yellow syrup: ^1H NMR (300 MHz, CDCl_3) δ 7.57-6.92 (m, 9H), 4.50 (s, 2H), 3.84 (t, 2H), 3.54 (t, 2H), 2.03-1.94 (m, 2H); MS (ES+) m/z 296.3 (M + 1), 318.3 (M + 23).

B. Synthesis of 1-[3-(benzyloxy)propyl]-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 1C, and making non-critical variations to replace 4-bromo-1-pentyl-1H-indole-2,3-dione with 1-[3-(benzyloxy)propyl]-1H-indole-2,3-dione, the title compound was obtained (70%): ^1H NMR (300 MHz, CDCl_3) δ 9.42 (s, 1H), 7.32-7.16 (m, 8H), 6.96 (d, 1H), 6.61 (s, 1H), 6.23 (s, 1H), 5.86-5.83 (m, 2H), 4.44 (s, 2H), 3.88-3.73 (m, 2H), 3.46 (t, 2H), 2.06-1.85 (m, 2H); MS (ES+) m/z 416.3 (M - 17), 456.3 (M + 23).

C. Synthesis of 1-[3-(benzyloxy)propyl]-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 1D, and making non-

critical variations to replace 4-bromo-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one with 1-[3-(benzyloxy)propyl]-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained (92%): ¹H NMR (300 MHz, CDCl₃) δ 7.42-6.95 (m, 9H), 6.56 (s, 1H), 6.24 (s, 1H), 5.86 (ABq, 1H), 5.81 (ABq, 1H), 4.99 (s, 1H), 4.42 (s, 2H), 3.91-3.76 (m, 2H), 3.46 (t, 2H), 2.03-1.93 (m, 2H); MS (ES+) *m/z* 418.3 (M + 1).

D. Synthesis of 1-[3-(benzyloxy)propyl]-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 1E, and making non-critical variations to replace 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one with 1-[3-(benzyloxy)propyl]-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained (93%): MS (ES+) *m/z* 448.2 (M + 1).

PREPARATION 10

15 Synthesis of methyl 2-[[3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]methyl]benzoate

A. Synthesis of methyl 2-[(2,3-dioxo-2,3-dihydro-1*H*-indol-1-yl)methyl]benzoate

Following the procedure as described in PREPARATION 2A, and making non-critical variations to replace (2-bromoethyl)cyclopropane with methyl 2-(bromomethyl)benzoate, the title compound was obtained (68%) as a yellow solid: ¹H NMR (300 MHz, CDCl₃) δ 8.05 (dd, 1H), 7.64 (dd, 1H), 7.50-7.31 (m, 3H), 7.22 (d, 1H), 7.10 (t, 1H), 6.72 (d, 1H), 5.41 (s, 2H), 3.95 (s, 3H).

B. Synthesis of methyl 2-[[3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]methyl]benzoate

25 Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1-(2-cyclopropylethyl)-1*H*-indole-2,3-dione with methyl 2-[(2,3-dioxo-2,3-dihydro-1*H*-indol-1-yl)methyl]benzoate, the title compound was obtained (97%) as a colorless solid: ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.29 (s, 1H), 7.97 (dd, 1H), 7.53-7.36 (m, 3H), 7.28 (s, 1H), 7.10 (td, 1H), 6.96-6.83 (m, 2H), 6.59 (d, 2H), 6.25 (s, 1H), 5.95-5.86 (m, 2H), 5.31-5.07 (m, 2H), 3.88 (s, 3H); MS (ES+) *m/z* 456.1 (M + 23).

C. Synthesis of methyl 2-[[3-(6-hydroxy-1,3-benzodioxol-5-yl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]methyl]benzoate

Following the procedure as described in PREPARATION 2C, and making non-

critical variations to replace 1-(2-cyclopropylethyl)-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2*H*-indol-2-one with methyl 2-[[3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]methyl]benzoate, the title compound was obtained (100%) as a white solid: ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.32 (s, 1H), 7.94 (dd, 1H), 7.50-7.34 (m, 2H), 7.26 (d, 1H), 7.08 (t, 1H), 7.00-6.86 (m, 2H), 6.76 (s, 1H), 6.64 (d, 1H), 6.38 (s, 1H), 5.93-5.86 (m, 2H), 5.34-5.12 (m, 2H), 4.83 (s, 1H), 3.87 (s, 3H); MS (ES+) *m/z* 418.2 (*M* + 1).

D. Synthesis of methyl 2-[[3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]methyl]benzoate

A solution of methyl 2-[[3-(6-hydroxy-1,3-benzodioxol-5-yl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]methyl]benzoate (17.1 g, 40.0 mmol) and paraformaldehyde (10.3 g, 330 mmol) in THF (500 mL) was degassed by bubbling through argon for 2 hours. To this solution was added lithium diisopropylamide solution (45.1 mL, 2 M solution, 90.0 mmol) slowly at -78 °C. The mixture was stirred at ambient temperature overnight and quenched with saturated ammonium chloride solution. The mixture was concentrated *in vacuo* to remove THF followed by the addition of ethyl acetate (500 mL). The organic layer was washed with water, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was recrystallized from ethyl acetate/hexanes to give the title compound (13.7 g, 75%): ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.20 (s, 1H), 7.95 (dd, 1H), 7.53-7.33 (m, 3H), 7.08-6.82 (m, 4H), 6.53 (d, 1H), 6.25 (s, 1H), 5.93-5.86 (m, 2H), 5.31-5.07 (m, 3H), 4.26-4.17 (m, 1H), 4.00-3.92 (m, 1H), 3.88 (s, 3H); MS (ES+) *m/z* 448.3 (*M* + 1).

PREPARATION 11

Synthesis of [3-(1,3-benzodioxol-5-yl)-2-oxo-1-pentyl-2,3-dihydro-1*H*-indol-3-yl]acetic acid

A. Synthesis of 1-pentyl-1*H*-indole-2,3-dione

Following the procedure as described in PREPARATION 2A, and making non-critical variations to replace (2-bromoethyl)cyclopropane with 1-bromopentane, the title compound was obtained (85%) as an orange solid: ¹H NMR (300 MHz, CDCl₃) δ 7.60-7.52 (m, 2H), 7.08 (td, 1H), 6.87 (d, 1H), 3.69 (t, 2H), 1.74-1.61 (m, 2H), 1.40-1.28 (m, 4H), 0.88 (t, 3H).

B. Synthesis of 3-(1,3-benzodioxol-5-yl)-3-hydroxy-1-pentyl-1,3-dihydro-2*H*-indol-2-one

To a solution of 1-pentyl-1*H*-indole-2,3-dione (2.80 g, 12.8 mmol) in THF (50.0

mL) was added 3,4-(methylenedioxy)phenylmagnesium bromide (14.0 mL, 1 M THF solution, 14.0 mmol) slowly at -78 °C. The mixture was stirred at 0 °C for 1 h and quenched with ammonium chloride solution. The mixture was poured into water (150 mL) and extracted with ethyl acetate (200 mL). The organic layer was washed with water, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to flash column chromatography to afford the title compound (3.10 g, 71%) as an orange oil: ¹H NMR (300 MHz, CDCl₃) δ 7.34-7.23 (m, 2H), 7.05 (t, 1H), 6.91-6.85 (m, 2H), 6.83-6.78 (m, 1H), 6.71 (d, 1H), 5.92-5.89 (m, 2H), 3.82-3.55 (m, 2H), 3.40 (br, 1H), 1.76-1.61 (m, 2H), 1.39-1.28 (m, 4H), 0.87 (t, 3H).

10 C. Synthesis of 3-(1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 2C, and making non-critical variations to replace 1-(2-cyclopropylethyl)-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2H-indol-2-one with 3-(1,3-benzodioxol-5-yl)-3-hydroxy-1-pentyl-1,3-dihydro-2H-indol-2-one, the title compound was obtained (90%) as an oil: ¹H NMR (300 MHz, CDCl₃) δ 7.30 (td, 1H), 7.14 (d, 1H), 7.03 (td, 1H), 6.89 (d, 1H), 6.75 (d, 1H), 6.67 (dd, 1H), 6.57 (d, 1H), 5.90 (s, 2H), 4.50 (s, 1H), 3.81-3.62 (m, 2H), 1.76-1.62 (m, 2H), 1.41-1.28 (m, 4H), 0.88 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 176.8, 148.1, 147.2, 143.5, 130.0, 129.4, 128.4, 125.1, 122.9, 122.0, 108.7, 108.6, 101.1, 51.9, 40.4, 29.0, 27.1, 22.3, 14.0.

20 D. Synthesis of methyl [3-(1,3-benzodioxol-5-yl)-2-oxo-1-pentyl-2,3-dihydro-1H-indol-3-yl]acetate

A solution of 3-(1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one (1.00 g, 3.10 mmol) and methyl bromoacetate (0.44 mL, 4.60 mmol) in THF (20.0 mL) was degassed by bubbling through argon for one hour. Sodium hydride (0.19 g, 4.60 mmol) was added at 0 °C. The mixture was stirred at 0 °C for 1 h and quenched with ammonium chloride solution. The mixture was poured into water (150 mL), and extracted with ethyl acetate (200 mL). The organic layer was washed with water, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to flash column chromatography to afford the title compound (0.94 g, 76%) as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 7.30 (td, 1H), 7.25 (dd, 1H), 7.06 (td, 1H), 6.89 (d, 1H), 6.81 (d, 1H), 6.74-6.65 (m, 2H), 5.90-5.87 (m, 2H), 3.71-3.64 (m, 2H), 3.45 (d, 1H), 3.41 (s, 3H), 3.18 (d, 1H), 1.74-1.60 (m, 2H), 1.39-1.22 (m, 4H), 0.85 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 177.8, 170.0, 147.9, 147.0, 143.9, 133.1, 131.3, 128.6, 124.6, 122.3, 119.9, 108.7, 108.1, 107.4, 101.2,

52.8, 51.6, 41.8, 40.4, 29.0, 26.8, 22.3, 14.0; MS (ES+) m/z 418.1 (M + 23), 396.1 (M + 1).

E. Synthesis of [3-(1,3-benzodioxol-5-yl)-2-oxo-1-pentyl-2,3-dihydro-1H-indol-3-yl]acetic acid

5 To a solution of methyl [3-(1,3-benzodioxol-5-yl)-2-oxo-1-pentyl-2,3-dihydro-1H-indol-3-yl]acetate (5.90 g, 15.0 mmol) in THF/water (2/1 v/v, 120 mL) was added lithium hydroxide monohydrate (1.26 g, 28.0 mmol). The mixture was stirred at ambient temperature overnight. Most THF was removed under vacuum and water (150 mL) was added. The solution was extracted with ethyl acetate/hexanes (1/3 v/v,
10 50.0 mL). The water layer was acidified with 1 N HCl solution until the pH value reached 2 and extracted with ethyl acetate (200 mL). The organic layer was washed with water, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness to afford the title compound (5.00 g, 88%) as a white solid: ^1H NMR (300 MHz, CDCl_3) δ 7.29 (td, 1H), 7.21 (dd, 1H), 7.05 (td, 1H), 6.87 (d, 1H), 6.76 (d, 1H), 6.72-6.64 (m, 2H), 5.90-5.86 (m, 2H), 3.65 (t, 2H), 3.43 (d, 1H), 3.11 (d, 1H), 1.70-1.55 (m, 2H), 1.36-1.22 (m, 4H), 0.85 (t, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 178.2, 174.0, 148.0, 147.1, 143.4, 132.6, 131.4, 128.7, 124.4, 122.7, 119.8, 108.9, 108.2, 107.2, 101.2, 52.6, 41.5, 40.4, 29.0, 26.6, 22.3, 14.0; MS (ES+) m/z 404.0 (M + 23), 382.0 (M + 1).

20 PREPARATION 12

Synthesis of 3-[3-(1,3-benzodioxol-5-yl)-2-oxo-1-pentyl-2,3-dihydro-1H-indol-3-yl]propanoic acid

A. Synthesis of methyl 3-[3-(1,3-benzodioxol-5-yl)-2-oxo-1-pentyl-2,3-dihydro-1H-indol-3-yl]propanoate

25 Following the procedure as described in PREPARATION 11D, and making non-critical variations to replace methyl bromoacetate with methyl 3-bromopropionate, the title compound was obtained (76%) as a colorless oil: ^1H NMR (300 MHz, CDCl_3) δ 7.28 (td, 1H), 7.17 (dd, 1H), 7.06 (td, 1H), 6.89 (d, 1H), 6.84 (d, 1H), 6.77 (dd, 1H), 6.68 (d, 1H), 5.89-5.84 (m, 2H), 3.67 (t, 2H), 3.53 (s, 3H), 2.69-2.56 (m, 1H), 2.54-2.41 (m, 1H), 2.21-2.08 (m, 1H), 1.99-1.86 (m, 1H), 1.72-1.59 (m, 2H), 1.38-1.24 (m, 4H), 0.85 (t, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 177.8, 173.1, 147.9, 146.9, 143.2, 133.5, 131.6, 128.5, 124.9, 122.6, 120.1, 108.7, 108.1, 107.6, 101.1, 55.2, 51.6, 40.2, 32.4, 29.5, 29.1, 27.1, 22.3, 14.0; MS (ES+) m/z 410.1 (M + 1), 432.0 (M + 23).

B. Synthesis of 3-[3-(1,3-benzodioxol-5-yl)-2-oxo-1-pentyl-2,3-dihydro-1*H*-indol-3-yl]propanoic acid

Following the procedure as described in PREPARATION 11E, and making non-critical variations to replace methyl [3-(1,3-benzodioxol-5-yl)-2-oxo-1-pentyl-2,3-dihydro-1*H*-indol-3-yl]acetate with methyl 3-[3-(1,3-benzodioxol-5-yl)-2-oxo-1-pentyl-2,3-dihydro-1*H*-indol-3-yl]propanoate, the title compound was obtained (92%) as a colorless solid: MS (ES-) *m/z* 394.2 (*M* - 1).

PREPARATION 13

Synthesis of 3-(4,5-difluoro-2-hydroxyphenyl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one

A. Synthesis of 3-(4,5-difluoro-2-hydroxyphenyl)-3-hydroxy-1-pentyl-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1-(2-cyclopropylethyl)-1*H*-indole-2,3-dione with 1-pentyl-1*H*-indole-2,3-dione, and 1,3-benzodioxol-5-ol with 3, 4-difluorophenol, the title compound was obtained (31%): ¹H NMR (300 MHz, CDCl₃) δ 9.69-9.65 (br, 1H), 7.51-7.41 (m, 2H), 7.26-7.21 (m, 1H), 6.99-6.57 (m, 3H), 4.18-4.14 (br, 1H), 3.78-3.58 (m, 2H), 1.76-1.62 (m, 2H), 1.40-1.28 (m, 4H), 0.87 (t, 3H); MS (ES+) *m/z* 330 (*M* - 17), 370 (*M* + 23).

B. Synthesis of 3-(4,5-difluoro-2-hydroxyphenyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 2C, and making non-critical variations to replace 1-(2-cyclopropylethyl)-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2*H*-indol-2-one with 3-(4,5-difluoro-2-hydroxyphenyl)-3-hydroxy-1-pentyl-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained (98%): ¹H NMR (300 MHz, CDCl₃) δ 7.46-7.19 (m, 3H), 7.03-6.68 (m, 3H), 5.03 (s, 1H), 3.76-3.67 (m, 2H), 1.76-1.62 (m, 2H), 1.40-1.28 (m, 4H), 0.87 (t, 3H); MS (ES+) *m/z* 332 (*M* + 1).

C. Synthesis of 3-(4,5-difluoro-2-hydroxyphenyl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 1E, and making non-critical variations to replace 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one with 3-(4,5-difluoro-2-hydroxyphenyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained (96%): MS (ES+) *m/z* 344 (*M* - 17), 384

(M + 23).

PREPARATION 14

Synthesis of 3-(5-fluoro-2-hydroxyphenyl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2H-indol-2-one

5 A. Synthesis of 3-(5-fluoro-2-hydroxyphenyl)-3-hydroxy-1-pentyl-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 1C, and making non-critical variations to replace 4-bromo-1-pentyl-1H-indole-2,3-dione with 1-pentyl-1H-indole-2,3-dione, and 1,3-benzodioxol-5-ol with 4-fluorophenol, the title compound was
10 obtained (53%): ¹H NMR (300 MHz, CDCl₃) δ 9.42-9.14 (br, 1H), 7.53-6.86 (m, 6H), 6.56-6.48 (m, 1H), 4.58-4.28 (br, 1H), 3.79-3.58 (m, 2H), 1.77-1.61 (m, 2H), 1.41-1.24 (m, 4H), 0.87 (t, 3H); MS (ES+) *m/z* 312 (M - 17), 352 (M + 23).

 B. Synthesis of 3-(5-fluoro-2-hydroxyphenyl)-1-pentyl-1,3-dihydro-2H-indol-2-one

To a solution of 3-(5-fluoro-2-hydroxyphenyl)-3-hydroxy-1-pentyl-1,3-dihydro-
15 2H-indol-2-one (2.42 g, 7.35 mmol) in dichloromethane (10.0 mL) were added trifluoroacetic acid (1.00 mL) and triethylsilane (1.00 mL) at ambient temperature. The reaction mixture was stirred at 40 °C for 15 hrs and concentrated *in vacuo* to dryness. The residue was triturated with ether to give the title compound (2.10 g, 91%) as a solid: MS (ES+) *m/z* 314 (M + 1).

20 C. Synthesis of 3-(5-fluoro-2-hydroxyphenyl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2H-indol-2-one

To a solution of 3-(5-fluoro-2-hydroxyphenyl)-1-pentyl-1,3-dihydro-2H-indol-2-one (2.10 g, 6.70 mmol) in THF (20.0 mL) were added paraformaldehyde (1.76 g, 58.8 mmol) and lithium diisopropylamide (7.35 mL, 2.0 M in THF, 14.7 mmol) at 0 °C. The
25 reaction mixture was stirred at 0 °C for 2 hrs followed by the addition of ammonium chloride solution (10.0 mL) and ethyl acetate (100 mL). The organic layer was washed with water and brine, dried over Na₂SO₄ and filtered. The filtrate was concentrated *in vacuo* to dryness to give the title compound: ¹H NMR (300 MHz, CDCl₃) δ 9.55-9.10 (br, 1H), 7.53-6.86 (m, 6H), 6.57-6.49 (m, 1H), 4.74-4.30 (br, 1H), 4.18-4.07 (m, 2H),
30 3.79-3.60 (m, 2H), 1.77-1.61 (m, 2H), 1.41-1.24 (m, 4H), 0.87 (t, 3H); MS (ES+) *m/z* 326 (M - 17), 366 (M + 23).

PREPARATION 15

Synthesis of 3-(5-bromo-2-hydroxyphenyl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2H-indol-2-one

A. Synthesis of 3-(5-bromo-2-hydroxyphenyl)-3-hydroxy-1-pentyl-1,3-dihydro-2H-indol-2-one

5

Following the procedure as described in PREPARATION 1C, and making non-critical variations to replace 4-bromo-1-pentyl-1H-indole-2,3-dione with 1-pentyl-1H-indole-2,3-dione, and 1,3-benzodioxol-5-ol with 4-bromophenol, the title compound was obtained (41%): ^1H NMR (300 MHz, CDCl_3) δ 9.46-9.25 (br, 1H), 7.51-6.80 (m, 7H), 4.73-4.51 (br, 1H), 3.79-3.56 (m, 2H), 1.76-1.60 (m, 2H), 1.41-1.22 (m, 4H), 0.87 (t, 3H); MS (ES+) m/z 377 (M - 17), 379 (M - 17), 412 (M + 23), 414 (M + 23).

10

B. Synthesis of 3-(5-bromo-2-hydroxyphenyl)-1-pentyl-1,3-dihydro-2H-indol-2-one

To a solution of 3-(5-bromo-2-hydroxyphenyl)-3-hydroxy-1-pentyl-1,3-dihydro-2H-indol-2-one (2.22 g, 5.64 mmol) in dichloromethane (10.0 mL) were added trifluoroacetic acid (1.00 mL) and triethylsilane (1.00 mL) at ambient temperature. The reaction mixture was stirred at 50 °C for 15 hrs and concentrated *in vacuo* to dryness to give the title compound: MS (ES+) m/z 374 (M + 1), 376 (M + 1).

15

C. Synthesis of 3-(5-bromo-2-hydroxyphenyl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 14C, and making non-critical variations to replace 3-(5-fluoro-2-hydroxyphenyl)-1-pentyl-1,3-dihydro-2H-indol-2-one with 3-(5-bromo-2-hydroxyphenyl)-1-pentyl-1,3-dihydro-2H-indol-2-one, the title compound was obtained: MS (ES+) m/z 386 (M - 17), 388 (M - 17), 426 (M + 23), 428 (M + 23).

20

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PREPARATION 16

Synthesis of 3-(5-chloro-4-fluoro-2-hydroxyphenyl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2H-indol-2-one

A. Synthesis of 3-(5-chloro-4-fluoro-2-hydroxyphenyl)-3-hydroxy-1-pentyl-1,3-dihydro-2H-indol-2-one

30

Following the procedure as described in PREPARATION 1C, and making non-critical variations to replace 4-bromo-1-pentyl-1H-indole-2,3-dione with 1-pentyl-1H-indole-2,3-dione, and 1,3-benzodioxol-5-ol with 4-chloro-3-fluorophenol, the title compound was obtained (33%): ^1H NMR (300 MHz, CDCl_3) δ 9.80 (s, 1H), 7.52-7.41 (m, 2H), 7.23 (t, 1H), 6.96 (d, 1H), 6.84 (d, 1H), 6.80 (d, 1H), 4.15 (s, 1H), 3.79-3.58

(m, 2H), 1.76-1.62 (m, 2H), 1.40-1.28 (m, 4H), 0.87 (t, 3H); MS (ES+) m/z 346 (M - 17), 386 (M + 23).

B. Synthesis of 3-(5-chloro-4-fluoro-2-hydroxyphenyl)-1-pentyl-1,3-dihydro-2H-indol-2-one

5 Following the procedure as described in PREPARATION 15B, and making non-critical variations to replace 3-(5-bromo-2-hydroxyphenyl)-3-hydroxy-1-pentyl-1,3-dihydro-2H-indol-2-one with 3-(5-chloro-4-fluoro-2-hydroxyphenyl)-3-hydroxy-1-pentyl-1,3-dihydro-2H-indol-2-one, the title compound was obtained (99%): ^1H NMR (300 MHz, CDCl_3) δ 10.0-9.70 (br, 1H), 7.45-7.18 (m, 3H), 6.98 (d, 1H), 6.90-6.82 (m, 2H),
10 5.01 (s, 1H), 3.75-3.66 (m, 2H), 1.76-1.62 (m, 2H), 1.40-1.28 (m, 4H), 0.87 (t, 3H); MS (ES+) m/z 348 (M + 1).

C. Synthesis of 3-(5-chloro-4-fluoro-2-hydroxyphenyl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 1E, and making non-critical variations to replace 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one with 3-(5-chloro-4-fluoro-2-hydroxyphenyl)-1-pentyl-1,3-dihydro-2H-indol-2-one, the title compound was obtained (46%): MS (ES+) m/z 360 (M - 17), 400 (M + 23).

PREPARATION 17

20 Synthesis of 3-(4-chloro-5-fluoro-2-hydroxyphenyl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2H-indol-2-one

A. Synthesis of 3-(4-chloro-5-fluoro-2-hydroxyphenyl)-3-hydroxy-1-pentyl-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 1C, and making non-critical variations to replace 4-bromo-1-pentyl-1H-indole-2,3-dione with 1-pentyl-1H-indole-2,3-dione, and 1,3-benzodioxol-5-ol with 3-chloro-4-fluorophenol, the title compound was obtained (14%): MS (ES+) m/z 346 (M - 17), 386 (M + 23).

B. Synthesis 3-(4-chloro-5-fluoro-2-hydroxyphenyl)-1-pentyl-1,3-dihydro-2H-indol-2-one

30 Following the procedure as described in PREPARATION 15B, and making non-critical variations to replace 3-(5-bromo-2-hydroxyphenyl)-3-hydroxy-1-pentyl-1,3-dihydro-2H-indol-2-one with 3-(4-chloro-5-fluoro-2-hydroxyphenyl)-3-hydroxy-1-pentyl-1,3-dihydro-2H-indol-2-one, the title compound was obtained: MS (ES+) m/z 348 (M + 1).

C. Synthesis of 3-(4-chloro-5-fluoro-2-hydroxyphenyl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 1E, and making non-critical variations to replace 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one with 3-(4-chloro-5-fluoro-2-hydroxyphenyl)-1-pentyl-1,3-dihydro-2H-indol-2-one, the title compound was obtained (50% for two steps): MS (ES+) m/z 360 (M - 17), 400 (M + 23).

PREPARATION 18

Synthesis of 3-(4,5-dichloro-2-hydroxyphenyl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2H-indol-2-one

A. Synthesis of 3-(4,5-dichloro-2-hydroxyphenyl)-3-hydroxy-1-pentyl-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 1C, and making non-critical variations to replace 4-bromo-1-pentyl-1H-indole-2,3-dione with 1-pentyl-1H-indole-2,3-dione, and 1,3-benzodioxol-5-ol with 3,4-dichlorophenol, the title compound was obtained (26%): ^1H NMR (300 MHz, CDCl_3) δ 9.60 (s, 1H), 7.50-7.40 (m, 2H), 7.22 (td, 1H), 7.11 (s, 1H), 6.95 (d, 1H), 6.86 (s, 1H), 4.31-4.12 (br, 1H), 3.79-3.59 (m, 2H), 1.76-1.62 (m, 2H), 1.40-1.27 (m, 4H), 0.88 (t, 3H); MS (ES+) m/z 363 (M - 17), 403 (M + 23).

B. Synthesis of 3-(4,5-dichloro-2-hydroxyphenyl)-1-pentyl-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 15B, and making non-critical variations to replace 3-(5-bromo-2-hydroxyphenyl)-3-hydroxy-1-pentyl-1,3-dihydro-2H-indol-2-one with 3-(4,5-dichloro-2-hydroxyphenyl)-3-hydroxy-1-pentyl-1,3-dihydro-2H-indol-2-one, the title compound was obtained (86%): ^1H NMR (300 MHz, CDCl_3) δ 10.0-9.50 (br, 1H), 7.42 (t, 1H), 7.32 (d, 1H), 7.22 (td, 1H), 7.09 (s, 1H), 6.95 (d, 1H), 6.93 (s, 1H), 5.04 (s, 1H), 3.77-3.68 (m, 2H), 1.77-1.62 (m, 2H), 1.40-1.27 (m, 4H), 0.88 (t, 3H); MS (ES+) m/z 348 (M + 1).

C. Synthesis of 3-(4,5-dichloro-2-hydroxyphenyl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 1E, and making non-critical variations to replace 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one with 3-(4,5-dichloro-2-hydroxyphenyl)-1-pentyl-1,3-dihydro-2H-indol-2-one, the title compound was obtained: MS (ES+) m/z 376 (M - 17), 416 (M +

23).

PREPARATION 19

Synthesis of 3-(hydroxymethyl)-3-[2-hydroxy-5-(trifluoromethyl)phenyl]-1-pentyl-1,3-dihydro-2*H*-indol-2-one

5 A. Synthesis of 3-hydroxy-3-[2-hydroxy-5-(trifluoromethyl)phenyl]-1-pentyl-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 1C, and making non-critical variations to replace 4-bromo-1-pentyl-1*H*-indole-2,3-dione with 1-pentyl-1*H*-indole-2,3-dione, and 1,3-benzodioxol-5-ol with α , α , α -trifluorocresol, the title
10 compound was obtained (46%): ¹H NMR (300 MHz, CDCl₃) δ 9.75 (s, 1H), 7.50-7.39 (m, 3H), 7.21 (td, 1H), 7.10-7.02 (m, 2H), 6.96 (d, 1H), 4.26 (s, 1H), 3.82-3.59 (m, 2H), 1.77-1.63 (m, 2H), 1.40-1.27 (m, 4H), 0.88 (t, 3H); MS (ES+) *m/z* 362 (M - 17), 402 (M + 23).

15 B. Synthesis of 3-[2-hydroxy-5-(trifluoromethyl)phenyl]-1-pentyl-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 15B, and making non-critical variations to replace 3-(5-bromo-2-hydroxyphenyl)-3-hydroxy-1-pentyl-1,3-dihydro-2*H*-indol-2-one with 3-hydroxy-3-[2-hydroxy-5-(trifluoromethyl)phenyl]-1-pentyl-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained (78%): ¹H NMR (300
20 MHz, CDCl₃) δ 8.20-8.00 (br, 1H), 7.43-7.14 (m, 5H), 7.02 (d, 1H), 6.95 (d, 1H), 5.11(s, 1H), 3.82-3.72 (m, 2H), 1.79-1.66 (m, 2H), 1.40-1.27 (m, 4H), 0.88 (t, 3H); MS (ES+) *m/z* 364 (M + 1).

25 C. Synthesis of 3-(hydroxymethyl)-3-[2-hydroxy-5-(trifluoromethyl)phenyl]-1-pentyl-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 1E, and making non-critical variations to replace 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one with 3-[2-hydroxy-5-(trifluoromethyl)phenyl]-1-pentyl-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained: MS (ES+) *m/z* 376 (M - 17), 416 (M + 23).

PREPARATION 20

Synthesis of 3-(2-hydroxy-4-methoxyphenyl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one

A. Synthesis of 3-(5-bromo-2-hydroxy-4-methoxyphenyl)-3-hydroxy-1-pentyl-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 1C, and making non-critical variations to replace 4-bromo-1-pentyl-1*H*-indole-2,3-dione with 1-pentyl-1*H*-indole-2,3-dione, and 1,3-benzodioxol-5-ol with 4-bromo-3-methoxyphenol, the title compound was obtained (48%): ¹H NMR (300 MHz, CDCl₃) δ 9.85 (s, 1H), 7.52-7.38 (m, 2H), 7.22 (td, 1H), 6.94 (d, 1H), 6.89 (s, 1H), 6.63 (s, 1H), 4.13-4.03 (br, 1H), 3.86 (s, 3H), 3.80-3.57 (m, 2H), 1.75-1.63 (m, 2H), 1.40-1.25 (m, 4H), 0.88 (t, 3H); MS (ES+) *m/z* 402 (M - 17), 404 (M - 17), 442 (M + 23), 444 (M + 23).

B. Synthesis of 3-(2-hydroxy-4-methoxyphenyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 15B, and making non-critical variations to replace 3-(5-bromo-2-hydroxyphenyl)-3-hydroxy-1-pentyl-1,3-dihydro-2*H*-indol-2-one with 3-(5-bromo-2-hydroxy-4-methoxyphenyl)-3-hydroxy-1-pentyl-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained (83%): ¹H NMR (300 MHz, CDCl₃) δ 9.78-9.20 (br, 1H), 7.43-7.31 (m, 2H), 7.19 (t, 1H), 6.97 (d, 1H), 6.79 (d, 1H), 6.70-6.64 (m, 1H), 6.38 (dd, 1H), 5.02 (s, 1H), 3.77 (s, 3H), 3.70 (t, 2H), 1.75-1.63 (m, 2H), 1.40-1.25 (m, 4H), 0.87 (t, 3H); MS (ES+) *m/z* 326 (M + 1).

C. Synthesis of 3-(2-hydroxy-4-methoxyphenyl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 1E, and making non-critical variations to replace 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one with 3-(2-hydroxy-4-methoxyphenyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained (41%): ¹H NMR (300 MHz, CDCl₃) δ 10.79 (s, 1H), 7.51-7.37 (m, 2H), 7.26 (td, 1H), 6.99 (d, 1H), 6.95 (d, 1H), 6.59 (d, 1H), 6.34 (dd, 1H), 4.67 (d, 1H), 4.14 (d, 1H), 3.76 (s, 3H), 3.78-3.69 (m, 2H), 1.75-1.63 (m, 2H), 1.40-1.25 (m, 4H), 0.87 (t, 3H); MS (ES+) *m/z* 338 (M - 17), 378 (M + 23).

PREPARATION 21

Synthesis of ethyl [3-(6-hydroxy-2,3-dihydro-1*H*-inden-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate

A. Synthesis of ethyl [3-hydroxy-3-(6-hydroxy-2,3-dihydro-1*H*-inden-5-yl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate

Following the procedure as described in PREPARATION 1C, and making non-critical variations to replace 4-bromo-1-pentyl-1*H*-indole-2,3-dione with ethyl (2,3-dioxo-2,3-dihydro-1*H*-indol-1-yl)acetate, and 1,3-benzodioxol-5-ol with 5-indanol, the title compound was obtained (84%): ¹H NMR (300 MHz, CDCl₃) δ 8.76 (s, 1H), 7.55 (d, 1H), 7.38 (td, 1H), 7.20 (t, 1H), 6.9 (s, 1H), 6.80 (d, 1H), 6.65 (s, 1H), 4.45 (ABq, 2H), 4.32-4.25 (br, 1H), 4.20 (q, 2H), 2.83 (t, 2H), 2.74-2.65 (m, 2H), 2.06-1.94 (m, 2H), 1.27 (t, 3H); MS (ES+) *m/z* 350 (M - 17), 390 (M + 23).

B. Synthesis of ethyl [3-(6-hydroxy-2,3-dihydro-1*H*-inden-5-yl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate

Following the procedure as described in PREPARATION 15B, and making non-critical variations to replace 3-(5-bromo-2-hydroxyphenyl)-3-hydroxy-1-pentyl-1,3-dihydro-2*H*-indol-2-one with ethyl [3-hydroxy-3-(6-hydroxy-2,3-dihydro-1*H*-inden-5-yl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate, the title compound was obtained: ¹H NMR (300 MHz, CDCl₃) δ 8.50-7.90 (br, 1H), 7.40-7.32 (m, 2H), 7.38 (td, 1H), 6.94 (s, 1H), 6.84 (d, 1H), 6.75 (s, 1H), 5.16 (s, 1H), 4.48 (ABq, 2H), 4.21 (q, 2H), 2.85 (t, 2H), 2.81-2.61 (m, 2H), 2.09-1.92 (m, 2H), 1.25 (t, 3H); MS (ES+) *m/z* 352 (M + 1).

C. Synthesis of ethyl [3-(6-hydroxy-2,3-dihydro-1*H*-inden-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate

Following the procedure as described in PREPARATION 1E, and making non-critical variations to replace 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one with ethyl [3-(6-hydroxy-2,3-dihydro-1*H*-inden-5-yl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate, the title compound was obtained: MS (ES+) *m/z* 364 (M - 17), 404 (M + 23).

PREPARATION 22

Synthesis of ethyl [3-(hydroxymethyl)-3-(3-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate

A. Synthesis of ethyl [3-hydroxy-3-(3-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate

Following the procedure as described in PREPARATION 1C, and making non-

critical variations to replace 4-bromo-1-pentyl-1*H*-indole-2,3-dione with ethyl (2,3-dioxo-2,3-dihydro-1*H*-indol-1-yl)acetate, and 1,3-benzodioxol-5-ol with 5, 6, 7, 8-tetrahydronaphthalen-2-ol, the title compound was obtained (81%): ¹H NMR (300 MHz, CDCl₃) δ 8.61 (s, 1H), 7.54 (dd, 1H), 7.38 (td, 1H), 7.20 (t, 1H), 6.80 (d, 1H), 6.76 (s, 1H), 6.50 (s, 1H), 4.45 (ABq, 2H), 4.21 (q, 2H), 4.18-4.14 (br, 1H), 2.73-2.47 (m, 4H), 1.77-1.63 (m, 4H), 1.24 (t, 3H); MS (ES+) *m/z* 364 (M - 17), 404 (M + 23)

B. Synthesis of ethyl [3-(3-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate

Following the procedure as described in PREPARATION 15B, and making non-critical variations to replace 3-(5-bromo-2-hydroxyphenyl)-3-hydroxy-1-pentyl-1,3-dihydro-2*H*-indol-2-one with ethyl [3-hydroxy-3-(3-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate, the title compound was obtained: ¹H NMR (300 MHz, CDCl₃) δ 7.42-7.32 (m, 2H), 7.20 (t, 1H), 6.84 (d, 1H), 6.78 (s, 1H), 6.61 (s, 1H), 5.12 (s, 1H), 4.47 (ABq, 2H), 4.21 (q, 2H), 2.76-2.44 (m, 4H), 1.78-1.64 (m, 4H), 1.24 (t, 3H); MS (ES+) *m/z* 366 (M + 1).

C. Synthesis of ethyl [3-(hydroxymethyl)-3-(3-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate

Following the procedure as described in PREPARATION 1E, and making non-critical variations to replace 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one with ethyl [3-(3-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate, the title compound was obtained: MS (ES+) *m/z* 378 (M-17), 418 (M + 23).

PREPARATION 23

Synthesis of ethyl [4-bromo-3-(4,5-difluoro-2-hydroxyphenyl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate

A. Synthesis of ethyl (4-bromo-2,3-dioxo-2,3-dihydro-1*H*-indol-1-yl)acetate

Following the procedure as described in PREPARATION 2A, and making non-critical variations to replace isatin with 4-bromoisatin and (2-bromoethyl)cyclopropane with ethyl bromoacetate, the title compound was obtained as a yellow solid (68%): ¹H NMR (300 MHz, CDCl₃) δ 7.39 (t, 1H), 7.27 (dd, 1H), 6.71 (dd, 1H), 4.47 (s, 2H), 4.23 (q, 2H), 1.27 (t, 3H); MS (ES+) *m/z* 312 (M + 1), 314 (M + 1), 334 (M + 23), 336 (M + 23).

B. Synthesis of ethyl [4-bromo-3-(4,5-difluoro-2-hydroxyphenyl)-3-hydroxy-2-oxo-2,3-dihydro-1H-indol-1-yl]acetate

Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1-(2-cyclopropylethyl)-1H-indole-2,3-dione with ethyl (4-bromo-2,3-dioxo-2,3-dihydro-1H-indol-1-yl)acetate and 1,3-benzodioxol-5-ol with 3,4-difluorophenol, the title compound was obtained as a white solid (42%); MS (ES+) *m/z* 424 (M - 17), 426 (M - 17), 464 (M + 23), 466 (M + 23).

C. Synthesis of ethyl [4-bromo-3-(4,5-difluoro-2-hydroxyphenyl)-2-oxo-2,3-dihydro-1H-indol-1-yl]acetate

A mixture of ethyl [4-bromo-3-(4,5-difluoro-2-hydroxyphenyl)-3-hydroxy-2-oxo-2,3-dihydro-1H-indol-1-yl]acetate (0.90 g, 2.00 mmol), triethylsilane (2.00 mL, 12.2 mmol) and trifluoroacetic acid (0.94 mL, 12.2 mmol) was heated at 90 °C for two days. After cooling down to ambient temperature, the mixture was diluted with ethyl acetate (200 mL), washed with water, dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography (ethyl acetate/hexanes, 1/3) to give the title compound (0.37 g, 43%); ¹H NMR (300 MHz, CDCl₃) δ 7.35-7.22 (m, 3H), 6.82-6.71 (m, 2H), 6.52 (t, 1H), 5.10 (s, 1H), 4.45 (s, 2H), 4.21 (q, 2H), 1.23 (t, 3H); MS (ES+) *m/z* 426.4 (M + 1), 428.4 (M + 1).

D. Synthesis of ethyl [4-bromo-3-(4,5-difluoro-2-hydroxyphenyl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1H-indol-1-yl]acetate

Following the procedure as described in PREPARATION 1E, and making non-critical variations to replace 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one with ethyl [4-bromo-3-(4,5-difluoro-2-hydroxyphenyl)-2-oxo-2,3-dihydro-1H-indol-1-yl]acetate, the title compound was obtained (83%); MS (ES+) *m/z* 456.3 (M + 1), 458.3 (M + 1).

PREPARATION 24

Synthesis of ethyl [4-bromo-3-(6-hydroxy-2,2-dimethyl-2,3-dihydro-1-benzofuran-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1H-indol-1-yl]acetate

A. Synthesis of 6-(benzyloxy)-2,2-dimethylbenzofuran-3(2H)-one

To a solution of 6-(benzyloxy)benzofuran-3(2H)-one (Adams, J. L., et al., *J. Med. Chem.* (1996), 39(26):5035-46) (1.60 g, 6.67 mmol) in DMF (50.0 mL) were added sodium hydride (0.59 g, 14.7 mmol) and iodomethane (1.46 mL, 23.3 mmol) at 0 °C. The reaction mixture was stirred at ambient temperature for 16 h and quenched

with saturated ammonium chloride (50.0 mL). The aqueous mixture was extracted with ethyl acetate (3 x 50.0 mL). The combined organic layers were dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography (ethyl acetate/hexane, 1/10) to give the title compound (0.85 g, 47%): ¹H NMR (300 MHz, CDCl₃) δ 7.55 (d, 1H), 7.44-7.30 (m, 5H), 6.69 (dd, 1H), 6.54 (d, 1H), 5.10 (s, 2H), 1.43 (s, 6H); MS (ES+) *m/z* 269.5 (M + 1).

B. Synthesis of 2,2-dimethyl-2,3-dihydrobenzofuran-6-ol

To a solution of 6-(benzyloxy)-2,2-dimethylbenzofuran-3(2H)-one (0.85 g, 3.20 mmol) in methanol (100 mL) was added palladium hydroxide (0.22 g, 20 wt. % loading, 0.32 mmol). The resulting mixture was hydrogenated for 16 hours under 60 psi of hydrogen. The reaction mixture was filtered through celite, washed with methanol. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography (ethyl acetate/hexane, 1/5) to give the title compound (0.46 g, 88%): ¹H NMR (300 MHz, CDCl₃) δ 6.92 (d, 1H), 6.30-6.21 (m, 2H), 4.77 (s, 1H), 2.90 (s, 2H), 1.44 (s, 6H).

C. Synthesis of ethyl [4-bromo-3-hydroxy-3-(6-hydroxy-2,2-dimethyl-2,3-dihydro-1-benzofuran-5-yl)-2-oxo-2,3-dihydro-1H-indol-1-yl]acetate

Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1-(2-cyclopropylethyl)-1H-indole-2,3-dione with ethyl (4-bromo-2,3-dioxo-2,3-dihydro-1H-indol-1-yl)acetate and 1,3-benzodioxol-5-ol with 2,2-dimethyl-2,3-dihydrobenzofuran-6-ol, the title compound was obtained: MS (ES+) *m/z* 498.5 (M + 23), 500.5 (M + 23).

D. Synthesis of ethyl [4-bromo-3-(6-hydroxy-2,2-dimethyl-2,3-dihydro-1-benzofuran-5-yl)-2-oxo-2,3-dihydro-1H-indol-1-yl]acetate

A mixture of ethyl [4-bromo-3-hydroxy-3-(6-hydroxy-2,2-dimethyl-2,3-dihydro-1-benzofuran-5-yl)-2-oxo-2,3-dihydro-1H-indol-1-yl]acetate (1.32 g, 2.80 mmol), triethylsilane (2.00 mL, 12.2 mmol) and trifluoroacetic acid (0.94 mL, 12.2 mmol) in dichloromethane (50.0 mL) was stirred at 35 °C for 3 hours. The mixture was diluted with dichloromethane (100 mL), washed with water, dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography (ethyl acetate/hexane, 1/3) to give the title compound (1.04 g, 81%): ¹H NMR (300 MHz, CDCl₃) δ 7.32-7.15 (m, 2H), 6.74 (d, 1H), 6.50-6.36 (br, 2H), 5.04 (s, 1H), 4.51-4.34 (m, 2H), 4.25-4.14 (m, 2H), 2.92-2.69 (m, 2H), 1.43 (s, 3H), 1.37 (s, 3H), 1.23 (t, 3H); MS (ES+) *m/z* 460.5 (M + 1), 462.5 (M +

1).

E. Synthesis of ethyl [4-bromo-3-(6-hydroxy-2,2-dimethyl-2,3-dihydro-1-benzofuran-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1H-indol-1-yl]acetate

Following the procedure as described in PREPARATION 1E, and making non-critical variations to replace 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one with ethyl [4-bromo-3-(6-hydroxy-2,2-dimethyl-2,3-dihydro-1-benzofuran-5-yl)-2-oxo-2,3-dihydro-1H-indol-1-yl]acetate, the title compound was obtained (25%): MS (ES+) m/z 490.5 (M + 1), 492.5 (M + 1).

PREPARATION 25

10 Synthesis of 3,3-dimethyl-2,3-dihydro-1-benzofuran-6-ol

A. Synthesis of 4-(benzyloxy)-1-bromo-2-(2-methylallyloxy)benzene

To a solution of 5-(benzyloxy)-2-bromophenol (Simas, A.B.C., et al, *Synthesis*, (1999):1017-21) (8.15 g, 29.3 mmol) in DMF (150 mL) was added potassium carbonate (4.46 g, 32.2 mmol) slowly at 0 °C. The mixture was stirred at ambient temperature for half an hour, followed by the addition of 3-bromo-2-methylpropene (3.35 mL, 32.2 mmol) during half an hour at 0 °C. The mixture was stirred at ambient temperature overnight and quenched with saturated ammonium chloride (50 mL). The aqueous mixture was extracted with ethyl acetate (3 x 200 mL). The combined organic layers was dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo*. The residue was subjected to column chromatography (ethyl acetate/hexane, 1/20) to give the title compound (10.0 g, 94%): ¹H NMR (300 MHz, CDCl₃) δ 7.43-7.29 (m, 5H), 6.53 (d, 1H), 6.45 (dd, 1H), 5.15-4.94 (m, 4H), 4.43 (s, 2H), 1.82 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 159.1, 155.6, 140.1, 136.5, 133.1, 128.6, 128.1, 127.5, 112.9, 107.2, 103.3, 102.0, 72.4, 70.3, 19.3.

25 B. Synthesis of 6-(benzyloxy)-3,3-dimethyl-2,3-dihydrobenzofuran

To a solution of 4-(benzyloxy)-1-bromo-2-(2-methylallyloxy)benzene (5.00 g, 15.1 mmol) in benzene (400 mL) was added tributyltin hydride (7.42 mL, 27.2 mmol) and benzoyl peroxide (0.70 g, 2.90 mmol) at 0 °C. The resulting mixture was refluxed at 100 °C overnight. After cooling down to ambient temperature, the mixture was washed with water, dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography (ethyl acetate/hexane, 1/20) to give the title compound (3.48 g, 91%): MS (ES+) m/z 255.6 (M + 1).

C. Synthesis of 3,3-dimethyl-2,3-dihydro-1-benzofuran-6-ol

To a solution of 6-(benzyloxy)-3,3-dimethyl-2,3-dihydrobenzofuran (3.48 g, 13.7 mmol) in methanol (200 mL) was added Pd/C (1.45 g) and the mixture was hydrogenated under 40 psi of hydrogen overnight. The reaction mixture was filtered through celite, washed with methanol. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography (ethyl acetate/hexane, 1/7) to give the title compound (1.66 g, 74%): MS (ES+) *m/z* 165.4 (M + 1).

PREPARATION 26

Synthesis of 1-(diphenylmethyl)-3-(5-hydroxy-2,3-dihydro-1-benzofuran-6-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one

A. Synthesis of 1-(diphenylmethyl)-3-hydroxy-3-(5-hydroxy-2,3-dihydro-1-benzofuran-6-yl)-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1,3-benzodioxol-5-ol with 2,3-dihydrobenzofuran-5-ol, (Alabaster, R.J., et al.; *Synthesis* (1988), 12:950-2) and 1-(2-cyclopropylethyl)-1*H*-indole-2,3-dione with 1-(diphenylmethyl)-1*H*-indole-2,3-dione, the title compound was obtained: MS (ES+) *m/z* 472.2 (M + 23).

B. Synthesis of 1-(diphenylmethyl)-3-(5-hydroxy-2,3-dihydro-1-benzofuran-6-yl)-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 2C, and making non-critical variations to replace 1-(2-cyclopropylethyl)-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2*H*-indol-2-one with 1-(diphenylmethyl)-3-hydroxy-3-(5-hydroxy-2,3-dihydro-1-benzofuran-6-yl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained: MS (ES+) *m/z* 434.4 (M + 1).

C. Synthesis of 1-(diphenylmethyl)-3-(5-hydroxy-2,3-dihydro-1-benzofuran-6-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one

To a solution of 1-(diphenylmethyl)-3-(5-hydroxy-2,3-dihydro-1-benzofuran-6-yl)-1,3-dihydro-2*H*-indol-2-one (1.01 g, 2.30 mmol) in THF (50.0 mL) was added paraformaldehyde (1.00 g, 30.0 mmol). Argon was bubbled through the reaction mixture for one hour followed by the addition of diisopropylamine (1.00 g, 10.0 mmol) at 0 °C. The reaction mixture was stirred at ambient temperature for 20 hours and diluted with ethyl acetate (100 mL). The resulting mixture was washed with water (2 x 50.0 mL), dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness to give 0.67 g (65%) of the title compound: MS (ES+) *m/z* 486.4 (M

+ 23).

PREPARATION 27

Synthesis of 3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-4-methoxy-1-[[5-(trifluoromethyl)-2-furyl]methyl]-1,3-dihydro-2*H*-indol-2-one

5 A. Synthesis of ethyl 2-(2-(*tert*-butoxycarbonylamino)-6-methoxyphenyl)-2-oxoacetate

To a solution of *tert*-butyl 3-methoxyphenylcarbamate (25.6 g, 0.11 mol) in THF (300 mL) was added *n*-BuLi (0.25 mol, 1.6 M solution in pentane) at -78 °C. The resulted solution was stirred at 0 °C for 3 hours and re-cooled to -78 °C followed by the
10 addition of diethyl oxalate (20.1 g, 0.14 mol). The mixture was stirred at -78 °C for 45 min and at ambient temperature for one hour, and quenched with 1 N HCl. The mixture was extracted with ether. The organic solution was dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography to give 3.70 g (27% based on recovered starting
15 material) of the title compound: MS (ES+) *m/z* 324.3 (*M* + 1).

 B. Synthesis of 4-methoxy-1*H*-indole-2,3-dione

A mixture of ethyl 2-(2-(*tert*-butoxycarbonylamino)-6-methoxyphenyl)-2-oxoacetate (3.70 g, 110 mmol) and 10% H₂SO₄ (100 mL) was heated at 100 °C for 10 hours. After cooling down to ambient temperature, the reaction mixture was extracted
20 with ether (3 x 100 mL). The combined ether solution was washed with water (2 x 50.0 mL), dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography to give 0.37 g (19%) of the title compound: MS (ES+) *m/z* 200.1 (*M* + 23).

 C. Synthesis of 4-methoxy-1-[[5-(trifluoromethyl)-2-furyl]methyl]-1*H*-indole-2,3-dione
25 dione

Following the procedure as described in PREPARATION 1A, and making non-critical variations to replace 4-bromoindole with 4-methoxy-1*H*-indole-2,3-dione, and 1-bromopentane with 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound was obtained (26%): MS (ES+) *m/z* 348.2 (*M* + 23).

30 D. Synthesis of 3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-4-methoxy-1-[[5-(trifluoromethyl)-2-furyl]methyl]-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1-(2-cyclopropylethyl)-1*H*-indole-2,3-dione with 4-methoxy-1-[[5-(trifluoromethyl)-2-furyl]methyl]-1*H*-indole-2,3-dione, the title compound was

obtained (56%): MS (ES+) m/z 486.4 ($M + 23$).

E. Synthesis of 3-(6-hydroxy-1,3-benzodioxol-5-yl)-4-methoxy-1-[[5-(trifluoromethyl)-2-furyl]methyl]-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 2C, and making non-critical variations to replace 1-(2-cyclopropylethyl)-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2H-indol-2-one with 3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-4-methoxy-1-[[5-(trifluoromethyl)-2-furyl]methyl]-1,3-dihydro-2H-indol-2-one, the title compound was obtained (86%): MS (ES+) m/z 448.4 ($M + 1$).

F. Synthesis of 3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-4-methoxy-1-[[5-(trifluoromethyl)-2-furyl]methyl]-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 26C, and making non-critical variations to replace 1-(diphenylmethyl)-3-(5-hydroxy-2,3-dihydro-1-benzofuran-6-yl)-1,3-dihydro-2H-indol-2-one with 3-(6-hydroxy-1,3-benzodioxol-5-yl)-4-methoxy-1-[[5-(trifluoromethyl)-2-furyl]methyl]-1,3-dihydro-2H-indol-2-one, the title compound was obtained (64%): MS (ES+) m/z 500.4 ($M + 23$).

PREPARATION 28

Synthesis of 4,7-dichloro-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2H-indol-2-one

A. Synthesis of 4,7-dichloro-1-pentyl-1H-indole-2,3-dione

To a mixture of sodium hydride (0.17 g, 6.94 mmol, 60% dispersion in mineral oil) in anhydrous *N,N*-dimethylformamide (5.00 mL) was added a solution of 4,7-dichloro-1H-indole-2,3-dione (1.00 g, 4.60 mmol) in *N,N*-dimethylformamide (5.00 mL) at 0 °C. The brown reaction mixture was stirred for 0.5 h followed by the addition of a solution of 1-bromopentane (0.84 g, 5.55 mmol) in anhydrous *N,N*-dimethylformamide (5.00 mL). The reaction mixture was stirred at ambient temperature for 16 h and poured into wet ethyl ether (30.0 mL). After the organic layer was separated, it was washed with water (2 x 20.0 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The gummy residue was dried under vacuum and the solid was triturated with ether to give the title compound (0.98 g, 98%): MS (ES+) m/z 286.2 ($M + 1$).

B. Synthesis of 4,7-dichloro-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1-(2-cyclopropylethyl)-1H-indole-2,3-dione with 4,7-

dichloro-1-pentyl-1*H*-indole-2,3-dione, the title compound was obtained (68%) as a white solid: ¹H NMR (300 MHz, CDCl₃) δ 8.61 (s, br, 1H), 7.26 (t, 1H), 7.03 (d, 1H), 6.52 (s, 1H), 6.12 (s, 1H), 5.86 (dd, 2H), 4.21 (s, br, 1H), 4.01-3.96 (m, 2H), 1.73-1.58 (m, 2H), 1.34-1.21 (m, 4H), 0.84 (t, 3H); MS (ES+) *m/z* 408.2 (*M* - 17).

5 C. Synthesis of 4,7-dichloro-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 2C, and making non-critical variations to replace 1-(2-cyclopropylethyl)-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2*H*-indol-2-one with 4,7-dichloro-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one, the title compound was
10 obtained (72%) as a white solid: ¹H NMR (300 MHz, CDCl₃) δ 7.27-7.23 (m, 1H), 7.03 (d, 1H), 6.55 (s, 1H), 6.04 (s, 1H), 5.84 (dd, 2H), 5.03 (s, 1H), 4.09-3.99 (m, 2H), 1.72-1.62 (m, 2H), 1.33-1.24 (m, 4H), 0.86 (t, 3H); MS (ES+) *m/z* 409.2 (*M* + 1).

15 D. Synthesis of 4,7-dichloro-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 1E, and making non-critical variations to replace 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one with 4,7-dichloro-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained (94%) as a gummy solid:
20 MS (ES+) *m/z* 439.3 (*M* + 1).

PREPARATION 29

Synthesis of ethyl 2-(4-chloro-3-(6-hydroxy-2,3-dihydrobenzofuran-5-yl)-3-(hydroxymethyl)-2-oxoindolin-1-yl)acetate

A. Synthesis of ethyl (4-chloro-2,3-dioxo-2,3-dihydro-1*H*-indol-1-yl)acetate

25 Following the procedure as described in PREPARATION 2A, and making non-critical variations to replace isatin with 4-chloro-1*H*-indole-2,3-dione, and (2-bromoethyl)cyclopropane with ethyl bromoacetate, the title compound was obtained (95%) as a colorless solid: ¹H NMR (300 MHz, CDCl₃) δ 7.48 (t, 1H), 7.08 (d, 1H), 6.67 (d, 1H), 4.47 (s, 2H), 4.23 (q, 2H), 1.27 (t, 3H); MS (ES+) *m/z* 268.6 (*M* + 1).

30 B. Synthesis of ethyl [4-chloro-3-hydroxy-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate

Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1-(2-cyclopropylethyl)-1*H*-indole-2,3-dione with ethyl (4-chloro-2,3-dioxo-2,3-dihydro-1*H*-indol-1-yl)acetate, the title compound was obtained

(75%) as a white solid: ^1H NMR (300 MHz, CDCl_3) δ 8.70 (br, 1H), 7.31 (t, 1H), 7.12 (d, 1H), 6.68 (d, 1H), 6.46 (d, 2H), 4.53-4.46 (m, 2H), 4.18 (q, 2H), 3.08-2.88 (m, 2H), 1.23 (t, 3H); MS (ES+) m/z 387.8 (M - 17).

C. Synthesis ethyl [4-chloro-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-2-oxo-2,3-dihydro-1H-indol-1-yl]acetate

Following the procedure as described in PREPARATION 2C, and making non-critical variations to replace 1-(2-cyclopropylethyl)-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2H-indol-2-one with ethyl [4-chloro-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-2-oxo-2,3-dihydro-1H-indol-1-yl]acetate, the title compound was obtained (75%) as a white solid: ^1H NMR (300 MHz, CDCl_3) δ 7.33-7.27 (m, 2H), 7.12 (d, 1H), 6.71 (d, 1H), 6.50-6.48 (m, 1H), 5.10 (s, 1H), 4.54-4.42 (m, 4H), 4.19 (q, 2H), 3.11-2.90 (m, 2H), 1.23 (t, 3H); MS (ES+) m/z 388.8 (M + 1).

D. Synthesis of ethyl [4-chloro-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1H-indol-1-yl]acetate

Following the procedure as described in PREPARATION 1E, and making non-critical variations to replace 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one with ethyl [4-chloro-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-2-oxo-2,3-dihydro-1H-indol-1-yl]acetate, the title compound was obtained (99%) as a gummy solid: MS (ES+) m/z 418.7 (M + 1).

20 PREPARATION 30

Synthesis of 3-hydroxy-3-[6-(hydroxymethyl)-1,3-benzodioxol-5-yl]-1-pentyl-1,3-dihydro-2H-indol-2-one

To a solution of (6-bromo-1,3-benzodioxol-5-yl)methanol (Mann, J., et al, *J. Chem. Soc. Perkin Trans. 1* (1984):2081-8) (1.27 g, 5.50 mmol) in THF (45.0 mL) was added n-BuLi (5.00 mL, 2.0 M, 10.0 mmol) dropwise at -75 °C. The reaction mixture was stirred at -75 °C for 45 min followed by the addition of a solution of 1-pentyl-1H-indole-2,3-dione (1.00 g, 4.60 mmol) in THF (20.0 mL) at -75 °C. The resulting mixture was stirred at ambient temperature for 12 hrs and quenched with ammonium chloride solution (5.00 mL). More ethyl acetate and water were added and separated. The organic layer was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography eluting with 50% EtOAc:Hexanes to yield the title compound (0.29 g, 25%) as a solid: ^1H NMR (300 MHz, CDCl_3) δ 7.38-7.24 (m, 2H), 7.11 (t, 1H), 6.91 (d, 1H), 6.81 (s, 1H), 6.43 (s, 1H), 5.90-5.87 (m, 2H), 4.77 (dd, 2H), 3.75-3.56 (m, 2H), 1.75-1.58 (m, 2H), 1.26-1.35 (m, 2H), 0.89-0.83 (m, 3H); ^{13}C NMR (75 MHz,

CDCl₃) δ 177.8, 147.4, 147.2, 142.8, 133.5, 132.2, 131.1, 130.1, 125.3, 123.8, 111.4, 109.2, 108.1, 101.5, 79.5, 64.7, 40.4, 29.0, 26.8, 22.3, 13.9; MS (ES+) m/z 352.1 (M - 17).

PREPARATION 31

- 5 Synthesis of ethyl [1-hexyl-3-(6-hydroxy-1,3-benzodioxol-5-yl)-2-oxo-2,3-dihydro-1*H*-indol-3-yl]acetate

A. Synthesis of 1-hexyl-1*H*-indole-2,3-dione

Following the procedure as described in PREPARATION 2A, and making non-critical variations to replace (2-bromoethyl)cyclopropane with n-bromohexane, the title
10 compound was obtained (90%) as a viscous gum: ¹H NMR (300 MHz, CDCl₃) δ 7.58-7.51 (m, 2H), 7.08 (t, 1H), 6.87 (d, 1H), 3.68 (t, 2H), 1.71-1.62 (m, 2H), 1.41-1.22 (m, 6H), 0.85 (t, 3H).

B. Synthesis of 1-hexyl-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2*H*-indol-2-one

15 Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1-(2-cyclopropylethyl)-1*H*-indole-2,3-dione with 1-hexyl-1*H*-indole-2,3-dione, the title compound was obtained (53%) as a colorless solid: ¹H NMR (300 MHz, CDCl₃) δ 9.44 (br, 1H), 7.47-7.44 (m, 1H), 7.40-7.34 (m, 1H), 7.17 (t, 1H), 6.89 (d, 1H), 6.55 (s, 1H), 6.21 (s, 1H), 5.84-5.82 (m, 2H), 4.58 (br, 1H), 3.71-3.56 (m,
20 2H), 1.67-1.62 (m, 2H), 1.32-1.21 (m, 6H), 0.84-0.80 (m, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 179.0, 152.3, 148.8, 142.5, 141.3, 130.3, 129.2, 126.1, 123.7, 117.2, 109.5, 106.8, 101.9, 101.4, 79.2, 40.4, 31.3, 27.1, 26.4, 22.4, 13.9; MS (ES+) m/z 352.5 (M - 17).

C. Synthesis of 1-hexyl-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2*H*-indol-2-one

25 Following the procedure as described in PREPARATION 2C, and making non-critical variations to replace 1-(2-cyclopropylethyl)-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2*H*-indol-2-one with 1-hexyl-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained (98%)
30 as a white solid: ¹H NMR (300 MHz, CDCl₃) δ 7.38-7.13 (m, 3H), 6.94 (d, 1H), 6.60 (s, 1H), 6.32 (s, 1H), 5.84 (dd, 2H), 5.02 (s, 1H), 3.74-3.63 (m, 2H), 1.70-1.61 (m, 2H), 1.37-1.19 (m, 6H), 0.83 (t, 3H); MS (ES+) m/z 354.2 (M + 1).

D. Synthesis of ethyl [1-hexyl-3-(6-hydroxy-1,3-benzodioxol-5-yl)-2-oxo-2,3-dihydro-1*H*-indol-3-yl]acetate

To a solution of diisopropylamine (1.14 g, 11.0 mmol) in THF (10.0 mL) was added n-butyl lithium (7.00 mL, 11.0 mmol, 1.6 M solution in hexane) at -75 °C. The resulting mixture was stirred at -75 °C for half an hour and added slowly to a solution of 1-hexyl-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2*H*-indol-2-one in THF (20.0 mL) at -75 °C. After stirring at -75 °C for another half an hour, ethyl bromoacetate was added. The mixture was stirred at ambient temperature for 18 hrs and quenched with saturated ammonium chloride solution. The organic solvent was removed *in vacuo* and the aqueous residue was diluted with ethyl acetate (100 mL). The organic layer was washed with saturated ammonium chloride (25.0 mL), brine (50.0 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography eluting with 40% EtOAc/Hexanes to yield the title compound (0.19 g, 8%) as an oil: MS (ES+) *m/z* 440.5 (*M* + 1).

PREPARATION 32

Synthesis of 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one

A. Synthesis of 4-bromo-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1-(2-cyclopropylethyl)-1*H*-indole-2,3-dione with 4-bromoisatin, the title compound was obtained (95%) as a beige solid: ¹H NMR (300 MHz, DMSO-*d*₆) δ 10.40 (s, 1H), 9.09 (s, 1H), 7.22 (s, 1H), 7.04 (t, 1H), 6.90 (d, 1H), 6.75 (d, 1H), 6.43 (br, 1H), 6.21 (s, 1H), 5.88 (d, 2H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 178.0, 148.7, 147.0, 145.8, 139.5, 131.3, 130.8, 125.4, 118.8, 118.4, 109.4, 108.9, 101.0, 97.4, 76.6; MS (ES+) *m/z* 366.4 (*M* + 1), 364.5 (*M* + 1).

B. Synthesis of 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 1D, and making non-critical variations to replace 4-bromo-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one with 4-bromo-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained (95%) as a cream solid: MS (ES+) *m/z* 348.5 (*M* + 1), 346.3 (*M* + 1).

C. Synthesis of 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 31D, and making non-critical variations to replace 1-hexyl-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2H-indol-2-one with 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2H-indol-2-one, and ethyl bromoacetate with *para*-formaldehyde, the title compound was obtained (70%) as a colorless solid: ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.00 (br, 1H), 7.13-6.95 (m, 3H), 6.84 (d, 1H), 6.16 (d, 1H), 5.90-5.84 (m, 2H), 5.16-4.83 (m, 2H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 177.8, 150.4, 147.1, 146.8, 139.8, 130.2, 129.3, 125.8, 117.7, 115.8, 109.3, 107.9, 101.2, 97.6, 63.5, 57.4.

PREPARATION 33

Synthesis of 4-bromo-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2H-indol-2-one

A. Synthesis of 4-bromo-3-hydroxy-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1-(2-cyclopropylethyl)-1H-indole-2,3-dione with 4-bromoisatin, and 1,3-benzodioxol-5-ol with 2,3-dihydrobenzofuran-6-ol, the title compound was obtained (78%) as a colorless solid: ¹H NMR (300 MHz, DMSO-*d*₆) δ 10.36 (s, 1H), 9.15 (s, 1H), 7.49 (1H), 7.04 (t, 1H), 6.89 (d, 1H), 6.74 (d, 1H), 6.35 (br, 1H), 5.90 (s, 1H), 4.45 (t, 2H), 3.05 (t, 2H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 178.4, 160.2, 154.0, 145.7, 131.6, 130.7, 125.5, 125.4, 118.9, 117.7, 116.1, 108.8, 96.8, 76.9, 71.8, 29.1; MS (ES-) *m/z* 344.4 (M - 17), 360.4 (M - 1).

B. Synthesis of 4-bromo-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 1D, and making non-critical variations to replace 4-bromo-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one with 4-bromo-3-hydroxy-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-1,3-dihydro-2H-indol-2-one, the title compound was obtained (62%) as a solid: MS (ES+) *m/z* 346.5 (M + 1), 348.5 (M + 1).

C. Synthesis of 4-bromo-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 31D, and making non-critical variations to replace 1-hexyl-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2H-

indol-2-one with 4-bromo-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-1,3-dihydro-2*H*-indol-2-one, and ethyl bromoacetate with *para*-formaldehyde, the title compound was obtained that was used directly for further reaction.

PREPARATION 34

- 5 Synthesis of 4-bromo-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-3-(hydroxymethyl)-1-(pyridin-2-ylmethyl)-1,3-dihydro-2*H*-indol-2-one

A. Synthesis of 4-bromo-1-(pyridin-2-ylmethyl)-1*H*-indole-2,3-dione

- To a solution of 4-bromoisatin (8.94 g, 39.5 mmol) in anhydrous *N,N*-dimethylformamide (100 mL) was added sodium hydride (3.34 g, 86.9 mmol, 60% dispersion in mineral oil) in portions at 0 °C. The brown reaction mixture was stirred for 30 min followed by the addition of a solution of 2-(bromomethyl)pyridine hydrobromide (10.0 g, 39.5 mmol) neutralized with sodium hydride (1.52 g, 39.5 mmol, 60% dispersion in mineral oil) in *N,N*-dimethylformamide at 0 °C. The reaction mixture was stirred for 16 h and quenched with water (100 mL). The reaction mixture was extracted with diethyl ether (3 x 100 mL) and the aqueous layer was extracted with ethyl acetate (3 x 100 mL). The combined organic layers was washed with water (5 x 200 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was triturated with ether to afford the title compound (10.6 g, 85%) as a brown solid: ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.53 (d, 1H), 7.67 (t, 1H), 7.30 (t, 2H), 7.25-7.19 (m, 2H), 6.94 (d, 1H), 5.04 (s, 2H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 180.5, 157.3, 154.2, 152.3, 149.5, 138.4, 137.5, 128.6, 123.3, 122.3, 121.5, 116.4, 110.3, 45.8.

B. Synthesis of 4-bromo-3-hydroxy-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-1-(pyridin-2-ylmethyl)-1,3-dihydro-2*H*-indol-2-one

- 25 Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1-(2-cyclopropylethyl)-1*H*-indole-2,3-dione with 4-bromo-1-(pyridin-2-ylmethyl)-1*H*-indole-2,3-dione, and 1,3-benzodioxol-5-ol with 2,3-dihydrobenzofuran-6-ol, the title compound was obtained (91%) as a colorless solid: mp >225 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.29 (s, 1H), 8.54 (d, 1H), 7.70 (dt, 1H), 7.61 (br, 1H), 7.32-7.26 (m, 2H), 7.07 (d, 1H), 7.00 (d, 1H), 6.72 (d, 1H), 6.60 (br, 1H), 6.02 (s, 1H), 4.91 (ABq, 2H), 4.47 (t, 2H), 3.06 (d, 2H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 176.9, 160.4, 156.3, 153.8, 149.6, 146.1, 137.5, 130.9, 130.8, 126.5, 125.8, 123.1, 121.5, 118.8, 117.3, 116.4, 108.3, 96.7, 76.6, 71.9, 45.7, 29.1; MS (ES+) *m/z* 455.4 (M + 1), 437.4 (M - 17).

C. Synthesis of 4-bromo-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-1-(pyridin-2-ylmethyl)-1,3-dihydro-2H-indol-2-one

To a solution of 4-bromo-3-hydroxy-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-1-(pyridin-2-ylmethyl)-1,3-dihydro-2H-indol-2-one (1.12 g, 2.48 mmol) in anhydrous dichloromethane (25.0 mL) was added triethylamine (1.40 mL, 9.91 mmol) and SOCl₂ (0.40 mL, 4.96 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 2 h and quenched with water (30.0 mL). The organic layer was separated, washed with water (3 x 30.0 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness to give a gummy material. The residue was dissolved in acetic acid/tetrahydrofuran (3.00 mL/22.0 mL) followed by the addition of zinc dust (0.81 g, 12.4 mmol) in one portion. The reaction mixture was stirred at ambient temperature for 16 h. After the solid was filtered, the solvent was removed *in vacuo*. The residue was dissolved in ethyl acetate (100 mL), washed with water (3 x 30.0 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness to give the title compound (1.50 g, 77%) as a gummy material: MS (ES+) *m/z* 437.3 (M + 1).

D. Synthesis of 4-bromo-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-3-(hydroxymethyl)-1-(pyridin-2-ylmethyl)-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 1E, and making non-critical variations to replace 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one with 4-bromo-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-1-(pyridin-2-ylmethyl)-1,3-dihydro-2H-indol-2-one, the title compound was obtained (34%): MS (ES+) *m/z* 468.4 (M + 1).

PREPARATION 35

25 Synthesis of 5-fluoro-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1-[[5-(trifluoromethyl)-2-furyl]methyl]-1,3-dihydro-2H-indol-2-one

A. Synthesis of 5-fluoro-1-[[5-(trifluoromethyl)-2-furyl]methyl]-1H-indole-2,3-dione

Following the procedure as described in PREPARATION 2A, and making non-critical variations to replace isatin with 5-fluoroisatin, and (2-bromoethyl)cyclopropane with 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound was obtained (59%) as a red solid: ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.54-7.50 (m, 1H), 7.47-7.44 (m, 1H), 7.20 (dd, 1H), 7.14-7.13 (m, 1H), 6.75 (d, 1H), 4.99 (s, 2H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 182.4 (d), 160.7, 158.5 (d), 157.5, 153.0 (d), 146.5 (d), 139.9 (q), 124.3, 119.3 (d), 114.5 (d), 112.7 (d), 112.0 (d), 110.5, 36.8.

B. Synthesis of 5-fluoro-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-[[5-(trifluoromethyl)-2-furyl]methyl]-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1-(2-cyclopropylethyl)-1H-indole-2,3-dione with 5-fluoro-1-
 5 [[5-(trifluoromethyl)-2-furyl]methyl]-1H-indole-2,3-dione, the title compound was obtained (66%) as a pale yellow solid: ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.15 (s, 1H), 7.21 (s, 1H), 7.15 (dd, 1H), 7.08-6.95 (m, 2H), 6.74 (s, 1H), 6.54 (s, 1H), 6.22 (d, 1H), 5.90 (d, 2H), 4.96 (s, 2H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 176.7, 160.57, 157.4, 154.0, 148.6, 147.4, 140.1 (m), 139.6 (m), 134.7 (d, ²J_{CF} = 29.4 Hz), 121.3, 119.5, 117.7,
 10 115.1 (d, ¹J_{CF} = 92.1 Hz), 114.5, 111.8 (d, ¹J_{CF} = 97.5 Hz), 109.7, 109.6, 107.2, 101.3, 97.8, 75.1, 36.9; MS (ES+) *m/z* 450.3 (M + 1)

C. Synthesis of 5-fluoro-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-[[5-(trifluoromethyl)-2-furyl]methyl]-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 1D, and making non-critical variations to replace 4-bromo-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one with 5-fluoro-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-[[5-(trifluoromethyl)-2-furyl]methyl]-1,3-dihydro-2H-indol-2-one, the title compound was obtained (72%) as a pale yellow solid: ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.31 (s, 1H), 7.13 (dd, 1H), 7.02 (dd, 2H), 6.82 (d, 1H), 6.59 (d, 2H), 6.39 (s, 1H),
 20 5.87 (d, 2H), 5.07-4.96 (m, 2H), 4.84 (s, 1H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 176.1, 160.5, 157.4, 153.9, 150.5, 147.5, 140.2, 139.6, 139.1, 132.3 (d, ²J_{CF} = 33.3 Hz), 115.3, 114.5 (m), 114.2, 113.9, 111.9 (d, ¹J_{CF} = 98.7 Hz), 109.9, 109.7 (d, ²J_{CF} = 32.7 Hz), 101.3, 98.3, 48.5, 36.8; MS (ES+) *m/z* 436.2 (M + 1).

D. Synthesis of 5-fluoro-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1-[[5-(trifluoromethyl)-2-furyl]methyl]-1,3-dihydro-2H-indol-2-one

A mixture of 5-fluoro-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-[[5-(trifluoromethyl)-2-furyl]methyl]-1,3-dihydro-2H-indol-2-one (3.64 g, 8.41 mmol), *para*-formaldehyde (2.52 g, 84.1 mmol) and lithium hydroxide monohydrate (1.06 g, 25.2 mmol) in tetrahydrofuran (84.0 mL) and water (10.0 mL) was stirred at 0 °C for 4 h. After the
 30 solvent was removed *in vacuo*, the residue was dissolved in ethyl acetate (100 mL), washed with 10% aqueous HCl (3 x 25.0 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography eluting with ethyl acetate/hexanes (50%) to give the title compound (0.65 g, 59%) as a colorless solid: ¹H NMR (300 MHz, DMSO-*d*₆) δ

9.11 (s, 1H), 7.12 (d, 1H), 6.99-6.87 (m, 3H), 6.80 (dd, 1H), 6.48 (d, 1H), 6.23 (s, 1H), 5.89 (d, 2H), 5.09 (br, 1H), 4.97 (ABq, 2H), 4.01 (ABq, 2H); ^{13}C NMR (75 MHz, DMSO- d_6) δ 176.1, 160.5; MS (ES+) m/z 466.2 (M + 1), 448.2 (M - 17).

PREPARATION 36

5 Synthesis of *tert*-butyl-(2-chloromethyl-5-trifluoromethylthiophen-3-yloxy)dimethylsilaneA. Synthesis of methyl 3-*tert*-butyl dimethylsilanyloxy-5-trifluoromethyl-2-thiophenecarboxylate

To a solution of methyl 3-hydroxy-5-trifluoromethyl-2-thiophenecarboxylate (Karp, G.M., et al, *Synthesis* (2000), 8:1078-1080) (19.4 g, 85.8 mmol) in *N,N*-dimethylformamide (50.0 mL) was added imidazole (8.77 g, 129 mmol) followed by *tert*-butyl dimethylsilyl chloride (19.4 g, 129 mmol) at 0 °C. The reaction mixture was stirred at ambient temperature overnight. More imidazole (7.50 g) and *tert*-butyl dimethylsilyl chloride (10.5 g) were added. The reaction mixture was stirred for another 4 h and quenched with water (100 mL). The reaction mixture was extracted with ether (3 x 500 mL). The combined organic layers was washed with water (3 x 500 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography eluting with ethyl acetate/hexanes (1/9) to give the title compound (26.5 g, 90%) as a yellow oil: ^1H NMR (300 MHz, CDCl_3) δ 6.91 (s, 1H), 3.82 (s, 3H), 0.21 (s, 6H), 0.06 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 161.5, 155.5, 133.7, 133.2, 123.6 (q, $^1J_{\text{CF}}$ = 14.4 Hz), 119.8, 51.9, 25.4, 18.2, -4.6.

B. Synthesis of [3-(*tert*-butyldimethylsilanyloxy)-5-trifluoromethylthiophen-2-yl]methanol

To a mixture of lithium aluminum hydride (1.67 g, 43.9 mmol) in anhydrous ether (75.0 mL) was added a solution of methyl 3-*tert*-butyl dimethylsilanyloxy-5-trifluoromethyl-2-thiophenecarboxylate (10.0 g, 29.3 mmol) in anhydrous ether (25.0 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 30 min and quenched by the slow addition of water (50.0 mL). After the aqueous layer was separated, the organic layer was washed with saturated ammonium chloride (3 x 20.0 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography eluting with ethyl acetate/hexanes (1/9) to give the title compound (6.95 g, 76%) as a yellow oil: ^1H NMR (300 MHz, CDCl_3) δ 6.89 (s, 1H), 4.68 (s, 2H), 2.11 (br, 1H), 0.96 (s, 9H), 0.88 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 148.0, 127.0, 124.0, 122.4 (q, $^1J_{\text{CF}}$ = 14.7 Hz), 120.5,

56.1, 25.5, 18.1, -4.6.

C. Synthesis of *tert*-butyl-(2-chloromethyl-5-trifluoromethylthiophen-3-yloxy)dimethylsilane

To a solution of [3-(*tert*-butyldimethylsilanyloxy)-5-trifluoromethylthiophen-2-yl]methanol in anhydrous dichloromethane (100 mL) was added triethylamine (4.05 g, 40.0 mmol) followed by thionyl chloride (2.38 g, 20.0 mmol) at 0 °C. The reaction mixture was stirred for 30 min and quenched with water (50.0 mL). After separation, the organic layer was washed with water (3 x 50.0 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography eluting with hexane to afford the title compound (2.31 g, 70%) as a yellow oil, which was directly used.

PREPARATION 37

Synthesis of 1-(diphenylmethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-5-methyl-1,3-dihydro-2*H*-indol-2-one

15 A. Synthesis of 1-(diphenylmethyl)-5-methyl-1*H*-indole-2,3-dione

Following the procedure as described in PREPARATION 2A, and making non-critical variations to replace isatin with 5-methylisatin, and (2-bromoethyl)cyclopropane with 1,1'-(bromomethylene)dibenzene, the title compound was obtained (74%) as a bright orange solid: ¹H NMR (300 MHz, CDCl₃) δ 7.42-7.26 (m, 11H), 7.09 (d, 1H), 6.95 (s, 1H), 6.37 (d, 1H), 2.24 (s, 3H).

B. Synthesis of 1-(diphenylmethyl)-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-5-methyl-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1-(2-cyclopropylethyl)-1*H*-indole-2,3-dione with 1-(diphenylmethyl)-5-methyl-1*H*-indole-2,3-dione, the title compound was obtained (92%) as a colorless solid: ¹H NMR (300 MHz, CDCl₃) δ 9.23 (br, 1H), 7.40-7.15 (m, 11H), 6.90-6.85 (m, 2H), 6.57 (s, 1H), 6.33 (d, 1H), 6.31 (s, 1H), 5.87 (s, 2H), 4.46 (br s, 1H), 2.28 (s, 3H); MS (ES+) *m/z* 448.4 (M - 17).

30 C. Synthesis of 1-(diphenylmethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-5-methyl-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 2C, and making non-critical variations to replace 1-(2-cyclopropylethyl)-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2*H*-indol-2-one with 1-(diphenylmethyl)-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-5-methyl-1,3-dihydro-2*H*-indol-2-one, the title compound

was obtained (84%) as a colorless solid: ^1H NMR (300 MHz, CDCl_3) δ 7.37-7.25 (m, 9H), 7.22-7.17 (m, 2H), 7.10 (s, 1H), 6.91 (s, 1H), 6.86 (d, 1H), 6.63 (s, 1H), 6.40 (s, 1H), 6.38 (d, 1H), 5.88 (ABq, 2H), 5.07 (s, 1H), 2.23 (s, 3H); MS (ES+) m/z 450.3 ($M + 1$).

5 D. Synthesis of 1-(diphenylmethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-5-methyl-1,3-dihydro-2H-indol-2-one

To a solution of 1-(diphenylmethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-5-methyl-1,3-dihydro-2H-indol-2-one (1.61 g, 3.60 mmol) and *para*-formaldehyde (0.43 g, 14.6 mmol) in dichloromethane (60.0 mL) was added diisopropylamine (7.20 mmol).

10 After stirring at ambient temperature for 3 h, the reaction was quenched with saturated aqueous ammonium chloride (60.0 mL). The organic layer was separated and washed with water (3 x 100 mL), dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography eluting with ethyl acetate/hexanes (20-60%) to afford the title
15 compound (1.07 g, 63%) as a colorless solid: ^1H NMR (300 MHz, CDCl_3) δ 10.09 (br, 1H), 7.37-7.16 (m, 12H), 6.99 (s, 1H), 6.87 (d, 1H), 6.62 (s, 1H), 6.54 (s, 1H), 6.37 (d, 1H), 5.87 (d, 2H), 4.45 (ABq, 2H), 2.33 (s, 3H); MS (ES+) m/z 480.4 ($M + 1$).

PREPARATION 38

Synthesis of 3-(hydroxymethyl)-3-(5-hydroxy-2-methyl-1,3-benzothiazol-6-yl)-1-pentyl-
20 1,3-dihydro-2H-indol-2-one

A. Synthesis of 3-hydroxy-3-(5-hydroxy-2-methyl-1,3-benzothiazol-6-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1-(2-cyclopropylethyl)-1H-indole-2,3-dione with 1-pentyl-
25 1H-indole-2,3-dione, and 1,3-benzodioxol-5-ol with 2-methyl-1,3-benzothiazol-5-ol, the title compound was obtained (81%) as a colorless solid: ^1H NMR (300 MHz, $\text{DMSO}-d_6$) δ 9.90 (br, 1H), 9.05 (br, 1H), 7.78 (d, 1H), 7.25 (dd, 1H), 7.10-6.95 (m, 2H), 6.90-6.80 (m, 2H), 3.81-3.58 (m, 2H), 2.75 (br, 3H), 1.80-1.60 (m, 2H), 1.50-1.31 (m, 4H), 0.90 (t, 3H); MS (ES+) m/z 383.4 ($M + 1$).

30 B. Synthesis of 3-(5-hydroxy-2-methyl-1,3-benzothiazol-6-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one

A suspension of 3-hydroxy-3-(5-hydroxy-2-methyl-1,3-benzothiazol-6-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one (0.50 g, 1.31 mmol) in hydroiodic acid (10.0 mL) was refluxed for 1.5 days. The reaction mixture was concentrated *in vacuo* to dryness.

The residue was used directly in next step.

C. Synthesis of 3-(hydroxymethyl)-3-(5-hydroxy-2-methyl-1,3-benzothiazol-6-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 1E, and making non-critical variations to replace 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one with 3-(5-hydroxy-2-methyl-1,3-benzothiazol-6-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one, the title compound was obtained: MS (ES+) m/z 367.5 (M + 1).

PREPARATION 39

Synthesis of (5-chloro-1,3,4-thiadiazol-2-yl)methanol

To a solution of ethyl 5-chloro-1,3,4-thiadiazole-2-carboxylate (0.51 g, 2.60 mmol) in anhydrous methanol (5.00 mL) was added sodium borohydride (0.30 g, 7.99 mmol) at 0 °C. The reaction mixture was stirred at ambient temperature for 16 h, diluted with acetic acid (3.00 mL) and extracted with ethyl acetate (2 x 150 mL). The combined organics was washed with aqueous saturated sodium bicarbonate (3 x 25.0 mL) and aqueous saturated sodium chloride (2 x 25.0 mL). The organic layer was dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness to give the title compound (0.30 g, 75%) as a light yellow semi-solid: ¹H NMR (300 MHz, CDCl₃) δ 5.04 (s, 2H), 2.80 (br, 1H); MS (ES+) 151.1 (M + 1), 153.1 (M + 1).

PREPARATION 40

Synthesis of 1-(diphenylmethyl)-3-(6-hydroxy-3,3-dimethyl-2,3-dihydro-1-benzofuran-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2H-indol-2-one

A. Synthesis of 1-(diphenylmethyl)-3-hydroxy-3-(6-hydroxy-3,3-dimethyl-2,3-dihydro-1-benzofuran-5-yl)-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1-(2-cyclopropylethyl)-1H-indole-2,3-dione with 1-(diphenylmethyl)-1H-indole-2,3-dione, and 1,3-benzodioxol-5-ol with 3,3-dimethyl-2,3-dihydro-1-benzofuran-6-ol, the title compound was obtained: MS (ES+) m/z 478.5 (M + 1).

B. Synthesis of 1-(diphenylmethyl)-3-(6-hydroxy-3,3-dimethyl-2,3-dihydro-1-benzofuran-5-yl)-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 2C, and making non-critical variations to replace 1-(2-cyclopropylethyl)-3-hydroxy-3-(6-hydroxy-1,3-

benzodioxol-5-yl)-1,3-dihydro-2*H*-indol-2-one with 1-(diphenylmethyl)-3-hydroxy-3-(6-hydroxy-3,3-dimethyl-2,3-dihydro-1-benzofuran-5-yl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained (73% for two steps): ¹H NMR (300 MHz, CDCl₃) δ 7.38-7.20 (m, 12H), 7.11-7.04 (m, 2H), 6.97 (s, 1H), 6.58 (s, 1H), 6.57-6.51 (m, 1H), 6.50 (s, 1H), 5.08 (s, 1H), 4.19 (s, 2H), 1.25 (s, 3H), 1.18 (s, 3H); MS (ES+) *m/z* 426.6 (M + 1).

C. Synthesis of 1-(diphenylmethyl)-3-(6-hydroxy-3,3-dimethyl-2,3-dihydro-1-benzofuran-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 26C, and making non-critical variations to replace 1-(diphenylmethyl)-3-(5-hydroxy-2,3-dihydro-1-benzofuran-6-yl)-1,3-dihydro-2*H*-indol-2-one with 1-(diphenylmethyl)-3-(6-hydroxy-3,3-dimethyl-2,3-dihydro-1-benzofuran-5-yl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained: MS (ES+) *m/z* 492.5 (M + 1)

PREPARATION 41

Synthesis of 7-fluoro-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2*H*-indol-2-one

15 A. Synthesis of 7-fluoro-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1-(2-cyclopropylethyl)-1*H*-indole-2,3-dione with 7-fluoro-1*H*-indole-2,3-dione, the title compound was obtained (80%): ¹H NMR (300 MHz, DMSO-*d*₆) δ 10.66 (s, 1H), 9.11 (s, 1H), 7.18 (s, 1H), 7.07-6.98 (m, 1H), 6.83-6.74 (m, 1H), 6.66 (d, 1H), 6.48 (s, 1H), 6.18 (s, 1H), 5.92-5.85 (m, 2H); MS (ES+) *m/z* 304.5 (M + 1).

B. Synthesis of 7-fluoro-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2*H*-indol-2-one

25 Following the procedure as described in PREPARATION 2C, and making non-critical variations to replace 1-(2-cyclopropylethyl)-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2*H*-indol-2-one with 7-fluoro-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained (100%): ¹H NMR (300 MHz, DMSO-*d*₆) δ 10.84 (s, 1H), 9.22 (s, 1H), 7.01 (t, 1H), 6.87-6.78 (m, 1H), 6.71 (d, 1H), 6.62 (s, 1H), 6.35 (s, 1H), 5.90-5.85 (m, 2H), 4.67 (s, 1H); MS (ES+) *m/z* 288.5 (M + 1).

PREPARATION 42

Synthesis of ethyl [4-bromo-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate

A. Synthesis of ethyl [4-bromo-3-hydroxy-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate

5

Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1-(2-cyclopropylethyl)-1*H*-indole-2,3-dione with ethyl (4-bromo-2,3-dioxo-2,3-dihydro-1*H*-indol-1-yl)acetate, and 1,3-benzodioxol-5-ol with 2,3-dihydrobenzofuran-6-ol, the title compound was obtained (68%) as a white solid: ¹H NMR (300 MHz, CDCl₃) δ 8.66 (br, 1H), 7.31-7.19 (m, 3H), 6.73 (dd, 1H), 6.49-6.45 (m, 1H), 5.09-4.36 (m, 4H), 4.20 (q, 2H), 3.14-2.90 (m, 2H), 1.23 (t, 3H); MS (ES+) *m/z* 432.2 (M - 17).

10

B. Synthesis of ethyl [4-bromo-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate

15

Following the procedure as described in PREPARATION 2C, and making non-critical variations to replace 1-(2-cyclopropylethyl)-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2*H*-indol-2-one with ethyl [4-bromo-3-hydroxy-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate, the title compound was obtained (81%) as a white solid: ¹H NMR (CDCl₃, 300 MHz) δ 7.31-7.19 (m, 3H), 6.75 (d, 1H), 6.50-6.45 (m, 1H), 5.08 (s, 1H), 5.09-4.36 (m, 4H), 4.20 (q, 2H), 3.14-2.90 (m, 2H), 1.23 (t, 3H); MS (ES+) *m/z* 433.3 (M + 1).

20

C. Synthesis of ethyl [4-bromo-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate

25

Following the procedure as described in PREPARATION 1E, and making non-critical variations to replace 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one with ethyl [4-bromo-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate, the title compound was obtained (99%); MS (ES+) *m/z* 463.2 (M + 1).

PREPARATION 43

30

Synthesis of ethyl [5-chloro-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate

A. Synthesis of ethyl (5-chloro-2,3-dioxo-2,3-dihydro-1*H*-indol-1-yl)acetate

Following the procedure as described in PREPARATION 2A, and making non-critical variations to replace isatin with 5-chloro-1*H*-indole-2,3-dione, and (2-

bromoethyl)cyclopropane with ethyl 2-bromoacetate, the title compound was obtained (98%) as solid: ^1H NMR (300 MHz, CDCl_3) δ 7.60 (d, 1H), 7.54 (dd, 1H), 6.74 (d, 1H), 4.46 (s, 2H), 4.23 (q, 2H), 1.27 (t, 3H); MS (ES+) m/z 268.6 ($M + 1$).

B. Synthesis of ethyl [5-chloro-3-hydroxy-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-2-oxo-2,3-dihydro-1H-indol-1-yl]acetate

Following the procedure as described in PREPARATION 1C, and making non-critical variations to replace 4-bromo-1-pentyl-1H-indole-2,3-dione with ethyl (5-chloro-2,3-dioxo-2,3-dihydro-1H-indol-1-yl)acetate, and 1,3-benzodioxol-5-ol with 2,3-dihydrobenzofuran-6-ol, the title compound was obtained (85%) as a white solid: ^1H NMR (300 MHz, CDCl_3) δ 8.70 (br, 1H), 7.31-7.24 (m, 2H), 6.92 (d, 1H), 6.68 (s, 1H), 6.46 (s, 1H), 4.53-4.46 (m, 2H), 5.09-4.40 (d, 2H), 4.18 (q, 2H), 3.08-2.88 (m, 2H), 1.23 (t, 3H); MS (ES+) m/z 387.8 ($M - 17$).

C. Synthesis of ethyl [5-chloro-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-2-oxo-2,3-dihydro-1H-indol-1-yl]acetate

Following the procedure as described in PREPARATION 1D, and making non-critical variations to replace 4-bromo-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one with ethyl [5-chloro-3-hydroxy-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-2-oxo-2,3-dihydro-1H-indol-1-yl]acetate, the title compound was obtained (94%) as a white solid: ^1H NMR (300 MHz, CDCl_3) δ 7.30-7.24 (m, 2H), 6.72 (d, 1H), 6.66 (s, 1H), 6.39 (s, 1H), 5.05 (s, 1H), 4.53-4.46 (m, 4H), 4.21 (q, 2H), 3.14-2.94 (m, 2H), 1.25 (t, 3H); MS (ES+) m/z 388.8 ($M + 1$).

D. Synthesis of ethyl [5-chloro-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1H-indol-1-yl]acetate

Following the procedure as described in PREPARATION 1E, and making non-critical variations to replace 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one with ethyl [5-chloro-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-2-oxo-2,3-dihydro-1H-indol-1-yl]acetate, the title compound was obtained (99%): MS (ES+) m/z 418.7 ($M + 1$).

PREPARATION 44

Synthesis of methyl [3-(4-chloro-2-hydroxyphenyl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1H-indol-1-yl]acetate

A. Synthesis of methyl (2,3-dioxo-2,3-dihydro-1H-indol-1-yl)acetate

Following the procedure as described in PREPARATION 2A, and making non-critical variations to replace (2-bromoethyl)cyclopropane with methyl bromoacetate, the

title compound was obtained (72%): ¹H NMR (300 MHz, CDCl₃) δ 7.64-7.53 (m, 2H), 7.14 (t, 1H), 6.77 (d, 1H), 4.48 (s, 2H), 3.76 (s, 3H); MS (ES+) *m/z* 220.4 (M + 1).

B. Synthesis of methyl [3-(4-chloro-2-hydroxyphenyl)-3-hydroxy-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate

- 5 Following the procedure as described in PREPARATION 1C, and making non-critical variations to replace 4-bromo-1-pentyl-1*H*-indole-2,3-dione with methyl (2,3-dioxo-2,3-dihydro-1*H*-indol-1-yl)acetate, and 1,3-benzodioxol-5-ol with 3-chlorophenol, the title compound was obtained (29%) as a yellow solid: ¹H NMR (300 MHz, CDCl₃) δ 9.10 (s, 1H), 7.48 (d, 1H), 7.38 (t, 1H), 7.19 (t, 1H), 7.01 (br, 1H), 6.80-6.64 (m, 3H),
10 5.28 (br s, 1H), 4.51 (d, 1H), 4.44 (d, 1H), 3.75 (s, 3H); MS (ES+) *m/z* 370.5 (M + 23), 372.4 (M + 23).

C. Synthesis of methyl [3-(4-chloro-2-hydroxyphenyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate

- Following the procedure as described in PREPARATION 2C, and making non-critical variations to replace 1-(2-cyclopropylethyl)-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2*H*-indol-2-one with methyl [3-(4-chloro-2-hydroxyphenyl)-3-hydroxy-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate, the title compound
15 was obtained (83%) as a semi-solid; ¹H NMR (300 MHz, CDCl₃) δ 7.36 (t, 1H), 7.29 (bd, 1H), 7.18 (t, 1H), 6.95 (br, 1H), 6.86-6.78 (m, 3H), 5.13 (br, 1H), 4.55 (d, 1H), 4.45
20 (d, 1H), 3.75 (s, 3H); MS (ES+) *m/z* 332.5 (M + 1), 334.5 (M + 1).

D. Synthesis of methyl [3-(4-chloro-2-hydroxyphenyl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate

- Following the procedure as described in PREPARATION 1E, and making non-critical variations to replace 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one with methyl [3-(4-chloro-2-hydroxyphenyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate, the title compound was obtained: MS (ES+) *m/z* 362.5 (M + 1)
25 364.5 (M + 1).

PREPARATION 45

- Synthesis of ethyl [3-(4,5-difluoro-2-hydroxyphenyl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate
30

A. Synthesis of ethyl [3-(4,5-difluoro-2-hydroxyphenyl)-3-hydroxy-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate

Following the procedure as described in PREPARATION 2B, and non-critical variations to replace 1-(2-cyclopropylethyl)-1*H*-indole-2,3-dione with ethyl (2,3-dioxo-

2,3-dihydro-1*H*-indol-1-yl)acetate, the title compound was obtained as a brown oil: MS (ES+) *m/z* 364.3 (*M* + 1), 348.5 (*M* - 17).

B. Synthesis of ethyl [3-(4,5-difluoro-2-hydroxyphenyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate

5 Following the procedure as described in PREPARATION 2C, and making non-critical variations to replace 1-(2-cyclopropylethyl)-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2*H*-indol-2-one with ethyl [3-(4,5-difluoro-2-hydroxyphenyl)-3-hydroxy-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate, the title compound was obtained (83%) as a light yellow oil: ¹H NMR (300 MHz, CDCl₃) δ 7.39 (t, 1H), 7.34 (d, 1H), 7.26-7.22 (m, 1H), 6.92-6.82 (m, 2H), 6.73 (dd, 1H), 5.11 (br, 1H), 4.50 (d, 1H), 4.43 (d, 1H), 4.21 (q, 2H), 1.23 (t, 3H); MS (ES+) *m/z* 448.5 (*M* + 1).

C. Synthesis of ethyl [3-(4,5-difluoro-2-hydroxyphenyl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate

15 Following the procedure as described in PREPARATION 1E, and making non-critical variations to replace 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one with methyl [3-(4-chloro-2-hydroxyphenyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate, the title compound was obtained: MS (ES+) *m/z* 378.3 (*M* + 1), 361.3 (*M* - 17).

PREPARATION 46

20 Synthesis of 3-(4-bromo-2-hydroxyphenyl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one

A. Synthesis of 3-(4-bromo-2-hydroxyphenyl)-3-hydroxy-1-pentyl-1,3-dihydro-2*H*-indol-2-one

25 Following the procedure as described in PREPARATION 1C, and making non-critical variations to replace 4-bromo-1-pentyl-1*H*-indole-2,3-dione with 1-pentyl-1*H*-indole-2,3-dione, and 1,3-benzodioxol-5-ol with 3-bromophenol, the title compound was obtained (48%) as a white solid: ¹H NMR (300 MHz, CDCl₃) δ 9.66 (br, 1H), 7.50-7.38 (m, 2H), 7.24-7.16 (m, 2H), 6.98-6.86 (m, 2H), 6.64 (d, 1H), 4.15 (br, 1H), 3.80-3.55 (m, 2H), 1.75-1.62 (m, 2H), 1.40-1.34 (m, 4H), 0.89 (t, 3H); MS (ES+) *m/z* 391.4 (M + 1), 393.4 (M + 1).

B. Synthesis of 3-(4-bromo-2-hydroxyphenyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 1D, and making non-critical variations to replace 4-bromo-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one with 3-(4-bromo-2-hydroxyphenyl)-3-hydroxy-1-

pentyl-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained (91%) as a white powder: ¹H NMR (300 MHz, CDCl₃) δ 7.40 (t, 1H), 7.31 (d, 1H) 7.24-7.23 (m, 2H), 7.01-6.91 (m, 2H), 6.74 (d, 1H), 5.05 (br, 1H), 3.80-3.65 (m, 2H), 1.75-1.63 (m, 2H), 1.38-1.29 (m, 4H), 0.88 (t, 3H); MS (ES+) *m/z* 374.4 (*M* + 1), 376.4 (*M* + 1).

5 C. Synthesis of 3-(4-bromo-2-hydroxyphenyl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 1E, and making non-critical variations to replace 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one with 3-(4-bromo-2-hydroxyphenyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained: *R*_f = 0.5 (EtOAc/Hexanes, ¼).

10

PREPARATION 47

Synthesis of 3-(5-bromo-2-hydroxyphenyl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one

15 A. Synthesis of 3-(5-bromo-2-hydroxyphenyl)-3-hydroxy-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1-(2-cyclopropylethyl)-1*H*-indole-2,3-dione with isatin, 1,3-benzodioxol-5-ol with 4-bromophenol, the title compound was obtained (71%) as a yellowish solid: MS (ES+) *m/z* 319.4 (*M* + 1), 321.4 (*M* + 1).

20 B. Synthesis of 3-(5-bromo-2-hydroxyphenyl)-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 1D, and making non-critical variations to replace 4-bromo-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one with 3-(5-bromo-2-hydroxyphenyl)-3-hydroxy-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained (98%) as a white powder: MS

25 (ES+) *m/z* 306.2 (*M* + 1), 304.2 (*M*+1).

30 C. Synthesis of 3-(5-bromo-2-hydroxyphenyl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 35D, and making non-critical variations to replace 5-fluoro-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-[[5-(trifluoromethyl)-2-furyl]methyl]-1,3-dihydro-2*H*-indol-2-one with 3-(5-bromo-2-hydroxyphenyl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained: MS

30 (ES+) *m/z* 334.2 (*M* + 1), 336.2 (*M* + 1).

PREPARATION 48

Synthesis of 1-(diphenylmethyl)-3-(hydroxymethyl)-3-[2-hydroxy-4-(trifluoromethoxy)phenyl]-1,3-dihydro-2*H*-indol-2-one

A. Synthesis of 1-(diphenylmethyl)-3-hydroxy-3-[2-hydroxy-4-(trifluoromethoxy)phenyl]-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1-(2-cyclopropylethyl)-1*H*-indole-2,3-dione with 1-(diphenylmethyl)-1*H*-indole-2,3-dione, and 1,3-benzodioxol-5-ol with 3-(trifluoromethoxy)phenol, the title compound was obtained (75%): MS (ES+) m/z 514.5 (M + 23).

B. Synthesis of 1-(diphenylmethyl)-3-[2-hydroxy-4-(trifluoromethoxy)phenyl]-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 2C, and making non-critical variations to replace 1-(2-cyclopropylethyl)-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2*H*-indol-2-one with 1-(diphenylmethyl)-3-hydroxy-3-[2-hydroxy-4-(trifluoromethoxy)phenyl]-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained (82%): MS (ES+) m/z 498.4 (M + 23).

C. Synthesis of 1-(diphenylmethyl)-3-(hydroxymethyl)-3-[2-hydroxy-4-(trifluoromethoxy)phenyl]-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 1E, and making non-critical variations to replace 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one with 1-(diphenylmethyl)-3-[2-hydroxy-4-(trifluoromethoxy)phenyl]-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained: MS (ES+) m/z 488 (M - 17), 528 (M + 23).

PREPARATION 49

Synthesis of 1-(diphenylmethyl)-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one

A. Synthesis of 1-(diphenylmethyl)-3-hydroxy-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1,3-benzodioxol-5-ol with 2,3-dihydrobenzofuran-6-ol (Foster et al., *J. Chem. Soc.* 1948:2254-2258) and 1-(2-cyclopropylethyl)-1*H*-indole-2,3-dione with 1-(diphenylmethyl)-1*H*-indole-2,3-dione, the title compound was obtained (68%) as a white solid: MS (ES+) m/z 450.4 (M + 1).

B. Synthesis of 1-(diphenylmethyl)-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 2C, and making non-critical variations to replace 1-(2-cyclopropylethyl)-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2H-indol-2-one with 1-(diphenylmethyl)-3-hydroxy-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-1,3-dihydro-2H-indol-2-one, the title compound was obtained (67%) as a white solid: MS (ES+) m/z 434.3 ($M + 1$).

C. Synthesis of 1-(diphenylmethyl)-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-(3-hydroxymethyl)-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 26C, and making non-critical variations to replace 1-(diphenylmethyl)-3-(5-hydroxy-2,3-dihydro-1-benzofuran-6-yl)-1,3-dihydro-2H-indol-2-one with 1-(diphenylmethyl)-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-1,3-dihydro-2H-indol-2-one, the title compound was obtained (45%) as a white solid: MS (ES+) m/z 464.5 ($M + 1$).

PREPARATION 50

Synthesis of 4-bromo-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2H-indol-2-one

A. Synthesis of 4-bromo-3-hydroxy-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1,3-benzodioxol-5-ol with 2,3-dihydrobenzofuran-6-ol and 1-(2-cyclopropylethyl)-1H-indole-2,3-dione with 4-bromo-1H-indole-2,3-dione, the title compound was obtained (78%) as a white solid: ^1H NMR (300 MHz, DMSO- d_6) δ 10.36 (s, 1H), 9.15 (s, 1H), 7.49 (1H), 7.04 (t, 1H), 6.89 (d, 1H), 6.74 (d, 1H), 6.35 (br, 1H), 5.90 (s, 1H), 4.45 (t, 2H), 3.05 (t, 2H); ^{13}C NMR (75 MHz, DMSO- d_6) δ 178.4, 160.2, 154.0, 145.7, 131.6, 130.7, 125.5, 125.4, 118.9, 117.7, 116.1, 108.8, 96.8, 76.9, 71.8, 29.1; MS (ES-) m/z 344.4 ($M - 17$), 360.4 ($M - 1$).

B. Synthesis of 4-bromo-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 2C, and making non-critical variations to replace 1-(2-cyclopropylethyl)-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2H-indol-2-one with 4-bromo-3-hydroxy-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-1,3-dihydro-2H-indol-2-one, the title compound was obtained (62%) as a white solid: MS (ES+) m/z 346.5 ($M + 1$), 348.5 ($M + 1$).

C. Synthesis of 4-bromo-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 14C, and making non-critical variations to replace 3-(5-fluoro-2-hydroxyphenyl)-1-pentyl-1,3-dihydro-2H-indol-2-one with 4-bromo-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-1,3-dihydro-2H-indol-2-one, the title compound was obtained (16%): $R_f = 0.21$ (EtOAc/Hexanes, 7/3).

PREPARATION 51

Synthesis of 7-fluoro-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1-[[5-(trifluoromethyl)-2-furyl]methyl]-1,3-dihydro-2H-indol-2-one

10 A. Synthesis of 7-fluoro-1-[[5-(trifluoromethyl)-2-furyl]methyl]-1H-indole-2,3-dione

Following the procedure as described in PREPARATION 1A, and making non-critical variations to replace 4-bromoindole with 7-fluoroisatin, and 1-bromopentane with 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound was obtained (34%): MS (ES+) m/z 336.2 ($M + 23$).

15 B. Synthesis of 7-fluoro-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-[[5-(trifluoromethyl)-2-furyl]methyl]-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1-(2-cyclopropylethyl)-1H-indole-2,3-dione with 7-fluoro-1-[[5-(trifluoromethyl)-2-furyl]methyl]-1H-indole-2,3-dione, the title compound was obtained (75%): MS (ES+) m/z 474.3 ($M + 23$).

C. Synthesis of 7-fluoro-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-[[5-(trifluoromethyl)-2-furyl]methyl]-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 2C, and making non-critical variations to replace 1-(2-cyclopropylethyl)-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2H-indol-2-one with 7-fluoro-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-[[5-(trifluoromethyl)-2-furyl]methyl]-1,3-dihydro-2H-indol-2-one, the title compound was obtained (65%): MS (ES+) m/z 436.4 ($M + 1$).

D. Synthesis of 7-fluoro-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1-[[5-(trifluoromethyl)-2-furyl]methyl]-1,3-dihydro-2H-indol-2-one

30 Following the procedure as described in PREPARATION 26C, and making non-critical variations to replace 1-(diphenylmethyl)-3-(5-hydroxy-2,3-dihydro-1-benzofuran-6-yl)-1,3-dihydro-2H-indol-2-one with 7-fluoro-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-[[5-(trifluoromethyl)-2-furyl]methyl]-1,3-dihydro-2H-indol-2-one, the title compound was obtained (67%): MS (ES+) m/z 488.4 ($M + 23$).

PREPARATION 52

Synthesis of 3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one

A. Synthesis of 3-hydroxy-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1-(2-cyclopropylethyl)-1*H*-indole-2,3-dione with 1-pentyl-1*H*-indole-2,3-dione, and 1,3-benzodioxol-5-ol with 2,3-dihydrobenzofuran-6-ol, the title compound was obtained (90%) as a white powder: MS (ES+) *m/z* 376.3 (*M* + 23).

B. Synthesis of 3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 2C, and making non-critical variations to replace 1-(2-cyclopropylethyl)-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2*H*-indol-2-one with 3-hydroxy-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained (76%): MS (ES+) *m/z* 338.3 (*M* + 1).

C. Synthesis of 3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 1E, and making non-critical variations to replace 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one with 3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained (46%): MS (ES+) *m/z* 368.3 (*M* + 1), 380.4 (*M* + 23).

PREPARATION 53

Synthesis of 3-(5-bromo-2-hydroxyphenyl)-1-(diphenylmethyl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one

A. Synthesis of 3-(5-bromo-2-hydroxyphenyl)-1-(diphenylmethyl)-3-hydroxy-1,3-dihydro-2*H*-indol-2-one

Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1-(2-cyclopropylethyl)-1*H*-indole-2,3-dione with 1-(diphenylmethyl)-1*H*-indole-2,3-dione, and 1,3-benzodioxol-5-ol with 4-bromophenol, the title compound was obtained (90%) as an orange solid: MS (ES+) *m/z* 486.2 (*M* + 1), 488.2 (*M* + 1).

B. Synthesis of 3-(5-bromo-2-hydroxyphenyl)-1-(diphenylmethyl)-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 15B, and making non-critical variations to replace 3-(5-bromo-2-hydroxyphenyl)-3-hydroxy-1-pentyl-1,3-dihydro-2H-indol-2-one with 3-(5-bromo-2-hydroxyphenyl)-1-(diphenylmethyl)-3-hydroxy-1,3-dihydro-2H-indol-2-one, the title compound was obtained (99%) as a white powder: ¹H NMR (300 MHz, CDCl₃) δ 7.39-7.20 (m, 11H), 7.11-7.06 (m, 4H), 6.82 (d, 1H), 6.57-6.51 (m, 1H), 5.04 (s, 1H); MS (ES+) *m/z* 471.2 (M + 1), 473.2 (M + 1).

C. Synthesis of 3-(5-bromo-2-hydroxyphenyl)-1-(diphenylmethyl)-3-(hydroxymethyl)-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 26C, and making non-critical variations to replace 1-(diphenylmethyl)-3-(5-hydroxy-2,3-dihydro-1-benzofuran-6-yl)-1,3-dihydro-2H-indol-2-one with 3-(5-bromo-2-hydroxyphenyl)-1-(diphenylmethyl)-1,3-dihydro-2H-indol-2-one, the title compound was obtained: MS (ES+) *m/z* 500.4 (M + 1), 502.4 (M + 1).

PREPARATION 54

Synthesis of 3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2H-indol-2-one

A. Synthesis of 1-pentyl-1H-indole-2,3-dione

Following the procedure as described in PREPARATION 2A, and making non-critical variations to replace (2-bromoethyl)cyclopropane with 1-bromopentane, the title compound was obtained (72%) as a red solid: ¹H NMR (300 MHz, CDCl₃) δ 7.90 (d, 1H), 7.53-7.45 (m, 1H), 7.03-6.97 (m, 1H), 6.82 (d, 1H), 3.64-3.57 (m, 2H), 1.68-1.52 (m, 2H), 1.34-1.21 (m, 4H), 0.79 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 183.6, 158.1, 151.0, 138.4, 125.3, 123.5, 117.5, 110.2, 40.2, 28.9, 26.9, 22.2, 13.9.

B. Synthesis of 3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 2B, and making non-critical variations to replace 1-(2-cyclopropylethyl)-1H-indole-2,3-dione with 1-pentyl-1H-indole-2,3-dione, the title compound was obtained (47%) as a colorless solid: ¹H NMR (300 MHz, CDCl₃) δ 9.41 (s, 1H), 7.46 (dd, 1H), 7.37 (dt, 1H), 7.16 (dt, 1H), 6.89 (d, 1H), 6.53 (s, 1H), 6.22 (s, 1H), 5.83 (dd, 2H), 4.70 (br, 1H), 3.73-3.54 (m, 2H), 1.69-1.60 (m, 2H), 1.34-1.26 (m, 4H), 0.85 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 178.9, 152.2, 148.8, 142.5, 141.3, 130.3, 129.3, 126.1, 123.8, 117.1, 109.5, 106.8, 101.8,

101.4, 79.3, 40.4, 28.9, 26.8, 22.3, 13.9; MS (ES+) m/z 355.5 ($M + 1$).

C. Synthesis of 3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 2C, and making non-critical variations to replace 1-(2-cyclopropylethyl)-3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2H-indol-2-one with 3-hydroxy-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one, the title compound was obtained (81%) as a colorless solid: ^1H NMR (300 MHz, CDCl_3) δ 9.67 (br, 1H), 7.39-7.29 (m, 2H), 7.18-7.13 (m, 1H), 6.94 (d, 1H), 6.62 (s, 1H), 6.32 (s, 1H), 5.84 (dd, 2H), 5.01 (s, 1H), 3.71-3.63 (m, 2H), 1.71-1.61 (m, 2H), 1.35-1.27 (m, 4H), 0.86 (t, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 178.8, 151.3, 147.6, 143.9, 141.53, 128.7, 126.4, 126.2, 123.1, 115.3, 109.4, 106.5, 101.5, 101.2, 47.4, 40.5, 28.9, 26.9, 22.3, 13.9; MS (ES+) m/z 340 ($M + 1$).

D. Synthesis of 3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2H-indol-2-one

Following the procedure as described in PREPARATION 1E, and making non-critical variations to replace 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one with 3-(6-hydroxy-1,3-benzodioxol-5-yl)-1-pentyl-1,3-dihydro-2H-indol-2-one, the title compound was obtained (67%): ^1H NMR (300 MHz, CDCl_3) δ 10.85-10.63 (br, 1H), 7.48-7.35 (m, 2H), 7.28-7.19 (m, 1H), 6.96 (d, 1H), 6.52 (d, 2H), 5.82 (dd, 2H), 4.63 (d, 1H), 4.11 (d, 1H), 3.70 (d, 2H), 2.04-1.74 (br, 1H), 1.65-1.62 (m, 2H), 1.31-1.24 (m, 4H), 0.84 (t, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 180.3, 152.6, 148.1, 143.2, 141.3, 129.2, 129.1, 126.2, 123.3, 112.4, 109.6, 108.2, 101.9, 101.3, 64.6, 59.8, 40.6, 28.9, 26.9, 22.2, 13.9; MS (ES+) m/z 370.1 ($M + 1$).

EXAMPLE 1

Synthesis of 1'-(2-cyclopropylethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'H)-one

To a solution of 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2H-indol-2-one (0.92 g, 2.51 mmol) in anhydrous THF (20.0 mL) was added triphenylphosphine (0.82 g, 3.13 mmol) and diethyl azodicarboxylate (0.55, 3.13 mmol) at -78°C . The brown reaction solution was stirred at ambient temperature for 16 h, and quenched with saturated ammonium chloride (50.0 mL). The organic solvent was removed under reduced pressure and the aqueous mixture was extracted with ethyl acetate (3 x 50.0 mL). The combined

organic layers were dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The brown residue was subjected to column chromatography eluting with ethyl acetate/hexane (5% to 20%, gradient) to give the title compound (0.63 g, 72%) which was crystallized from ether to afford a colorless solid: mp 125-127 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.30-7.25 (m, 1H), 7.14 (d, 1H), 7.02 (t, 1H), 6.89 (d, 1H), 6.49 (s, 1H), 6.11 (s, 1H), 5.84 (m, 2H), 4.76 (m, 2H), 3.93-3.74 (m, 2H), 1.65-1.57 (m, 2H), 0.76-0.56 (m, 1H), 0.48-0.41 (m, 2H), 0.08-0.03 (m, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 177.4, 155.9, 148.8, 142.6, 142.3, 132.4, 128.8, 124.0, 123.1, 119.5, 108.6, 103.1, 101.5, 93.6, 80.6, 58.2, 40.5, 32.5, 30.8, 8.7, 4.4; MS (ES+) *m/z* 350.3 (M + 1).

EXAMPLE 1.1

Synthesis of 1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one

Following the procedure as described in Example 1, and making non-critical variations using 3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one to replace 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained (80%) as a white solid: mp 85-87 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.28 (t, 1H), 7.15 (d, 1H), 7.02 (t, 1H), 6.89 (d, 1H), 6.49 (s, 1H), 6.11 (s, 1H), 5.84 (dd, 2H), 4.77 (ABq, 2H), 3.85-3.62 (m, 2H), 1.76-1.66 (m, 2H), 1.40-1.33 (m, 4H), 0.89 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 177.3, 155.9, 148.8, 142.4, 142.3, 132.5, 128.9, 123.9, 119.6, 108.6, 103.0, 101.5, 93.6, 80.5, 58.2, 40.4, 29.0, 27.1, 22.3, 14.0; MS (ES+) *m/z* 352 (M + 1).

EXAMPLE 1.2

Synthesis of 4'-bromo-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one

Following the procedure as described in EXAMPLE 1, and making non-critical variations using 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one to replace 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained as a colorless solid: ¹H NMR (300 MHz, CDCl₃) δ 7.16 (d, 1H), 7.15 (s, 1H), 6.84 (dd, 1H), 6.45 (s, 1H), 6.06 (s, 1H), 5.86 (dd, 2H), 4.90 (ABq, 2H), 3.83-3.60 (m, 2H), 1.74-1.64 (m, 2H), 1.39-1.28 (m, 4H), 0.89 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 177.1, 157.2, 149.1, 144.6, 142.0, 130.3, 130.1, 127.0, 120.0, 116.5, 107.6, 102.5, 101.5, 93.3, 77.3, 59.6, 40.6, 29.0, 27.0, 22.3, 14.0; MS (ES+) *m/z* 430 (M + 1).

EXAMPLE 1.3

Synthesis of ethyl (2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)acetate

Following the procedure as described in EXAMPLE 1, and making non-critical variations using ethyl [3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate to replace 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained as a white powder in 90% yield: ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.31-7.26 (m, 1H), 7.17-7.00 (m, 3H), 6.67 (s, 1H), 6.18 (s, 1H), 5.90-5.89 (m, 2H), 4.76-4.66 (m, 2H), 4.59 (s, 2H), 4.13 (q, 2H), 1.17 (t, 3H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 177.3, 168.3, 155.6, 148.8, 142.4, 142.1, 132.0, 129.3, 124.1, 123.7, 120.4, 109.6, 103.3, 101.9, 93.8, 79.8, 61.8, 57.8, 41.8, 14.5; MS (ES+) *m/z* 390.2 (M + 23).

EXAMPLE 1.4

Synthesis of methyl 2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)methyl]benzoate

Following the procedure as described in EXAMPLE 1, and making non-critical variations using methyl 2-[[3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]methyl]benzoate to replace 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained as a white powder in 74% yield: mp 166-167 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.05 (m, 1H), 7.44 (m, 1H), 7.34 (t, 1H), 7.22-7.10 (m, 3H), 7.03 (m, 1H), 6.70 (d, 1H), 6.52 (s, 1H), 6.21 (s, 1H), 5.90-5.84 (m, 2H), 5.52-5.33 (m, 2H), 4.99 (d, 1H), 4.72 (d, 1H), 3.95 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 177.8, 167.5, 156.0, 148.9, 142.4, 142.3, 137.4, 132.8, 132.1, 131.4, 129.0, 128.6, 127.4, 126.5, 123.9, 123.6, 119.4, 109.5, 103.1, 101.5, 93.7, 80.7, 58.4, 52.3, 42.4; MS (ES+) *m/z* 430.3 (M + 1), 452.3 (M + 23).

EXAMPLE 1.5

Synthesis of methyl 3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)methyl]benzoate

Following the procedure as described in EXAMPLE 1, and making non-critical variations using methyl 3-[[3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]methyl]benzoate to replace 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained as a white powder in 73% yield; ¹H NMR (300 MHz, CDCl₃) δ

7.97-7.95 (m, 2H), 7.53-7.50 (m, 1H), 7.45-7.40 (m, 1H), 7.21-7.15 (m, 2H), 7.04-6.99 (m, 1H), 6.73-6.71 (m, 1H), 6.52 (s, 1H), 6.20 (s, 1H), 5.86 (s, 1H), 5.18 (d, 1H), 4.72 (d, 1H), 4.80 (d, 1H), 4.69 (d, 1H), 3.89 (s, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 177.7, 166.6, 156.0, 149.0, 142.4, 141.7, 136.1, 132.2, 131.7, 130.9, 129.2, 128.1, 124.0, 123.7, 119.4, 109.2, 103.1, 101.6, 93.7, 80.5, 64.3, 58.3, 52.3, 43.7; MS (ES+) m/z 430 (M + 1).

EXAMPLE 1.6

Synthesis of methyl 4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)methyl]benzoate

Following the procedure as described in EXAMPLE 1, and making non-critical variations using methyl 4-[[3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]methyl]benzoate to replace 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained as a white powder in 87% yield: ^1H NMR (300 MHz, CDCl_3) δ 8.01 (d, 2H), 7.38 (d, 2H), 7.18 (t, 2H), 7.02 (t, 1H), 6.72 (d, 1H), 6.52 (s, 1H), 6.12 (s, 1H), 5.86 (m, 2H), 5.11 (d, 1H), 4.96 (d, 1H), 4.86 (d, 1H), 4.69 (d, 1H), 3.89 (s, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 177.7, 166.6, 156.0, 149.0, 142.4, 141.8, 140.8, 132.1, 130.3, 129.8, 129.0, 127.3, 124.1, 123.7, 119.3, 109.2, 103.0, 102.0, 93.7, 80.5, 58.3, 52.2, 43.9; MS (ES+) m/z 430.1 (M + 1).

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EXAMPLE 1.7

Synthesis of 1'-(diphenylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one

Following the procedure as described in EXAMPLE 1, and making non-critical variations using 1-(diphenylmethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one to replace 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained as a white powder in 26% yield: MS (ES+) m/z 462.3 (M + 1).

EXAMPLE 1.8

Synthesis of spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one

To a solution of 1'-(diphenylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one (2.10 g, 4.70 mmol) in EtOAc (100 mL) and acetic acid (0.10 mL) was

added palladium on carbon (1.00 g). The reaction mixture was hydrogenated under 60 psi of hydrogen at ambient temperature for 5 days and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography to yield the title compound (0.87 g, 66%) as a white powder: mp 252 °C (dec.); ¹H NMR (300 MHz, CDCl₃) δ 10.55 (s, 1H), 7.25-6.84 (m, 4H), 6.64 (s, 1H), 6.22 (s, 1H), 5.88 (s, 2H), 4.76-4.57 (dd, 2H); MS (ES+) *m/z* 282.2 (M + 1).

EXAMPLE 1.9

Synthesis of 2-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)propyl]-1*H*-isoindole-1,3(2*H*)-dione

Following the procedure as described in EXAMPLE 1, and making non-critical variations using 2-{3-[3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]propyl}-1*H*-isoindole-1,3(2*H*)-dione to replace 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained in 45% yield: ¹H NMR (300 MHz, CDCl₃) δ 7.83-7.80 (m, 2H), 7.70-7.68 (m, 2H), 7.28-7.26 (m, 1H), 7.15 (d, 1H), 7.05-7.00 (m, 1H), 6.86 (d, 1H), 6.48 (s, 1H), 6.23 (s, 1H), 5.85-5.83 (m, 2H), 4.91 (d, 1H), 4.65 (d, 1H), 3.94-3.68- (m, 4H), 2.15-2.10- (m, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 177.4, 168.2, 155.9, 148.8, 142.4, 141.9, 134.0, 132.5, 132.0, 128.9, 124.1, 123.4, 123.3, 119.4, 108.4, 103.2, 101.5, 93.6, 80.4, 58.2, 38.0, 35.6, 26.8; MS (ES+) *m/z* 469.3 (M + 1), 491.3 (M + 23).

EXAMPLE 1.10

Synthesis of 2-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)ethyl]-1*H*-isoindole-1,3(2*H*)-dione

Following the procedure as described in EXAMPLE 1, and making non-critical variations using 2-{2-[3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]ethyl}-1*H*-isoindole-1,3(2*H*)-dione to replace 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained in 61% yield: ¹H NMR (300 MHz, CDCl₃) δ 7.81-7.73 (m, 2H), 7.71-7.62 (m, 2H), 7.18-7.08 (m, 2H), 6.98 (t, 1H), 6.87 (d, 1H), 6.43 (s, 1H), 6.29 (s, 1H), 5.91-5.81 (ABq, 2H), 4.79 (d, 1H), 4.58 (d, 1H), 4.18-3.92 (m, 4H), 3.06 (t, 2H), 1.59-1.35 (br, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 178, 168.2, 156.1, 148.7, 142.2, 141.9, 134.1, 132.4, 131.8, 128.7, 124.1, 123.4, 123.3, 119.0, 107.8, 103.7, 101.4, 93.4, 80.9, 58.1, 39.0, 35.6; MS (ES+) *m/z* 455 (M + 1), 477 (M +

23).

EXAMPLE 1.11

Synthesis of 1'-[3-(Benzyloxy)propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one

5 Following the procedure as described in EXAMPLE 1, and making non-critical variations using 1-[3-(benzyloxy)propyl]-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one to replace 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained in 98% yield as a pale yellow syrup: ¹H NMR (300 MHz, CDCl₃) δ 7.38-6.95 (m, 9H), 6.49 (s, 1H), 6.08 (s, 1H), 5.83 (dd, 2H), 5.86 (ABq, 1H), 4.58 (ABq, 1H), 3.96-3.79 (m, 2H), 3.53 (t, 2H), 2.06-2.00 (m, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 177.4, 155.9, 148.8, 142.5, 142.2, 138.1, 132.3, 128.9, 127.9, 127.6, 123.9, 123.1, 119.5, 108.7, 103.0, 101.4, 93.6, 80.4, 73.1, 67.4, 58.1, 37.7, 27.9; MS (ES+) *m/z* 430.3 (M + 1).

15

EXAMPLE 1.12

Synthesis of 5,6-difluoro-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(*1'H*)-one

Following the procedure as described in EXAMPLE 1, and making non-critical variations using 3-(4,5-difluoro-2-hydroxyphenyl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one to replace 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained in 71% yield: mp 48-50 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.33 (td, 1H), 7.18-7.12 (m, 2H), 6.93 (d, 1H), 6.77 (dd, 1H), 6.51 (dd, 1H), 4.96 (d, 1H), 4.71 (d, 1H), 3.87-3.64 (m, 2H), 1.82-1.65 (m, 2H), 1.46-1.28 (m, 4H), 0.92 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 176.6, 156.8, 152.9, 149.8, 144.2, 142.6, 131.8, 129.4, 124.1, 123.5, 111.7, 109.0, 100.2, 80.9, 57.9, 40.6, 29.1, 27.2, 22.5, 14.1; MS (ES+) *m/z* 344 (M + 1).

25

EXAMPLE 1.13

Synthesis of 5-fluoro-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(*1'H*)-one

Following the procedure as described in EXAMPLE 1, and making non-critical variations using 3-(5-fluoro-2-hydroxyphenyl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one to replace 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained in 3% yield: ¹H NMR (300 MHz, CDCl₃) δ 7.37-7.28 (m, 1H), 7.18-7.11 (m, 1H), 7.09-7.01 (m,

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1H), 6.98-6.82 (m, 3H), 6.45-6.37 (m, 1H), 4.95 (d, 1H), 4.69 (d, 1H), 3.89-3.63 (m, 2H), 1.81-1.65 (m, 2H), 1.48-1.28 (m, 4H), 0.92 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 176.7, 159.4, 156.6, 132.2, 130.1, 129.3, 124.1, 123.4, 116.3, 110.8, 110.5, 108.9, 80.4, 58.4, 40.6, 29.2, 27.3, 22.5, 14.1; MS (ES+) *m/z* 326 (*M* + 1).

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EXAMPLE 1.14

Synthesis of 5-bromo-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one

Following the procedure as described in EXAMPLE 1, and making non-critical variations using 3-(5-bromo-2-hydroxyphenyl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one to replace 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained in 4% yield: ¹H NMR (300 MHz, CDCl₃) δ 7.38-7.23 (m, 2H), 7.17-7.01 (m, 2H), 6.93 (d, 1H), 6.84 (d, 1H), 6.79 (d, 1H), 4.95 (d, 1H), 4.69 (d, 1H), 3.89-3.64 (m, 2H), 1.81-1.65 (m, 2H), 1.48-1.28 (m, 4H), 0.92 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 176.7, 160.1, 142.6, 132.7, 132.1, 131.4, 129.3, 126.5, 124.1, 123.5, 113.1, 112.2, 108.9, 80.3, 58.0, 40.6, 29.2, 27.3, 22.5, 14.2; MS (ES+) *m/z* 386 (*M* + 1), 388 (*M* + 23).

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EXAMPLE 1.15

Synthesis of 5-chloro-6-fluoro-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one

Following the procedure as described in EXAMPLE 1, and making non-critical variations using 3-(5-chloro-4-fluoro-2-hydroxyphenyl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one to replace 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained in 80% yield; mp 74-76 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.38-7.27 (m, 1H), 7.18-7.02 (m, 2H), 6.94 (d, 1H), 6.77 (d, 1H), 6.69 (d, 1H), 4.98 (d, 1H), 4.72 (d, 1H), 3.87-3.64 (m, 2H), 1.82-1.65 (m, 2H), 1.47-1.28 (m, 4H), 0.92 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 176.5, 160.6, 157.4, 142.6, 133.9, 131.8, 129.5, 124.6, 124.1, 123.5, 113.1, 109.0, 100.0, 81.2, 57.5, 40.6, 29.2, 27.2, 22.5, 14.1; MS (ES+) *m/z* 360 (*M* + 1).

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EXAMPLE 1.16

Synthesis of 6-methoxy-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one

Following the procedure as described in EXAMPLE 1, and making non-critical variations using 3-(2-hydroxy-4-methoxyphenyl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one to replace 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained in

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99% yield: ^1H NMR (300 MHz, CDCl_3) δ 7.30 (td, 1H), 7.14 (dd, 1H), 7.03 (t, 1H), 6.91 (d, 1H), 6.58 (d, 1H), 6.52 (d, 1H), 6.36 (dd, 1H), 4.93 (d, 1H), 4.69 (d, 1H), 3.91-3.63 (m, 2H), 3.77 (s, 3H), 1.81-1.65 (m, 2H), 1.46-1.29 (m, 4H), 0.91 (t, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 177.4, 162.1, 161.5, 142.5, 132.9, 128.8, 123.9, 123.5, 123.1, 121.0, 108.5, 107.5, 96.6, 80.5, 57.6, 55.6, 40.3, 29.0, 27.1, 22.3, 14.0; MS (ES+) m/z 338 ($M + 1$).

EXAMPLE 1.17

Synthesis of 6-chloro-5-fluoro-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'-(1'*H*)-one

Following the procedure as described in EXAMPLE 1, and making non-critical variations using 3-(4-chloro-5-fluoro-2-hydroxyphenyl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one to replace 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained in 44% yield: ^1H NMR (300 MHz, CDCl_3) δ 7.34 (td, 1H), 7.14 (dd, 1H), 7.06 (td, 1H), 6.98 (d, 1H), 6.93 (d, 1H), 6.50 (d, 1H), 4.96 (d, 1H), 4.70 (d, 1H), 3.87-3.63 (m, 2H), 1.81-1.65 (m, 2H), 1.47-1.29 (m, 4H), 0.91 (t, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 176.2, 156.9, 154.8, 151.6, 142.5, 131.5, 129.4, 128.6, 123.7, 121.7, 121.9, 111.2, 108.9, 80.6, 57.9, 40.5, 29.0, 27.1, 22.3, 14.0; MS (ES+) m/z 360 ($M + 1$).

EXAMPLE 1.18

Synthesis of 1'-pentyl-5-(trifluoromethyl)spiro[1-benzofuran-3,3'-indol]-2'-(1'*H*)-one

Following the procedure as described in EXAMPLE 1, and making non-critical variations using 3-(hydroxymethyl)-3-[2-hydroxy-5-(trifluoromethyl)phenyl]-1-pentyl-1,3-dihydro-2*H*-indol-2-one to replace 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained in 27% yield: ^1H NMR (300 MHz, CDCl_3) δ 7.48 (dd, 1H), 7.35 (td, 1H), 7.16-6.90 (m, 5H), 5.02 (d, 1H), 4.76 (d, 1H), 3.91-3.65 (m, 2H), 1.82-1.67 (m, 2H), 1.47-1.29 (m, 4H), 0.91 (t, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 176.5, 163.3, 142.6, 131.8, 129.8, 129.3, 127.7, 124.1, 124.0, 123.9, 123.6, 121.0, 110.6, 108.9, 80.5, 57.6, 40.5, 29.0, 27.1, 22.3, 13.9; MS (ES+) m/z 376 ($M + 1$).

EXAMPLE 1.19

Synthesis of 5,6-dichloro-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'-(1'*H*)-one

Following the procedure as described in EXAMPLE 1, and making non-critical variations using 3-(4,5-dichloro-2-hydroxyphenyl)-3-(hydroxymethyl)-1-pentyl-1,3-

dihydro-2*H*-indol-2-one to replace 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained in 43% yield. ¹H NMR (300 MHz, CDCl₃) δ 7.35 (td, 1H), 7.17-7.03 (m, 3H), 6.94 (d, 1H), 6.76 (s, 1H), 4.98 (d, 1H), 4.72 (d, 1H), 3.88-3.65 (m, 2H), 1.82-1.67 (m, 2H), 1.47-1.29 (m, 4H), 0.92 (t, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 176.2, 159.9, 142.5, 133.3, 131.5, 129.4, 124.6, 124.5, 123.9, 123.4, 112.4, 108.9, 80.8, 57.5, 40.5, 29.0, 27.1, 22.3, 14.0; MS (ES+) *m/z* 376 (*M* + 1), 378 (*M* + 1).

EXAMPLE 1.20

Synthesis of 1'-(diphenylmethyl)-5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'-(1'*H*)-one

Following the procedure as described in EXAMPLE 1, and making non-critical variations using 1-(diphenylmethyl)-3-(6-hydroxy-3,3-dimethyl-2,3-dihydro-1-benzofuran-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one to replace 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained: mp 190-192 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.40-7.26 (m, 10H), 7.19-7.15 (m, 1H), 7.07-6.93 (m, 3H), 6.55-6.51 (m, 1H), 6.38 (s, 1H), 6.20 (s, 1H), 4.98 (d, 1H), 4.71 (d, 1H), 4.17 (s, 2H), 1.17 (s, 3H), 1.14 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 178.1, 161.1, 161.0, 141.8, 137.9, 137.2, 132.8, 130.0, 128.6, 128.5, 128.4, 128.2, 128.0, 127.8, 123.9, 123.1, 120.8, 116.1, 112.1, 93.4, 85.4, 80.4, 58.7, 57.4, 41.3, 27.7, 27.6; MS (ES+) *m/z* 474.5 (*M* + 1).

EXAMPLE 1.21

Synthesis of 5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'-(1'*H*)-one

To a solution of 1'-(diphenylmethyl)-5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'-(1'*H*)-one (0.23 g, 0.49 mmol) in methanol (50.0 mL) was added palladium on carbon (0.10 g). The mixture was hydrogenated under 120 psi of hydrogen at ambient temperature overnight. The reaction mixture was filtered through celite, washed with methanol. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography (ethyl acetate/hexane, 1/2) to give the title compound (0.10 g, 68%): mp 95-100 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.74 (s, 1H), 7.28-7.20 (m, 1H), 7.15 (d, 1H), 7.03 (t, 1H), 6.95 (d, 1H), 6.43 (s, 1H), 6.40 (s, 1H), 4.94 (d, 1H), 4.66 (d, 1H), 4.19 (s, 2H), 1.20 (s, 3H), 1.16 (3H); ¹³C NMR (75 MHz, CDCl₃) δ 180.4, 161.3, 161.0, 140.3, 133.0, 130.1, 128.8, 124.2, 123.4, 120.0, 116.6,

110.1, 93.4, 85.5, 80.6, 58.3, 41.4, 27.7, 27.6; MS (ES+) m/z 308.6 ($M + 1$).

EXAMPLE 1.22

Synthesis of 4',7'-dichloro-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

5 To a solution of 4,7-dichloro-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one (0.69 g, 1.57 mmol) in anhydrous tetrahydrofuran (15.0 mL) was added triphenylphosphine (0.54 g, 2.04 mmol) followed by slow addition of diisopropyl azodicarboxylate (0.41 g, 2.04 mmol) at 0 °C. The brown reaction mixture was stirred at ambient temperature for 16 h and quenched with
10 ammonium chloride solution (2.00 mL). The organic solvent was removed *in vacuo*. The residue was dissolved in ethyl acetate (20.0 mL), washed with 10% aqueous HCl solution (10.0 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography eluting with ethyl acetate/hexane (35%) to give a solid, which was
15 crystallized from ethyl acetate/ether to give the title compound (0.13 g, 20%) as a colorless solid: mp 106-108 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.24-7.16 (m, 1H), 6.81 (d, 1H), 6.44 (s, 1H), 6.07 (s, 1H), 5.86 (dd, 2H), 4.87 (dd, 2H), 4.12-4.07 (m, 2H), 1.76-1.66 (m, 2H) 1.36-1.31 (m, 4H), 0.89 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 177.5, 157.0, 149.2, 142.1, 140.0, 132.3, 131.0, 130.2, 124.6, 116.0, 113.8, 102.3, 101.5,
20 93.3, 77.2, 58.5, 42.1, 29.5, 28.7, 22.3, 14.0; MS (ES+) m/z 420.4 ($M + 1$).

EXAMPLE 1.23

Synthesis of 4'-bromospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure as described in EXAMPLE 1.22, and making non-critical variations using 4-bromo-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-
25 1,3-dihydro-2*H*-indol-2-one to replace 4,7-dichloro-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained in 71% yield as a colorless solid: ¹H NMR (300 MHz, DMSO-*d*₆) δ 10.79 (s, 1H), 7.19-7.08 (m, 2H), 6.90 (dd, 1H), 6.58 (s, 1H), 6.25 (s, 1H), 5.90 (d, 2H), 4.74 (ABq, 2H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 178.5, 157.0, 148.8, 144.5, 141.9, 131.2,
30 130.6, 126.1, 119.2, 117.5, 109.8, 103.3, 101.8, 93.3, 77.6, 59.7; MS (ES-) m/z 360.4 ($M - 1$), 358.4 ($M - 1$).

EXAMPLE 1.24

Synthesis of 4'-bromo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'-(1'*H*)-one

To a solution of 4-bromo-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one (1.80 g, 4.80 mmol) in anhydrous ethyl acetate (50 mL) was added tributylphosphine (1.26 g, 1.54 mL, 6.24 mmol) at 0 °C under nitrogen. A solution of di-*tert*-butyl azodicarboxylate (1.44 g, 6.24 mmol) in anhydrous ethyl acetate (15.0 mL) was added over 10 min. The reaction solution was stirred for 2 h, and then quenched with saturated ammonium chloride solution (30.0 mL). After the aqueous layer was separated, the organic layer was washed with 10% aqueous HCl solution (2 x 25.0 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography eluting with ethyl acetate-hexane (70%) to obtain a solid which was triturated with diethyl ether to give the title compound (0.64 g, 37%) as a colorless solid: ¹H NMR (300 MHz, DMSO-*d*₆) δ 10.77 (s, 1H), 7.18-7.13 (m, 1H), 7.08 (d, 1H), 6.90 (d, 1H), 6.47 (s, 1H), 6.30 (s, 1H), 4.80 (ABq, 2H), 4.46 (t, 2H), 2.92 (t, 2H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 178.7, 162.2, 161.7, 144.5, 131.1, 131.0, 126.1, 119.8, 119.2, 119.1, 118.3, 109.7, 92.4, 77.6, 72.5, 59.2, 28.8; MS (ES-) *m/z* 358.4 (M - 1), 356.3 (M - 1).

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EXAMPLE 1.25

Synthesis of 4'-bromo-1'-(pyridin-2-ylmethyl)-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'-(1'*H*)-one

A mixture of 4-bromo-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-3-(hydroxymethyl)-1-(pyridin-2-ylmethyl)-1,3-dihydro-2*H*-indol-2-one (1.81 g, 3.88 mmol), triphenylphosphine (2.04 g, 7.77 mmol) and diisopropyl azodicarboxylate (1.57 g, 7.77 mmol) in anhydrous dioxane (60 mL) was heated at reflux for 16 h. After cooling down to ambient temperature, the solvent was removed *in vacuo*. The gummy residue was diluted with ethyl acetate (50.0 mL), washed with water (3 x 25.0 mL), brine (3 x 25.0 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography eluting with ethyl acetate/hexane (80%) to give the title compound (0.64 g, 37%) as colorless solid: mp >200 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.47 (d, 1H), 7.77 (dt, 1H), 7.37 (d, 1H), 7.27 (dt, 1H), 7.19-7.13 (m, 2H), 6.94 (dd, 1H), 6.61 (s, 1H), 6.33 (s, 1H), 5.08 (d, 1H), 5.03 (d, 1H), 4.93 (d, 1H), 4.74 (d, 1H), 4.48 (t, *J* = 8.6 Hz, 2H), 2.96 (t, 2H); ¹³C NMR

5 Synthesis of 5'-fluoro-1'-[[5-(trifluoromethyl)-2-furyl]methyl]spiro[furo[2,3-
f][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

To a solution of 5-fluoro-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-
1'-[[5-(trifluoromethyl)-2-furyl]methyl]-1,3-dihydro-2*H*-indol-2-one (3.34 g, 7.18 mmol) in
anhydrous tetrahydrofuran (80.0 mL) was added tributylphosphine (2.18 g, 2.70 mL,
10 10.8 mmol) under nitrogen. A solution of di-*tert*-butyl azodicarboxylate (2.49 g, 10.8
mmol) in anhydrous tetrahydrofuran (25.0 mL) was added over 10 min. The reaction
solution was stirred for 1 h, and quenched with saturated ammonium chloride (30.0
mL). After the solvent was removed under reduced pressure, the gummy material was
extracted with ethyl acetate (3 x 75.0 mL). The organic layer was washed with 10%
15 aqueous HCl solution (2 x 25.0 mL), saturated aqueous sodium hydrogen carbonate (3
x 25.0 mL), brine (3 x 25.0 mL), dried over anhydrous sodium sulfate and filtered. The
filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column
chromatography eluting with ethyl acetate/hexane (30%) to afford the title compound
(1.10 g, 34%) as a colorless solid: mp 139-141 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.02-
20 6.96 (m, 1H), 6.93-6.89 (m, 2H), 6.74-6.73 (m, 1H), 6.50 (s, 1H), 6.38 (d, 1H), 6.09 (s,
1H), 5.87 (dd, 2H), 4.95 (ABq, 2H), 4.78 (ABq, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 176.9,
161.5, 158.3, 155.9, 151.7, 149.2, 142.6, 137.1, 137.1, 133.7, 118.6, 115.6, 115.3,
112.7, 112.4, 112.0, 109.7, 109.6, 109.4, 102.8, 101.7, 93.8, 80.1, 58.6, 37.1; MS
(ES+) *m/z* 448.2 (M + 1).

Synthesis of 1'-(diphenylmethyl)-5'-methylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one

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(60.0 mL). The organic layer was separated and washed with 1.0 N hydrochloric acid solution (3 x 100 mL), dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography eluting with ethyl acetate/hexane (10-50%) to afford the title compound (0.98 g, 78% yield): ¹H NMR (300 MHz, CDCl₃) δ 7.40-7.25 (m, 10H), 7.02, (s, 1H), 6.96 (s, 1H), 6.79 (d, 1H), 6.50 (s, 1H), 6.36 (d, 1H), 6.08 (s, 1H), 5.86 (d, 2H), 4.82 (ABq, 2H), 2.20 (s, 3H).

EXAMPLE 1.28

Synthesis of 5'-methylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

10 A stainless steel hydrogenating vessel was successively charged with 1'-(diphenylmethyl)-5'-methylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one (0.90 g, 1.95 mmol), glacial acetic acid (50.0 mL) and palladium hydroxide (0.10 g, 1.35 mmol, 20 wt % on carbon). The vessel was flushed with nitrogen, sealed then heated to 60 °C and placed under 120 Psi of H₂. After 4 days of stirring, the reaction mixture was diluted with ethyl acetate and passed through a bed of celite. The filtrate was washed with water (6 x 100 mL), dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography eluting with ethyl acetate/hexane (40-50%) to afford the title compound (0.25 g, 43%): mp 269-271 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 10.45 (s, 1H), 7.00 (d, 1H), 6.87 (s, 1H), 6.76 (d, 1H), 6.63 (s, 1H), 6.21 (s, 1H), 5.87 (d, 2H), 4.64 (ABq, 2H), 2.17 (s, 3H); MS (ES+) *m/z* 296.28 (M + 1).

EXAMPLE 1.29

Synthesis of 5'-methyl-1'-{[5-(trifluoromethyl)-2-furyl]methyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

25 To a suspension of sodium hydride (0.03 g, 0.63 mmol, 60% dispersion in mineral oil) in *N,N*-dimethylformamide (5.00 mL) was slowly added a solution of 5'-methylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one (0.10 g, 0.33 mmol) in *N,N*-dimethylformamide (5.00 mL) at 0 °C. After stirring for 15 minutes at 0 °C, a solution of 2-(bromomethyl)-5-(trifluoromethyl)furan (0.11 g, 0.49 mmol) in *N,N*-dimethylformamide (40.0 mL) was added. The resulting mixture was stirred at ambient temperature for 4 h and quenched with water (20.0 mL). The mixture was extracted with ethyl acetate (3 x 25.0 mL). The combined organic layers was washed with water (50.0 mL) and brine (2 x 25.0 mL), dried over sodium sulfate and filtered. The filtrate

was concentrated *in vacuo*. The residue was subjected to column chromatography eluting with ethyl acetate/hexane (15-50%) to afford the title compound (0.11 g, 77% yield): mp 96-98 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.09 (d, 1H), 7.00 (s, 1H), 6.87 (d, 1H), 6.74 (d, 1H), 6.52 (s, 1H), 6.38 (d, 1H), 6.11 (s, 1H), 5.88 (d, 2H), 4.96 (ABq, 2H),
5 4.80 (ABq, 2H), 2.29 (s, 3H); MS (ES+) *m/z* 444.2 (M + 1).

EXAMPLE 1.30

Synthesis of 6-bromo-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(1'H)-one

Following the procedure as described in EXAMPLE 1.22, and making non-critical variations using 3-(4-bromo-2-hydroxyphenyl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one to replace 4,7-dichloro-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained in 82% yield as a colorless solid: ¹H NMR (300 MHz, CDCl₃) δ 7.33 (td, 1H), 7.15-7.14 (m, 2H), 7.04 (dd, 1H), 6.96-6.90 (m, 2H), 6.56 (d, 1H), 4.95 (d, 1H), 4.69 (d, 1H), 3.89-3.64 (m, 2H), 1.80-1.68 (m, 2H), 1.43-1.34 (m, 4H), 0.92 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 176.6, 161.6, 142.5, 132.1, 129.1, 128.4, 124.4, 123.9, 123.3, 122.8, 114.1,
15 108.8, 80.4, 57.6, 40.4, 29.0, 27.1, 22.3, 14.0; MS (ES+) *m/z* 386.3 (M + 1), 388.3 (M + 1).

EXAMPLE 1.31

Synthesis of 5-bromo-1'-(diphenylmethyl)spiro[1-benzofuran-3,3'-indol]-2'(1'H)-one

20 Following the procedure as described in Example 1, and making non-critical variations using 3-(5-bromo-2-hydroxyphenyl)-1-(diphenylmethyl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one to replace 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained (72%) as a white solid: ¹H NMR (300 MHz, CDCl₃) δ 7.43-7.25 (m, 11H),
25 7.14-6.93 (m, 4H), 6.83 (d, 1H), 6.71 (d, 1H), 6.52 (d, 1H), 5.0 (d, 1H), 4.73 (d, 1H); MS (ES+) *m/z* 484.4 (M + 1), 482.4 (M + 1).

EXAMPLE 1.32

Synthesis of 2-methyl-1'-pentylspiro[furo[2,3-*f*][1,3]benzothiazole-7,3'-indol]-2'(1'H)-one

Following the procedure as described in EXAMPLE 1.22, and making non-critical variations using 3-(hydroxymethyl)-3-(5-hydroxy-2-methyl-1,3-benzothiazol-6-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one to replace 4,7-dichloro-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained (50%) as a white solid: mp 105-107 °C; ¹H NMR (300 MHz,
30

CDCl₃) δ 7.59 (d, 1H), 7.28 (dt, 1H), 7.02-6.92 (m, 2H), 5.02 (d, 1H), 4.77 (d, 1H), 4.01 (m, 1H), 3.64 (m, 1H), 2.54 (s, 3H), 1.92-1.71 (m, 2H), 1.54-1.34 (m, 4H), 0.92 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 176.7, 169.2, 160.2, 149.2, 142.7, 138.3, 132.7, 129.0, 128.6, 123.5, 122.7, 122.1, 120.2, 108.6, 108.3, 80.1, 58.1, 40.7, 29.1, 27.0, 22.5, 20.2, 14.1; MS (ES+) *m/z* 379.5 (M + 1).

EXAMPLE 1.33

Synthesis of 5-bromo-1'-[[5-(trifluoromethyl)-2-furyl]methyl]spiro[1-benzofuran-3,3'-indol]-2'-(1'*H*)-one

Following the procedure as described in EXAMPLE 1.22, and making non-critical variations using 3-(hydroxymethyl)-3-(5-hydroxy-2-methyl-1,3-benzothiazol-6-yl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one to replace 4,7-dichloro-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained (30%) as a white solid: mp 143-145 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.35-7.27 (m, 2H), 7.17-6.98 (m, 3H), 6.84 (d, 1H), 6.78-6.73 (m, 2H), 6.40 (d, 1H), 5.07-4.87 (m, 3H), 4.69 (d, 1H); MS (ES+) *m/z* 464.2 (M + 1), 466.2 (M + 1).

EXAMPLE 1.34

Synthesis of 5-bromospiro[1-benzofuran-3,3'-indol]-2'-(1'*H*)-one

Following the procedure as described in EXAMPLE 1, and making non-critical variations using 3-(5-bromo-2-hydroxyphenyl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one to replace 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained (25%) as a white solid: mp 225-228 °C; ¹H NMR (300 MHz, CDCl₃) δ 10.65 (s, 1H), 7.35 (dd, 1H), 7.24 (dt, 1H), 7.11 (d, 1H), 6.99-6.88 (m, 3H), 6.83 (d, 1H), 4.81 (d, 1H), 4.69 (d, 1H); MS (ES+) *m/z* 316.1 (M + 1), 318.1 (M + 1).

EXAMPLE 1.35

Synthesis of 1'-(diphenylmethyl)-6-(trifluoromethoxy)spiro[1-benzofuran-3,3'-indol]-2'-(1'*H*)-one

To a solution of 1-(diphenylmethyl)-3-(hydroxymethyl)-3-[2-hydroxy-4-(trifluoromethoxy)phenyl]-1,3-dihydro-2*H*-indol-2-one (17.3 mmol) in anhydrous THF (200 mL) was added triphenylphosphine (6.34 g, 24.2 mmol) followed by diethyl azodicarboxylate (4.39 mL, 24.2 mmol) at 0 °C. The reaction mixture was stirred at ambient temperature for 16 h, quenched with saturated ammonium chloride (40.0 mL).

The aqueous mixture was extracted with ethyl acetate (3 x 150 mL). The combined organic layers was dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo*. The residue was subjected to column chromatography (ethyl acetate/hexane, 1/4) to give the title compound (6.00 g, 71%): ¹H NMR (300 MHz, CDCl₃) δ 7.45-6.51 (m, 18H), 5.08 (d, 1H), 4.81 (d, 1H); MS (ES+) *m/z* 488 (M + 1).

EXAMPLE 1.36

Synthesis of 6-(trifluoromethoxy)spiro[1-benzofuran-3,3'-indol]-2'-(1'*H*)-one

To a suspension of 1'-(diphenylmethyl)-6-(trifluoromethoxy)spiro[1-benzofuran-3,3'-indol]-2'-(1'*H*)-one (6.00 g, 12.3 mmol) in methanol (100 mL) and acetic acid (1.00 mL) was added 10 % palladium on carbon (0.65 g, 0.62 mmol), and the mixture was hydrogenated at ambient temperature under 130 psi of hydrogen for 5 days. The reaction mixture was filtered over celite and the filtrate was concentrated *in vacuo* to dryness. The residue was subjected to flash chromatography eluting with 30% ethyl acetate in hexane to give the title compound (2.95 g, 75%) as a white solid: mp 180-182 °C; ¹H NMR (300 MHz, CDCl₃) δ 9.19 (s, 1H), 7.29-6.92 (m., 4H), 6.86-6.64 (m, 3H), 5.03 (d, 1H), 4.75 (d, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 179.9, 161.9, 150.6, 132.3, 129.4, 127.4, 125.6, 124.3, 124.2, 123.8, 120.5, 114.1, 110.7, 104.3, 80.8, 58.2; MS (ES+) *m/z* 322 (M + 1).

EXAMPLE 1.37

Synthesis of ethyl (4'-bromo-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'-(2'*H*)-yl)acetate

Following the procedure as described in EXAMPLE 1.22, and making non-critical variations using ethyl [4-bromo-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate to replace 4,7-dichloro-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained (41%) as a colorless solid: MS (ES+) *m/z* 445.5 (M + 1).

EXAMPLE 1.38

Synthesis of ethyl (4'-chloro-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'-(2'*H*)-yl)acetate

Following the procedure as described in EXAMPLE 1.22, and making non-critical variations using ethyl [4-chloro-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate to replace 4,7-dichloro-3-(6-

hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained in 63% yield as a colorless solid: MS (ES+) *m/z* 400.8 (*M* + 1).

EXAMPLE 1.39

5 Synthesis of ethyl (4'-bromo-6,6-dimethyl-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)acetate

Following the procedure as described in EXAMPLE 1, and making non-critical variations using ethyl [4-bromo-3-(6-hydroxy-2,2-dimethyl-2,3-dihydro-1-benzofuran-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate to replace 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained in 52% yield: ¹H NMR (300 MHz, CDCl₃) δ 7.22-7.10 (m, 2H), 6.70 (d, 1H), 6.48 (s, 1H), 6.30 (s, 1H), 5.0 (d, 1H); 4.86 (d, 1H), 4.63 (d, 1H), 4.35 (d, 1H), 4.28-4.18 (m, 2H), 2.79 (s, 2H), 1.43 (s, 3H), 1.39 (s, 3H), 1.28 (t, 3H); MS (ES+) *m/z* 472.5 (*M* + 1), 474.5 (*M* + 1).

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EXAMPLE 1.40

Synthesis of ethyl (4'-bromo-5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2' *H*)-yl)acetate

Following the procedure as described in EXAMPLE 1, and making non-critical variations using ethyl [4-bromo-3-(4,5-difluoro-2-hydroxyphenyl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate to replace 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained in 81% yield: MS (ES+) *m/z* 438.4 (*M* + 1), 440.4 (*M* + 1).

EXAMPLE 1.41

25 Synthesis of ethyl (5'-chloro-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)acetate

Following the procedure as described in EXAMPLE 1.22, and making non-critical variations using ethyl [5-chloro-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate to replace 4,7-dichloro-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained in 90% yield as a colorless solid: MS (ES+) *m/z* 400.8 (*M* + 1).

EXAMPLE 1.42

Synthesis of 7'-fluorospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one

A solution of 7-fluoro-3-(6-hydroxy-1,3-benzodioxol-5-yl)-1,3-dihydro-2*H*-indol-2-one (2.00 g, 7.00 mmol) and paraformaldehyde (2.10 g, 61.0 mmol) in THF (50 mL) was degassed by bubbling through argon for one hour, followed by the slow addition of lithium diisopropylamide (48.8 mL, freshly made 0.50 M solution, 25 mmol) at -78 °C. The mixture was stirred at ambient temperature overnight and quenched with saturated ammonium chloride (50.0 mL). The mixture was extracted with ethyl acetate (3 x 100 mL). The combined organic layers was dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was dissolved in anhydrous ethyl acetate (50 mL) followed by the addition of tributylphosphine (2.10 mL, 8.00 mmol) and di-*tert*-butyl azodicarboxylate (1.90 g, 8.00 mmol) at 0 °C. The reaction mixture was stirred at ambient temperature for 16 h and quenched with saturated ammonium chloride (30.0 mL). The organic layer was separated, dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was dissolved in methanol (70.0 mL) followed by the addition of saturated sodium bicarbonate solution (30.0 mL). The resulted mixture was refluxed at 100 °C for one hour. After cooling down to ambient temperature, the mixture was extracted with ethyl acetate (3 x 50.0 mL). The combined organic layers was dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography (ethyl acetate/hexane, 1/5) to give the title compound (0.27 g, 17%): ¹H NMR (300 MHz, DMSO-*d*₆) δ 11.06 (s, 1H), 7.17-7.08 (m, 1H), 7.00-6.88 (m, 2H), 6.64 (s, 1H), 6.33 (s, 1H), 5.92-5.85 (m, 2H), 4.74 (d, 1H), 4.62 (d, 1H).

EXAMPLE 1.43

Synthesis of methyl (6-chloro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'-(2'*H*)-yl)acetate

Following the procedure as described in EXAMPLE 1.22, and making non-critical variations using methyl [3-(4-chloro-2-hydroxyphenyl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate to replace 4,7-dichloro-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained in 74% yield as a colorless solid: ¹H NMR (300 MHz, CDCl₃) δ 7.29 (dt, 1H), 7.14 (dd, 1H), 7.06 (t, 1H), 6.95 (d, 1H), 6.81-6.74 (m, 3H), 5.03 (d, 1H), 4.74 (d, 1H), 4.65 (d, 1H), 4.44 (d, 1H), 3.75 (s, 3H); MS (ES+) *m/z* 344.5 (M + 1), 346.5 (M + 1).

EXAMPLE 1.44

Synthesis of ethyl (5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2'H)-yl)acetate

Following the procedure as described in EXAMPLE 1.22, and making non-critical variations using ethyl [3-(4,5-difluoro-2-hydroxyphenyl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate to replace 4,7-dichloro-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1-pentyl-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained in 46% yield as a light yellow oil: ¹H NMR (300 MHz, CDCl₃) δ 7.31 (dt, 1H), 7.16 (dd, 1H), 7.08 (dt, 1H), 6.81-6.71 (m, 2H), 6.67 (dd, 1H), 4.98 (d, 1H), 4.74 (d, 1H), 4.64 (d, 1H), 4.37 (d, 4.24 (q, 7.1 Hz), 1.28 (t, 3H); MS (ES+) *m/z* 360.5 (M + 1).

EXAMPLE 1.45

Synthesis of ethyl (2'-oxo-6,7-dihydro-5*H*-spiro[indeno[5,6-*b*]furan-3,3'-indol]-1'(2'H)-yl)acetate

To a solution of ethyl [3-(6-hydroxy-2,3-dihydro-1*H*-inden-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate (4.20 mmol) in anhydrous THF (60.0 mL) was added triphenylphosphine (1.43 g, 5.46 mmol) and diethyl azodicarboxylate (0.95 g, 5.46 mmol) at 0 °C. The reaction mixture was stirred at ambient temperature for 16 h and quenched with saturated ammonium chloride (20.0 mL). The mixture was extracted with ethyl acetate (3 x 50.0 mL). The combined organic layers was dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography (ethyl acetate/hexane, 1/4) to give the title compound (0.25 g, 16 % in three steps): ¹H NMR (300 MHz, CDCl₃) δ 7.29 (td, 1H), 7.22-7.17 (m, 1H), 7.07 (t, 1H), 6.81 (s, 1H), 6.78 (d, 1H), 6.65 (s, 1H), 4.95 (d, 1H), 4.71 (d, 1H), 4.64 (d, 1H), 4.42 (d, 1H), 4.24 (q, 2H), 2.84 (t, 2H), 2.73-2.65 (m, 2H), 2.10-1.95 (m, 2H), 1.29 (t, 3H); MS (ES+) *m/z* 364 (M + 1).

EXAMPLE 1.46

Synthesis of ethyl (2-oxo-5',6',7',8'-tetrahydrospiro[indole-3,3'-naphtho[2,3-*b*]furan]-1(2*H*)-yl)acetate

Following the procedure as described in EXAMPLE 1.45, and making non-critical variations using ethyl [3-(hydroxymethyl)-3-(3-hydroxy-5,6,7,8-tetrahydronaphthalen-2-yl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate to replace ethyl [3-(6-hydroxy-2,3-dihydro-1*H*-inden-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-

yl]acetate, the title compound was obtained (24 % in three steps): ^1H NMR (300 MHz, CDCl_3) δ 7.29 (td, 1H), 7.19 (d, 1H), 7.07 (t, 1H), 6.79 (d, 1H), 6.66 (s, 1H), 6.51 (s, 1H), , 4.91 (d, 1H), 4.67 (d, 1H), 4.52 (ABq, 2H), 4.24 (q, 2H), 2.77-2.51 (m, 4H), 1.77-1.64 (m, 4H), 1.29 (t, 3H); MS (ES+) m/z 378 ($M + 1$).

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EXAMPLE 1.47

Synthesis of ethyl (4'-bromo-5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2'*H*)-yl)acetate

Following the procedure as described in EXAMPLE 1.45, and making non-critical variations using ethyl [4-bromo-3-(4,5-difluoro-2-hydroxyphenyl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate to replace ethyl [3-(6-hydroxy-2,3-dihydro-1*H*-inden-5-yl)-3-(hydroxymethyl)-2-oxo-2,3-dihydro-1*H*-indol-1-yl]acetate, the title compound was obtained (41%): mp 133-134 °C; ^1H NMR (300 MHz, CDCl_3) δ 7.26-7.15 (m, 3 H), 6.78-6.58 (m, 2H), 5.08 (d, 1H), 4.91 (d, 1H), 4.63 (d, 1H), 4.35 (d, 1H), 4.24 (q, 2H), 1.29 (t, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 176.5, 166.8, 157.1, 143.7, 130.7, 129.0, 127.8, 120.0, 111.8, 111.6, 107.5, 99.8, 99.5, 62.2, 59.1, 41.7, 14.1; MS (ES+) m/z 438 ($M + 1$), 440 ($M + 1$), 460 ($M + 23$), 462 ($M + 23$).

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EXAMPLE 1.48

Synthesis of 1'-(diphenylmethyl)-6,7-dihydrospiro[benzo[1,2-*b*:4,5-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one

Following the procedure described in EXAMPLE 1, and making non-critical variations using 1-(diphenylmethyl)-3-(5-hydroxy-2,3-dihydro-1-benzofuran-6-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one to replace 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained (43%): MS (ES+) m/z 446.4 ($M + 1$).

20

EXAMPLE 1.49

Synthesis of 6,7-dihydrospiro[benzo[1,2-*b*:4,5-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one

A mixture of 1'-(diphenylmethyl)-6,7-dihydrospiro[benzo[1,2-*b*:4,5-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one (0.29 g, 0.65 mmol) and palladium hydroxide (0.10 g, 20% on activated carbon) in acetic acid (20.0 mL) was hydrogenated at 60 °C under normal pressure of hydrogen for 20 hours. The reaction mixture was filtered through celite and washed with acetone (50.0 mL). The filtrate was concentrated *in vacuo* to dryness to give the title compound (0.13 g, 69%): MS (ES+) m/z 280.2 ($M + 1$).

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EXAMPLE 1.50

Synthesis of 1'-(diphenylmethyl)-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one

Following the procedure described in EXAMPLE 1, and making non-critical variations using 1-(diphenylmethyl)-3-(6-hydroxy-2,3-dihydro-1-benzofuran-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one to replace 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained (51%) as a white solid: MS (ES+) *m/z* 446.3 (*M* + 1).

EXAMPLE 1.51

Synthesis of 5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one

Following the procedure as described in EXAMPLE 1.49, and making non-critical variations using 1'-(diphenylmethyl)-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one to replace 1'-(diphenylmethyl)-6,7-dihydrospiro[benzo[1,2-*b*:4,5-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one, the title compound was obtained (68%): mp 208-210 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 10.53 (s, 1H), 7.39-6.76 (m, 4H), 6.45 (s, 1H), 6.35 (s, 1H), 4.68 (ABq, 2H), 4.45 (t, 2H), 2.92 (t, 2H); MS (ES+) *m/z* 280.2 (*M* + 1).

EXAMPLE 1.52

Synthesis of ethyl (2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)acetate

A mixture of 5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]2'(1'*H*)-one (0.28 g, 1.00 mmol), ethyl 2-bromoacetate (0.17 g, 1.00 mmol) and cesium carbonate (0.98 g, 3.00 mmol) in acetone (20.0 mL) was stirred at reflux for 5 hours. After cooling down to ambient temperature, the mixture was filtered. The filtrate was evaporated under reduced pressure and the residue was subjected to column chromatography to give the title compound (0.23 g, 63%) as a white solid: MS (ES+) *m/z* 366.4 (*M* + 1).

EXAMPLE 1.53

Synthesis of 4'-methoxy-1'{{[5-(trifluoromethyl)-2-furyl]methyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure described in EXAMPLE 1, and making non-critical variations using 3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-4-methoxy-1-{{[5-(trifluoromethyl)-2-furyl]methyl}-1,3-dihydro-2*H*-indol-2-one to replace 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-

2*H*-indol-2-one, the title compound was obtained (33%) as a white solid: mp 149-153 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.32-7.24 (m, 1H), 6.82-6.62 (m, 3H), 6.46 (s, 1H), 6.40 (d, 1H), 6.08 (s, 1H), 5.87 (ABq, 2H), 4.92 (ABq, 2H), 4.82 (ABq, 2H), 3.70 (s, 3H); MS (ES+) *m/z* 460.3 (M + 1).

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EXAMPLE 1.54

Synthesis of 7'-fluoro-1'-{[5-(trifluoromethyl)-2-furyl]methyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one

Following the procedure described in EXAMPLE 1, and making non-critical variations using 7-fluoro-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1-*[[*5-(trifluoromethyl)-2-furyl]methyl]-1,3-dihydro-2*H*-indol-2-one to replace 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained (32%) as a white solid: mp 116-118 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.36-6.88 (m, 4H), 6.67 (s, 1H), 6.62 (d, 1H), 6.19 (s, 1H), 5.90 (d, 2H), 5.07 (q, 2H), 4.75 (dd, 2H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 176.9, 155.8, 154.1, 149.1, 148.8, 145.6, 142.4, 140.9, 140.3, 139.2, 139.2, 135.2, 135.2, 128.5, 128.4, 124.9, 128.4, 124.9, 124.8, 124.7, 121.2, 120.4, 120.4, 119.8, 117.6, 117.2, 117.0, 114.5, 114.5, 109.5, 103.2, 102.0, 93.8, 80.1, 58.3, 58.2, 39.0, 38.9; MS (ES+) *m/z* 448.3 (M + 1).

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EXAMPLE 2

20 Synthesis of (2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(*2'H*)-yl)acetic acid

To a suspension of ethyl (2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(*2'H*)-yl)acetate (10.5 g, 24.5 mmol) in THF (200 mL) and water (100 mL) was added lithium hydroxide monohydrate (3.98 g, 95.0 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 30 min and at ambient temperature for 17 h. The mixture was neutralized with of 4 M HCl (15.0 mL). The residue obtained upon removing the solvent was acidified by the addition of 4 M HCl (6.2 mL) to pH 3. The solid was filtered, washed with water and hexane, and dried under the reduced pressure to give the title compound (8.48 g, 87%) as a white solid: ¹H NMR (300 MHz, CDCl₃) δ 7.32-7.06 (m, 4H), 6.79 (d, 1H), 6.49 (s, 1H), 6.23 (s, 1H), 5.84 (m, 2H), 4.92 (m, 1H), 4.69-4.63 (m, 2H), 4.45 (m, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 177.8, 171.8, 155.8, 149.0, 142.4, 141.2, 132.0, 129.0, 124.1, 124.0, 119.2, 108.3, 103.4, 101.5, 93.5, 80.2, 58.2, 41.1; MS (ES-) *m/z* 338.2 (M-1).

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EXAMPLE 2.1

Synthesis of (2'-oxo-6,7-dihydro-5*H*-spiro[indeno[5,6-*b*]furan-3,3'-indol]-1'(2'*H*)-yl)acetic acid

Following the procedure as described in EXAMPLE 2, and making non-critical variations using ethyl (2'-oxo-6,7-dihydro-5*H*-spiro[indeno[5,6-*b*]furan-3,3'-indol]-1'(2'*H*)-yl)acetate to replace ethyl (2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetate, the title compound was obtained in 74% yield; MS (ES-) *m/z* 354 (M – 1).

EXAMPLE 2.2

10 Synthesis of (4'-chloro-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)acetic acid

Following the procedure as described in EXAMPLE 2, and making non-critical variations using ethyl (4'-chloro-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)acetate to replace ethyl (2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetate, the title compound was obtained in 92% yield as a colorless solid: mp 228-229 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.26-7.21 (m, 1H), 7.03 (dd, 1H), 6.71 (dd, 1H), 6.52 (s, 1H), 6.36 (s, 1H), 4.93 (dd, 2H), 4.69-4.63 (m, 1H), 4.54-4.51 (m, 3H), 2.95 (t, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 177.8, 170.9, 162.1, 162.1, 143.1, 131.7, 130.0, 128.6, 124.7, 119.6, 118.7, 117.0, 106.7, 92.8, 77.2, 72.3, 58.1, 41.2, 20 28.9; MS (ES-) *m/z* 370.4 (M-1).

EXAMPLE 2.3

Synthesis of (4'-bromo-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)acetic acid

Following the procedure as described in EXAMPLE 2, and making non-critical variations using ethyl (4'-bromo-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)acetate to replace ethyl (2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetate, the title compound was obtained (98%) as a colorless solid: MS (ES-) *m/z* 415.2 (M-1).

EXAMPLE 2.4

30 Synthesis of (5'-chloro-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)acetic acid

Following the procedure as described in EXAMPLE 2, and making non-critical variations using ethyl (5'-chloro-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-

indol]-1'(2'*H*)-yl)acetate to replace ethyl (2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetate, the title compound was obtained in 98% yield as a colorless solid: ¹H NMR (300 MHz, CDCl₃) δ 7.27-7.25 (m, 1H), 7.16 (d, 1H), 6.72 (d, 1H), 6.54 (s, 1H), 6.39 (s, 1H), 4.93 (dd, 2H), 4.69-4.63 (m, 1H), 4.54-4.51 (m, 3H), 2.95 (t, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 177.8, 170.9, 162.1, 162.1, 143.1, 131.7, 130.0, 128.6, 124.7, 119.6, 118.7, 117.0, 106.7, 92.8, 77.2, 72.3, 58.1, 41.2, 28.9; MS (ES-) *m/z* 370.4 (M - 1).

EXAMPLE 2.5

Synthesis of (2-oxo-5',6',7',8'-tetrahydrospiro[indole-3,3'-naphtho[2,3-*b*]furan]-1(2'*H*)-yl)acetic acid

Following the procedure as described in Example 2, and making non-critical variations using ethyl (2-oxo-5',6',7',8'-tetrahydrospiro[indole-3,3'-naphtho[2,3-*b*]furan]-1(2'*H*)-yl)acetate to replace ethyl (2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetate, the title compound was obtained (99%): MS (ES-) *m/z* 348 (M - 1).

EXAMPLE 2.6

Synthesis of (2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)acetic acid

A mixture of ethyl (2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)acetate (0.23 g, 0.63 mmol) and LiOH (0.10 g, 4.20 mmol) in MeOH/H₂O (1/1, 20.0 mL) was stirred at ambient temperature for 20 hours. The mixture was acidified with 0.1 M HCl until pH 2-3. The solid was filtered off and dried to give the title compound (0.15 g, 70%): MS (ES-) *m/z* 336.3 (M-1).

EXAMPLE 3

Synthesis of *N*-(4-chlorobenzyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide

A. Preparation of stock solution of isobutyl (2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetyl carbonate

To a solution of (2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetic acid (0.30 g, 0.88 mmol) in dichloromethane (12.5 mL) was added *N*-methylmorpholine (0.09 g, 0.88 mmol) and *iso*-butyl chloroformate (0.12 g, 0.88 mmol) dropwise at 0 °C. The mixture was stirred at 0 °C for 1.5 h and at ambient temperature for 3 h. This mixture was used as a mixed anhydride for the next step amide formation.

B. Synthesis of *N*-(4-chlorobenzyl)-2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetamide

To the above mixed anhydride stock solution (2.50 mL, 0.18 mmol) was added a solution of 4-chlorobenzylamine in dichloromethane (0.35 mL, 0.50 M, 0.18 mmol) at ambient temperature. The reaction mixture was stirred at ambient temperature for 23 h, washed with saturated aqueous sodium carbonate and water. After removal of the solvent, diethyl ether was added and the precipitate was collected by filtration to give the title compound (0.04 g, 46%): ¹H NMR (300 MHz, CDCl₃) δ 7.39-6.97 (m, 8H), 6.49 (s, 1H), 6.29 (br, 1H), 6.01 (s, 1H), 5.85 (m, 2H), 4.87 (m, 1H), 4.65 (m, 1H), 4.53-4.29 (m, 4H); MS (ES⁺), *m/z* 485.2 (M + 23).

EXAMPLE 3.1

The compounds listed in the following table were synthesized using similar conditions as described in Example 3. The compound numbers listed below do not correspond to the compound numbers provided in the general Reaction Schemes above.

Compound Number	Name	MS (<i>m/z</i> , M + 1)
1	<i>N</i> -(3-fluorophenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	433.2
2	<i>N</i> -butyl-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	395.2
3	1'-(2-oxo-2-piperidin-1-ylethyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	407.2
4	<i>N</i> -butyl- <i>N</i> -methyl-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	409.3
5	2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)- <i>N</i> -phenylacetamide	415.2
6	<i>N</i> -(4-fluorophenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	433.3
7	<i>N</i> -(3-fluorobenzyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	447.3
8	<i>N</i> -(3-chlorophenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	449.2
9	<i>N</i> -(2-fluorophenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	433.3

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
10	<i>N</i> -(2-ethylphenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	443.2
11	<i>N</i> -(4-ethylphenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	443.3
12	<i>N</i> -(3-methylphenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	429.3
13	<i>N</i> -(2,3-dimethylphenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	443.3
14	<i>N</i> -(3,5-dimethylphenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	443.4
15	2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)- <i>N</i> -pentylacetamide	409.4
16	2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)- <i>N</i> -propylacetamide	381.3
17	<i>N</i> -isopropyl-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	381.4
18	<i>N</i> -(3-methylbutyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	409.3
19	<i>N</i> -isobutyl-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	395.3
20	<i>N</i> -hexyl-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	423.4
21	<i>N</i> -cyclohexyl-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	421.4
22	<i>N</i> -cyclopentyl-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	407.3
23	<i>N</i> -heptyl-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	437.5
24	<i>N</i> -(2-chlorobenzyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	463.2
25	<i>N</i> -(2,6-dimethylphenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	443.3
26	<i>N</i> -(2-methoxyphenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	445.3
27	<i>N</i> -[(5-methyl-2-furyl)methyl]-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	433.2

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
28	<i>N</i> -ethyl-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	367.4
29	<i>N</i> -methyl-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	353.3
30	<i>N</i> -(2-fluorobenzyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	447.2
31	<i>N</i> -[2-(3-methoxyphenyl)ethyl]-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	473.3
32	<i>N</i> -(2-ethoxyethyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	411.3
33	<i>N</i> -(4-methoxybenzyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	459.3
34	<i>N</i> -(2,4-dimethylphenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	443.3
35	<i>N</i> -(3-isopropoxypropyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	439.4
36	<i>N</i> -(2-furylmethyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	419.3
37	<i>N</i> -(cyclohexylmethyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	435.3
38	<i>N</i> -(3-fluoro-2-methylphenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	447.3
39	<i>N</i> -(4-methoxyphenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	445.3
40	<i>N</i> -cyclobutyl-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	393.4
41	<i>N</i> -(2,5-difluorophenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	451.3
42	<i>N</i> -benzyl-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	429.3
43	<i>N</i> -(cyclopropylmethyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	393.2
44	<i>N</i> -butyl- <i>N</i> -ethyl-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	423.3

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
45	<i>N</i> -octyl-2-(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	451.2
46	<i>N</i> -(3,3-dimethylbutyl)-2-(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	423.2
47	<i>N</i> -(4-chloro-2-methylphenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	463.1
48	<i>N</i> -(3-methoxyphenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	445.0
49	<i>N</i> -(2-fluoro-4-methylphenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	447.0
50	<i>N</i> -(3,4-dimethylphenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	443.1
51	<i>N</i> -(3-chlorobenzyl)-2-(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	463.1
52	<i>N</i> -(3-methoxybenzyl)-2-(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	459.1
53	<i>N</i> -(3,4-difluorophenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	451.1
54	<i>N</i> -(3-methylbenzyl)-2-(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	443.1
55	<i>N</i> -(2-methoxybenzyl)-2-(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	459.2
56	<i>N</i> -(4-isopropylphenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	457.2
57	<i>N</i> -(2,3-difluorophenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	451.1
58	2-(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)- <i>N</i> -(tetrahydrofuran-2-ylmethyl)acetamide	423.1
59	<i>N</i> -[2-(4-methylphenyl)ethyl]-2-(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	457.1
60	<i>N</i> -[2-(3-chlorophenyl)ethyl]-2-(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	477.1
61	<i>N</i> -(4-cyanophenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	440.1

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
62	<i>N</i> -(2,3-dihydro-1 <i>H</i> -inden-1-yl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	455.1
63	<i>N</i> -(2-methoxyethyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	397.1
64	<i>N</i> -[2-(4-methoxyphenyl)ethyl]-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	473.1
65	<i>N</i> -(2-cyanoethyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	392.1
66	<i>N</i> -(2,4-dichlorobenzyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	497.0
67	<i>N</i> -(3,5-difluorobenzyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	465.0
68	<i>N</i> -(2,4-difluorobenzyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	465.0
69	<i>N</i> -(2-methylbenzyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	443.1
70	<i>N</i> -(3,4-difluorobenzyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	465.1
71	<i>N</i> -(2,5-difluorobenzyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	465.1
72	2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)- <i>N,N</i> -dipropylacetamide	423.2
73	<i>N,N</i> -dibutyl-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	451.2
74	<i>N</i> -(2,6-difluorobenzyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	465.1
75	<i>N</i> -[2-(methylthio)phenyl]-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	461.1
76	<i>N</i> -(2-isopropylphenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	457.2
77	<i>N</i> -(4-bromophenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	493.0
78	<i>N</i> -(4-chlorophenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	449.0

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
79	<i>N</i> -(2,4-dichlorophenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	483.0
80	<i>N</i> -(3,5-dichlorophenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	483.1
81	<i>N,N</i> -diethyl-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	395.1
82	<i>N</i> -methyl-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)- <i>N</i> -phenylacetamide	429.1
83	<i>N</i> -(4-hydroxybutyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	411.1
84	<i>N</i> -allyl-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	379.1
85	<i>N</i> -(2-fluoro-5-methylphenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	447.1
86	<i>N</i> -(1,3-benzodioxol-5-ylmethyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	473.1
87	<i>N</i> -cyclopropyl-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	379.1
88	<i>N</i> -(2-cyclopropylethyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	407.2
89	<i>N</i> -(3,4-dichlorobenzyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	497.1
90	<i>N</i> -(2,3-dichlorobenzyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	497.1
91	<i>N</i> -(2,5-dimethylphenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	443.1
92	<i>N</i> -(3,4-dichlorophenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	483.3
93	<i>N,N</i> -dimethyl-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	367.2
94	<i>N</i> -methyl-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)- <i>N</i> -(2-phenylethyl)acetamide	457.2
95	2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)- <i>N</i> -(2-phenylpropyl)acetamide	457.2

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
96	<i>N</i> -[(1 <i>R</i>)-1-cyclohexylethyl]-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	449.2
97	<i>N</i> -[(1 <i>S</i>)-1-cyclohexylethyl]-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	449.2
98	2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)- <i>N</i> -(2-piperidin-1-ylethyl)acetamide	451.4
99	2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)- <i>N</i> -[3-(trifluoromethyl)phenyl]acetamide	483.1
100	<i>N</i> -(3-cyanophenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	440.1
101	1'-(2-morpholin-4-yl-2-oxoethyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	409.1
102	2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)- <i>N</i> -(2-phenylethyl)acetamide	443.1
103	<i>N</i> -(4-bromo-2-chlorophenyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	527.0
104	<i>N</i> -(2-biphenyl-4-ylethyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	519.2

EXAMPLE 3.2

Synthesis of *N*-(2-fluorophenyl)-2-(2'-oxo-6,7-dihydro-5*H*-spiro[indeno[5,6-*b*]furan-3,3'-indol]-1'(2'*H*)-yl)acetamide

- 5 To a solution of 2'-oxo-6,7-dihydro-5*H*-spiro[indeno[5,6-*b*]furan-3,3'-indol]-1'(2'*H*)-yl)acetic acid (0.18 g, 0.54 mmol) in chloroform (5.00 mL) was added oxalyl chloride (0.09 mL, 1.07 mmol) with one drop of DMF. The mixture was refluxed for 2 hours, and evaporated under reduced vacuum to dryness. To the above residue were added Et₃N (0.66 mL, 4.72 mmol), 2-fluoroaniline (0.10 mL, 1.00 mmol) and THF (5.00
- 10 mL). The reaction mixture was stirred at ambient temperature overnight, evaporated to dryness. The residue was subjected to column chromatography (25% ethyl acetate in hexane) to yield the title compound (0.04 g, 17%): ¹H NMR (300 MHz, CDCl₃) δ 8.26 (t, 1H), 8.05-7.90 (br, 1H), 7.33 (td, 1H), 7.26-6.96 (m, 6H), 6.83 (s, 1H), 6.61 (s, 1H), 4.98 (d, 1H), 4.73 (d, 1H), 4.71 (d, 1H), 4.52 (d, 1H), 2.85 (t, 2H), 2.69 (t, 2H), 2.12-
- 15 1.94 (m, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 178.6, 165.0, 159.8, 146.9, 141.5, 137.5, 132.5, 129.2, 126.3, 125.2, 124.8, 124.4, 124.3, 121.9, 118.9, 115.2, 114.9, 109.0,

106.8, 79.9, 58.2, 45.3, 33.2, 32.0, 26.1; MS (ES+) m/z 429 ($M + 1$), 451 ($M + 23$).

EXAMPLE 3.3

Synthesis of *N*-(2-fluorophenyl)-2-(2-oxo-5',6',7',8'-tetrahydrospiro[indole-3,3'-naphtho[2,3-*b*]furan]-1(2*H*)-yl)acetamide

- 5 Following the procedure as described in EXAMPLE 3.2, and making non-critical variations using (2-oxo-5',6',7',8'-tetrahydrospiro[indole-3,3'-naphtho[2,3-*b*]furan]-1(2*H*)-yl)acetic acid to replace 2'-oxo-6,7-dihydro-5*H*-spiro[indeno[5,6-*b*]furan-3,3'-indol]-1'(2'*H*)-yl)acetic acid, the title compound was obtained in 5% yield: ¹H NMR (300 MHz, CDCl₃) δ 8.27 (t, 1H), 8.04-7.90 (br, 1H), 7.33 (td, 1H), 7.26-6.97 (m, 6H), 6.69
10 (s, 1H), 6.48 (s, 1H), 4.94 (d, 1H), 4.69 (d, 1H), 4.71 (d, 1H), 4.52 (d, 1H), 2.81-2.45 (m, 4H), 1.82-1.60 (m, 4H); MS (ES+) m/z 443 ($M + 1$), 465 ($M + 23$).

EXAMPLE 3.4

Synthesis of 2-(4'-bromo-5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2'*H*)-yl)-*N*-(2-fluorophenyl)acetamide

- 15 A. Synthesis of (4'-bromo-5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2' *H*)-yl)acetic acid

- Following the procedure as described in EXAMPLE 2, and making non-critical variations using ethyl (4'-bromo-5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2' *H*)-yl)acetate to replace ethyl (2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetate, the title compound was obtained in 100% yield. The product was
20 used directly in the next step.

- B. Synthesis of 2-(4'-bromo-5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2' *H*)-yl)-*N*-(2-fluorophenyl)acetamide

- To a solution of (4'-bromo-5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2'*H*)-yl)acetic acid (0.24 g, 0.59 mmol) and oxalyl chloride (0.15 mL, 1.76 mmol) in
25 toluene (7.00 mL) was added one drop of DMF and the resulted mixture was stirred at ambient temperature overnight. The mixture was concentrated under vacuum. The residue was dissolved in dichloromethane (5.00 mL) and 2-fluoroaniline (0.18 mL, 1.89 mmol) was added at ambient temperature. The mixture was stirred at ambient
30 temperature for one hour. More dichloromethane (100 mL) was added. The organic layer was washed with water, dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo*. The residue was subjected to column chromatography (ethyl acetate/hexane, 1/5) to give the title compound (0.23 g, 76%):

¹H NMR (300 MHz, CDCl₃) δ 8.20 (t, 1H), 7.80 (br, 1H), 7.27-7.17 (m, 2H), 7.16-7.03 (m, 3H), 6.97-6.88 (m, 1H), 6.78-6.60 (m, 2H), 5.08 (d, 1H), 4.93 (d, 1H), 4.68 (d, 1H), 4.49 (d, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 177.1, 163.9, 157.8, 143.6, 131.0, 128.8, 128.1, 124.7, 121.8, 120.0, 115.0, 111.6, 108.1, 99.8, 77.5, 59.2, 44.7; MS (ES+) *m/z* 503.4 (*M* + 1), 505.4 (*M* + 1).

EXAMPLE 3.5

Synthesis of 2-(4'-bromo-6,6-dimethyl-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)-*N*-(2-fluorophenyl)acetamide

A. Synthesis of (4'-bromo-6,6-dimethyl-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)acetic acid

Following the procedure as described in EXAMPLE 2, and making non-critical variations using ethyl (4'-bromo-6,6-dimethyl-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)acetate to replace ethyl (2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetate, the title compound was obtained. The product was used directly in the next step.

B. Synthesis of 2-(4'-bromo-6,6-dimethyl-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)-*N*-(2-fluorophenyl)acetamide

Following the procedure as described in EXAMPLE 3.4B, and making non-critical variations using (4'-bromo-6,6-dimethyl-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)acetic acid to replace (4'-bromo-5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2'*H*)-yl)acetic acid, the title compound was obtained (61% for two steps): MS (ES+) *m/z* 537.4 (*M* + 1), 539.4 (*M* + 1).

EXAMPLE 3.6

Synthesis of 2-(4'-chloro-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)-*N*-(2-fluorophenyl)acetamide

Following the procedure as described in EXAMPLE 3.4B, and making non-critical variations using (4'-chloro-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)acetic acid to replace (4'-bromo-5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2'*H*)-yl)acetic acid, the title compound was obtained (69%) as a colorless solid: mp 243-245 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.19 (t, 1H), 7.96 (s, 1H), 7.21-7.27 (m, 1H), 7.10-7.02 (m, 4H), 6.88 (d, 1H), 6.55 (s, 1H), 6.35 (s, 1H), 4.96 (dd, 2H), 4.70 (d, 1H), 4.57-4.53 (m, 3H), 2.97 (t, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 178.2, 164.4, 162.2, 162.1, 143.2, 131.6, 130.2, 128.5, 125.2, 125.1, 124.9, 124.6,

121.9, 119.7, 118.6, 116.8, 115.1, 114.8, 107.3, 92.9, 77.2, 72.4, 58.2, 44.9, 28.9; MS (ES+) m/z 465.5 (M + 1).

EXAMPLE 3.7

Synthesis of 2-(5'-chloro-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)-*N*-(2-fluorophenyl)acetamide

Following the procedure as described in EXAMPLE 3.4B, and making non-critical variations using (5'-chloro-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)acetic acid to replace (4'-bromo-5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2'*H*)-yl)acetic acid, the title compound was obtained (91%) as a colorless solid: mp 229-230 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.21 (t, 1H), 7.88 (s, 1H), 7.28-7.25 (m, 1H), 7.18 (d, 1H), 7.13-7.04 (m, 3H), 6.90 (d, 1H), 6.57 (s, 1H), 6.40 (s, 1H), 4.95 (d, 1H), 4.70-4.66 (m, 2H), 4.56-4.43 (m, 3H), 2.99 (t, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 177.8, 170.9, 162.1, 162.1, 143.1, 131.7, 130.0, 128.6, 124.7, 119.6, 118.7, 117.0, 106.7, 92.8, 77.2, 72.3, 58.1, 41.2, 28.9; MS (ES+) m/z 465.4 (M + 1).

EXAMPLE 3.8

Synthesis of 2-(6-chloro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2'*H*)-yl)-*N*-(2-fluorophenyl)acetamide

Following the procedure as described in EXAMPLE 3.4B, and making non-critical variations using (6-chloro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2'*H*)-yl)acetic acid to replace (4'-bromo-5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2'*H*)-yl)acetic acid, the title compound was obtained (10%) as a white solid: mp 70-75 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.21 (t, 1H), 7.99 (br, 1H), 7.32 (dt, 1H), 7.19-6.93 (m, 7H), 6.80 (dd, 1H), 6.73 (d, 1H), 5.01 (d, 1H), 4.75 (d, 1H), 4.69 (d, 1H), 4.50 (d, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 177.7, 164.6, 161.4, 141.4, 135.5, 131.6, 129.4, 127.3, 125.2, 125.0, 124.7, 124.6, 124.4, 124.3, 124.1, 121.9, 121.8, 115.1, 114.8, 111.3, 109.0, 80.3, 57.6, 44.9; MS (ES+) m/z 423.4 (M + 1).

EXAMPLE 3.9

Synthesis of 2-(5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2'*H*)-yl)-*N*-(2-fluorophenyl)acetamide

Following the procedure as described in EXAMPLE 3.4B, and making non-critical variations using (5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2'*H*)-yl)acetic acid to replace (4'-bromo-5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2'

H)-yl)acetic acid, the title compound was obtained (35%) as a white solid: mp 97-100 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.20-8.10 (m, 2H), 7.31 (dt, 1H), 7.19-7.00 (m, 5H), 6.95 (d, 1H), 6.77-6.40 (m, 2H), 5.02 (d, 1H), 4.74 (d, 1H), 4.69 (d, 1H), 4.51 (d, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 177.4, 164.3, 141.4, 131.2, 129.7, 125.6, 125.5, 125.3, 125.2, 125.1, 124.7, 124.4, 124.1, 121.8, 115.1, 114.9, 112.1, 111.8, 109.1, 100.3, 100.0, 80.7, 57.9; MS (ES+) *m/z* 425.5 (M + 1).

EXAMPLE 3.10

Synthesis of 2-(5-bromo-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2'*H*)-yl)-*N*-(2-fluorophenyl)acetamide

10 Following the procedure as described in EXAMPLE 3.4B, and making non-critical variations using (5-bromo-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2'*H*)-yl)acetic acid to replace (4'-bromo-5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2'*H*)-yl)acetic acid, the title compound was obtained (94%) as a light yellow solid: mp 100-103 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.26 (dd, 1H), 7.92 (br, 1H), 7.39-7.31 (m, 2H), 7.22-7.01 (m, 6H), 6.91 (d, 1H), 6.87 (d, 1H), 5.02 (d, 1H), 4.76 (d, 1H), 4.67 (d, 1H), 4.57 (d, 1H); MS (ES+) *m/z* 467.3 (M + 1).

EXAMPLE 3.11

Synthesis of 2-(4'-fluoro-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)-*N*-(2-fluorophenyl)acetamide

20 Following the procedure as described in EXAMPLE 3.4B, and making non-critical variations using (4'-fluoro-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)acetic acid to replace (4'-bromo-5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2'*H*)-yl)acetic acid, the title compound was obtained: ¹H NMR (300 MHz, CDCl₃) δ 8.20 (t, 1H), 7.91 (s, 1H), 7.29 (dt, 1H), 7.13-7.04 (m, 3H), 6.81-6.75 (m, 2H), 6.61 (s, 1H), 6.39 (s, 1H), 4.95-4.87 (m, 2H), 4.70 (d, 1H), 4.55-4.44 (m, 3H), 2.98 (t, 2H); MS (ES+) *m/z* 449.5 (M + 1)

EXAMPLE 3.12

Synthesis of 2-(4'-bromo-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)-*N*-(2-fluorophenyl)acetamide

30 Following the procedure as described in EXAMPLE 3.4B, and making non-critical variations using (4'-bromo-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)acetic acid to replace (4'-bromo-5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2'*H*)-yl)acetic acid, the title compound was obtained (75%) as

a colorless solid: mp 245-246 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.20 (t, 1H), 7.90 (s, 1H), 7.20-7.03 (m, 5H), 6.92 (dd, 1H), 6.53 (s, 1H), 6.36 (s, 1H), 5.05 (d, 1H), 4.90 (d, 1H), 4.69 (d, 1H), 4.55-4.43 (m, 3H), 2.97 (t, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 178.3, 164.3, 162.4, 162.2, 143.4, 130.4, 130.0, 128.0, 125.5, 125.2, 124.7, 121.9, 120.0, 119.7, 118.6, 116.7, 115.1, 114.8, 107.8, 92.8, 77.2, 72.4, 59.1, 44.9, 28.9; MS (ES+) *m/z* 509 (M + 1), 511 (M + 1).

EXAMPLE 3.13

Synthesis of *N*-(2-fluorophenyl)-2-(2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)acetamide

Following the procedure as described in EXAMPLE 3.4B, and making non-critical variations using (2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)acetic acid to replace (4'-bromo-5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2'*H*)-yl)acetic acid, the title compound was obtained (68%) as a white solid: mp 210-212 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 10.18 (s, 1H), 8.17-7.67 (m, 1H), 7.55-6.90 (m, 7H), 6.54 (s, 1H), 6.38 (s, 1H), 4.68 (m, 4H), 4.46 (t, 2H), 2.93 (t, 2H); MS (ES+) *m/z* 431.4 (M + 1).

EXAMPLE 3.14

Synthesis of 2-(4'-fluoro-7'-methyl-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)-*N*-(2-fluorophenyl)acetamide

Following the procedure as described in EXAMPLE 3.4B and making non-critical variations using (4'-fluoro-7'-methyl-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)acetic acid to replace (4'-bromo-5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2'*H*)-yl)acetic acid, the title compound was obtained (21%) as a white solid: mp 250-255 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 10.23 (s, 1H), 7.99-7.69 (m, 1H), 7.36-7.01 (m, 4H), 6.74 (t, 1H), 6.63 (s, 1H), 6.42 (s, 1H), 5.90 (d, 2H), 4.88 (t, 2H), 4.76 (ABq, 2H), 3.30 (s, 3H); MS (ES+) *m/z* 463.4 (M + 1).

EXAMPLE 4

Synthesis of 4'-[6-(dimethylamino)pyridin-3-yl]-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

To an oven-dried flask was charged with [6-(dimethylamino)pyridin-3-yl]boronic acid (37.0 mg, 0.17 mmol), Pd(PPh₃)₄ (13.5 mg, 0.012 mmol) followed by flashing with nitrogen. To the flask was added a solution of 4'-bromo-1'-pentylspiro[furo[2,3-

f[[1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one (50.0 mg, 0.12 mmol) in anhydrous dioxane (2.00 mL) followed by the addition of 2.0 M Na₂CO₃ (0.24 mL). The reaction mixture was heated at reflux for 48 h. After cooling down to ambient temperature, the solvent was removed under reduced pressure. The residue was diluted with ethyl acetate (2.00 mL), washed with saturated ammonium chloride (2.00 mL), and concentrated *in vacuo* to dryness. The residue was subjected to column chromatography to yield the title compounds: ¹H NMR (300 MHz, CDCl₃) δ 7.77 (d, 1H), 7.32 (t, 1H), 6.87 (dd, 2H), 6.71 (dd, 1H), 6.23 (d, 1H), 6.20 (s, 1H), 5.88 (d, 2H), 4.56 (ABq, 2H), 3.89-3.80 (m, 1H), 3.69-3.59 (m, 1H), 3.05 (s, 6H), 1.78-1.69 (m, 2H), 1.39-1.35 (m, 4H), 0.90 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 177.9, 158.3, 156.1, 148.8, 147.3, 142.9, 142.0, 137.8, 137.2, 129.9, 128.9, 125.6, 122.0, 121.0, 107.6, 104.3, 102.5, 101.5, 93.6, 77.8, 58.5, 40.5, 38.2, 29.1, 27.2, 22.4, 14.0; MS (ES+, *m/z*) 472.0 (*M* + 1).

EXAMPLE 4.1

The compounds listed in the following table were synthesized using similar conditions as described in Example 4. As previously noted, the compound numbers listed below do not correspond to the compound numbers provided in the general Reaction Schemes above.

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
105	4'-(3,5-dimethoxyphenyl)-1'-pentylspiro[furo[2,3- <i>f</i> [[1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	488.4
106	4'-(4-fluorophenyl)-1'-pentylspiro[furo[2,3- <i>f</i> [[1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	447.3
107	4'-(3,5-dichlorophenyl)-1'-pentylspiro[furo[2,3- <i>f</i> [[1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	496.3
108	4'-[4-(dimethylamino)phenyl]-1'-pentylspiro[furo[2,3- <i>f</i> [[1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	471.3
109	1'-pentyl-4'-(3,4,5-trimethoxyphenyl)spiro[furo[2,3- <i>f</i> [[1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	518.3
110	4-(2'-oxo-1'-pentyl-1',2'-dihydrospiro[furo[2,3- <i>f</i> [[1,3]benzodioxole-7,3'-indol]-4'-yl)benzonitrile	453.3
111	4'-dibenzo[b,d]furan-4-yl-1'-pentylspiro[furo[2,3- <i>f</i> [[1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	518.3

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
112	4'-(1-benzyl-1 <i>H</i> -pyrazol-4-yl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	508.4
113	4'-(2-methoxypyrimidin-5-yl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	460.3
114	4'-(2,4-dimethoxypyrimidin-5-yl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	490.4
115	4-(2'-oxo-1'-pentyl-1',2'-dihydrospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-4'-yl)benzamide	471.3
116	4'-{4-[(dimethylamino)methyl]phenyl}-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	484.6
117	4'-(1-benzofuran-2-yl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	467.5
118	4'-(6-methoxypyridin-3-yl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	458.5
119	<i>N,N</i> -dimethyl-4-(2'-oxo-1'-pentyl-1',2'-dihydrospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-4'-yl)benzamide	498.6
120	4'-dibenzo[<i>b,d</i>]thien-4-yl-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	533.6
121	3-(2'-oxo-1'-pentyl-1',2'-dihydrospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-4'-yl)benzonitrile	452.5
122	1'-pentyl-4'-pyridin-3-ylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	428.5
123	4'-(3-fluoro-4-methoxyphenyl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	475.5
124	1'-pentyl-4'-[2-(trifluoromethoxy)phenyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	511.5
125	4'-[3,5-bis(trifluoromethyl)phenyl]-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	563.5

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
126	1'-pentyl-4'-[4-(trifluoromethyl)pyridin-3-yl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	496.5
127	4'-(2-fluoro-5-methoxyphenyl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	475.5
128	4'-(4-ethoxy-3-fluorophenyl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	489.5
129	4'-(1-benzothien-2-yl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	483.6
130	4'-isobutyl-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	407.5
131	1'-pentyl-4'-[4-(trifluoromethoxy)phenyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	511.5
132	4'-(5-fluoro-2-methoxyphenyl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	475.5
133	4'-(1,3-benzodioxol-5-yl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	471.5
134	1'-pentyl-4'-phenylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	427.5
135	1'-pentyl-4'-[2-(trifluoromethyl)phenyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	495.5
136	4'-(4-chlorophenyl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	461.9
137	4'-(2,3-dihydro-1,4-benzodioxin-6-yl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	485.5
138	1'-pentyl-4'-quinolin-3-ylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	478.5
139	4'-(3,5-difluorophenyl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	463.5

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
140	4'-isoquinolin-4-yl-1'-pentylspiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	478.5
141	4'-(6-methoxypyridin-2-yl)-1'-pentylspiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	458.5
142	4'-(1 <i>H</i> -indol-5-yl)-1'-pentylspiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	466.5
143	<i>N</i> -[2-(2'-oxo-1'-pentyl-1',2'-dihydrospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-4'- yl)phenyl]acetamide	484.5
144	4'-(4-fluoro-2-methylphenyl)-1'-pentylspiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	459.5
145	1'-pentyl-4'-quinolin-6-ylspiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	478.5
146	<i>N</i> -[4-(2'-oxo-1'-pentyl-1',2'-dihydrospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-4'- yl)phenyl]methanesulfonamide	520.6
147	4'-(5-chloro-2-methoxyphenyl)-1'-pentylspiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	492.0
148	1'-pentyl-4'-[3-(trifluoromethoxy)phenyl]spiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	511.5
149	1'-pentyl-4'-(4-phenoxyphenyl)spiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	519.6
150	4'-(2,4-dimethoxyphenyl)-1'-pentylspiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	487.5
151	4'-(3-furyl)-1'-pentylspiro[furo[2,3-f][1,3]benzodioxole- 7,3'-indol]-2'(1' <i>H</i>)-one	417.5
152	4'-(3,4-dimethoxyphenyl)-1'-pentylspiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	487.5
153	<i>N</i> -[4-(2'-oxo-1'-pentyl-1',2'-dihydrospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-4'- yl)phenyl]acetamide	484.5

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
154	1'-pentyl-4'-[(<i>E</i>)-2-phenylvinyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	453.5
155	4'-(4-methoxyphenyl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	457.5
156	4'-(6-fluoropyridin-3-yl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	446.5
157	4'-(3-chloro-4-fluorophenyl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	479.9
158	4'-(3-chlorophenyl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	461.9
159	4'-(1-benzothien-3-yl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	483.6
160	1'-pentyl-4'-(2-phenoxyphenyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	519.6
161	4'-(4-isopropoxyphenyl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	485.6
162	4'-[(<i>E</i>)-2-(4-fluorophenyl)vinyl]-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	471.5
163	4'-(6-fluoropyridin-2-yl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	446.5
164	1'-pentyl-4'-[1-(phenylsulfonyl)-1 <i>H</i> -indol-3-yl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	606.7
165	4'-(3-fluorophenyl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	445.5
166	4'-(3-acetylphenyl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	469.5
167	4'-(2-furyl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	417.5
168	4'-(4-methylphenyl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	441.5

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
169	4'-(1-methyl-1H-pyrrol-3-yl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	430.5
170	4'-(2,5-difluorophenyl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	463.5
171	4'-(2-fluorophenyl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	445.5
172	4'-(2-chlorophenyl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	461.9
173	4'-(2,4-difluorophenyl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	463.5
174	4'-(4-morpholin-4-ylphenyl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	512.6
175	tert-butyl 5-methoxy-3-(2'-oxo-1'-pentyl-1',2'-dihydrospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-4'-yl)-1 <i>H</i> -indole-1-carboxylate	596.7
176	1'-pentyl-4'-pyrimidin-5-ylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	429.5
177	tert-butyl 4-[2-(2'-oxo-1'-pentyl-1',2'-dihydrospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-4'-yl)phenyl]piperazine-1-carboxylate	611.7
178	4'-(2-methoxypyridin-3-yl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	458.5
179	4'-(5-methoxypyridin-3-yl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	458.5
180	4'-(4-butoxy-3-fluorophenyl)-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	517.6
181	1'-pentyl-4'-pyridin-4-ylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	428.5
182	1'-pentyl-4'-phenoxathiin-4-ylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	549.6
183	4'-[(1 <i>Z</i>)-3-chloroprop-1-en-1-yl]-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	425.9

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
184	1'-pentyl-4'-(3-thienyl)spiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	433.5
185	4'-(2,3-dimethoxyphenyl)-1'-pentylspiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	487.5
186	4'-(4-butylphenyl)-1'-pentylspiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	483.6
187	4'-(3-fluoro-5-methoxyphenyl)-1'-pentylspiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	475.5
188	4'-[3-fluoro-4-(pentyloxy)phenyl]-1'- pentylspiro[furo[2,3-f][1,3]benzodioxole-7,3'- indol]-2'(1' <i>H</i>)-one	531.6
189	4'-(2-butoxy-5-fluorophenyl)-1'-pentylspiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	517.6
190	4'-(3-butoxyphenyl)-1'-pentylspiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	499.6
191	4'-(4-butoxyphenyl)-1'-pentylspiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	499.6
192	4'-(4-isobutoxyphenyl)-1'-pentylspiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	499.6
193	4'-(2-chloro-4-[(3,5-dimethoxybenzyl)oxy]phenyl)-1'- pentylspiro[furo[2,3-f][1,3]benzodioxole-7,3'- indol]-2'(1' <i>H</i>)-one	628.1
194	4'-[4-(benzyloxy)-3-chlorophenyl]-1'- pentylspiro[furo[2,3-f][1,3]benzodioxole-7,3'- indol]-2'(1' <i>H</i>)-one	568.1
195	4'-(1-methyl-1 <i>H</i> -indol-5-yl)-1'-pentylspiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	480.6
196	4'-(4-methoxypyridin-3-yl)-1'-pentylspiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	458.5
197	4'-[(6-methoxypyridin-3-yl)amino]-1'- pentylspiro[furo[2,3-f][1,3]benzodioxole-7,3'- indol]-2'(1' <i>H</i>)-one	473.5

EXAMPLE 4.2

Synthesis of 2-(5,6-difluoro-2'-oxo-4'-pyrimidin-5-ylspiro[1-benzofuran-3,3'-indol]-1'(2'
H)-yl)-*N*-(2-fluorophenyl)acetamide

To a solution of 2-(4'-bromo-5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-
5 1'(2' *H*)-yl)-*N*-(2-fluorophenyl)acetamide (0.15 g, 0.30 mmol) in anhydrous 1,4-dioxane
(5.00 mL) was added Pd(PPh₃)₄ (0.03 g, 0.03 mmol) and stirred at ambient
temperature for 10 min. Pyrimidine-5-boronic acid (0.06 g, 0.45 mmol) and sodium
carbonate (0.90 mL of 2 M solution, 1.80 mmol) were added. The reaction mixture was
relaxed at 120 °C for 16 h, diluted with ethyl acetate (50.0 mL). The organic layer was
10 washed with water, dried over anhydrous sodium sulfate and filtered. The filtrate was
concentrated *in vacuo*. The residue was subjected to column chromatography (ethyl
acetate/hexane, 1/1) to give the title compound (0.13 g, 84%): ¹H NMR (300 MHz,
CDCl₃) δ 9.13 (s, 1H), 8.29-8.10 (m, 3H), 7.62 (s, 1H), 7.44 (t, 1H), 7.16-7.03 (m, 4H),
6.91 (d, 1H), 6.85-6.76 (m, 1H), 6.46-6.37 (m, 1H), 4.85-4.73 (m, 2H), 4.61-4.47 (m,
15 2H); ¹³C NMR (75 MHz, CDCl₃) δ 177.1, 163.9, 157.7, 156.4, 155.7, 141.9, 132.9,
130.0, 126.0, 124.7, 121.9, 115.0, 111.6, 109.8, 100.2, 79.4, 57.9, 44.7; MS (ES+) *m/z*
503.5 (M + 1).

EXAMPLE 4.3

Synthesis of 2-(6,6-dimethyl-2'-oxo-4'-pyrimidin-5-yl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-
20 *b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)-*N*-(2-fluorophenyl)acetamide

Following the procedure as described in EXAMPLE 4.2, making variation using
2-(4'-bromo-6,6-dimethyl-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-
1'(2'*H*)-yl)-*N*-(2-fluorophenyl)acetamide to replace 2-(4'-bromo-5,6-difluoro-2'-
oxospiro[1-benzofuran-3,3'-indol]-1'(2'*H*)-yl)-*N*-(2-fluorophenyl)acetamide, the title
25 compound was obtained (95%): mp > 250 °C; ¹H NMR (300 MHz, CDCl₃) δ 9.10 (s,
1H), 8.24 (t, 1H), 8.15 (s, 2H), 8.00 (s, 1H), 7.40 (t, 1H), 7.16-7.03 (m, 4H), 6.88 (d,
1H), 6.61 (s, 1H), 5.99 (s, 1H), 4.84-4.73 (m, 2H), 4.54 (d, 1H), 4.44 (d, 1H), 2.79 (s,
2H), 1.45 (s, 3H), 1.39 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 178.4, 164.5, 161.1, 157.4,
155.8, 154.1, 150.8, 141.7, 132.9, 132.2, 131.3, 129.4, 125.9, 125.5, 125.2, 124.7,
30 121.9, 120.8, 119.3, 118.8, 115.0, 109.5, 93.5, 88.5, 78.9, 58.0, 45.0, 42.0, 28.0, 27.9;
MS (ES+) *m/z* 537.5 (M + 1).

EXAMPLE 4.4

Synthesis of 4'-(3-furyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one

Following the procedure as described in EXAMPLE 4, making variations using 4'-bromospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one to replace 4'-bromo-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one, and 3-furanboronic acid to replace [6-(dimethylamino)pyridin-3-yl]boronic acid, the title compound was obtained (66%) as a colorless solid: mp 270-272 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.32 (t, 1H), 7.25 (d, 2H), 6.97 (d, 1H), 6.91 (d, 1H), 6.83 (s, 1H), 6.44 (s, 1H), 6.30 (s, 1H), 6.04 (d, 1H), 5.89 (dd, 2H), 4.68 (ABq, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 180.4, 156.2, 149.2, 142.9, 142.1, 141.2, 140.4, 131.3, 129.2, 128.5, 125.3, 122.6, 120.6, 111.0, 109.5, 102.9, 101.6, 94.0, 77.2, 59.0; MS (ES+) *m/z* 348.4 (M + 1).

EXAMPLE 4.5

Synthesis of 4'-dibenzo[*b,d*]furan-4-ylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one

Following the procedure as described in EXAMPLE 4, and making non-critical variations using 4'-bromospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one to replace 4'-bromo-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one, and dibenzo[*b,d*]furan-4-ylboronic acid to replace [6-(dimethylamino)pyridin-3-yl]boronic acid, the title compound was obtained (10%) as a colorless solid: mp >230 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 10.77 (s, 1H), 8.04 (d, 1H), 7.97 (dd, 1H), 7.43-7.42 (m, 3H), 7.34-7.29 (m, 3H), 7.16 (t, 1H), 6.98 (d, 1H), 6.89 (d, 1H), 6.25 (s, 1H), 5.69 (d, 2H), 4.41 (ABq, 2H); MS (ES+) *m/z* 448.5 (M + 1).

EXAMPLE 4.6

Synthesis of 4'-(6-methoxypyridin-3-yl)-1'-{[5-(trifluoromethyl)-2-furyl]methyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one

Following the procedure as described in EXAMPLE 4, and making non-critical variations using 4'-bromo-1'-{[5-(trifluoromethyl)-2-furyl]methyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one to replace 4'-bromo-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one, and (6-methoxypyridin-3-yl)boronic acid to replace [6-(dimethylamino)pyridin-3-yl]boronic acid, the title compound was obtained (51%) as a colorless solid: mp 174-176 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.73 (d, 1H), 7.69 (d, 1H), 7.34 (t, 1H), 7.03 (d, 1H), 6.89-6.86 (m, 2H), 6.65 (d, 1H), 6.61 (d, 1H), 6.56 (d, 1H), 6.17 (d, 2H), 5.87 (d, 2H), 4.99 (ABq, 2H), 4.56 (ABq, 2H), 3.90 (s, 3H);

¹³C NMR (75 MHz, CDCl₃) δ 177.7, 163.5, 158.4, 156.1, 151.8, 151.8, 149.2, 147.8, 146.1, 142.3, 141.6, 138.8, 136.9, 132.6, 130.0, 129.1, 127.8, 127.2, 126.2, 119.9, 112.7, 112.7, 110.9, 109.6, 109.5, 108.5, 102.3, 101.6, 93.6, 78.2, 58.5, 53.6, 37.0; MS (ES+) *m/z* 537.4 (*M* + 1).

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EXAMPLE 4.7

Synthesis of 4'-[6-(dimethylamino)pyridin-3-yl]-1'-[5-(trifluoromethyl)-2-furyl]methyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure as described in EXAMPLE 4, and making non-critical variations using 4'-bromo-1'-[5-(trifluoromethyl)-2-furyl]methyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 4'-bromo-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one, the title compound was obtained (37%) as a colorless solid: mp 174-176 °C; MS (ES+) *m/z* 550.4 (*M* + 1).

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EXAMPLE 4.8

Synthesis of 4'-pyrimidin-5-ylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure as described in EXAMPLE 4, and making non-critical variations using 4'-bromospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 4'-bromo-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one, and pyrimidin-5-ylboronic acid to replace [6-(dimethylamino)pyridin-3-yl]boronic acid, the title compound was obtained (32%) as a colorless solid: mp 185-187 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 10.85 (s, 1H), 9.02 (s, 1H), 8.19 (s, 2H), 7.33 (t, 1H), 7.00 (d, 1H), 6.83 (d, 1H), 6.37 (s, 1H), 6.19 (s, 1H), 5.89 (d, 2H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 178.7, 157.5, 156.0, 155.6, 148.8, 142.3, 133.1, 132.6, 131.8, 129.5, 124.5, 120.3, 110.9, 103.2, 101.9, 93.3, 79.5, 66.8, 58.5; MS (ES+) *m/z* 360.4 (*M* + 1).

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EXAMPLE 4.9

Synthesis of 4'-(3-furyl)-1'-(pyridin-2-ylmethyl)-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one

Following the procedure as described in EXAMPLE 4, and making non-critical variations using 4'-bromo-1'-(pyridin-2-ylmethyl)-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one to replace 4'-bromo-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one, and 3-furanboronic acid to replace [6-(dimethylamino)pyridin-3-yl]boronic acid, the title compound was obtained (75%) as a colorless solid: mp 195-197 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.58 (d, 1H), 7.68 (t, 1H), 7.32-7.21 (m, 4H), 6.97 (d, 1H), 6.92 (d, 1H), 6.77 (s, 1H), 6.60 (s, 1H), 6.35 (s, 1H),

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5.99 (s, 1H), 5.12 (ABq, 2H), 4.71 (ABq, 2H), 4.57 (t, 2H), 3.03 (t, 2H); MS (ES+) *m/z* 437.4 (M + 1).

EXAMPLE 4.10

Synthesis of 1'-(pyridin-2-ylmethyl)-4'-pyrimidin-5-yl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one

Following the procedure as described in EXAMPLE 4, and making non-critical variations using 4'-bromo-1'-(pyridin-2-ylmethyl)-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one to replace 4'-bromo-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one, and pyrimidin-5-ylboronic acid to replace [6-(dimethylamino)pyridin-3-yl]boronic acid, the title compound was obtained (16%) as a colorless solid: mp >200 °C; ¹H NMR (300 MHz, CDCl₃) δ 9.09 (s, 1H), 8.59 (d, 1H), 8.14 (s, 2H), 7.74 (t, 1H), 7.67 (d, 1H), 7.63 (d, 1H), 7.52 (d, 1H), 7.47-7.42 (m, 1H), 7.37 (d, 1H), 7.30 (d, 1H), 7.09 (d, 1H), 6.82 (d, 1H), 6.62 (s, 1H), 6.07 (s, 1H), 5.18 (ABq, 2H), 4.62 (ABq, 2H), 4.62-4.48 (m, 2H), 3.02 (t, 2H); MS (ES+) *m/z* 449.5 (M + 1).

EXAMPLE 4.11

Synthesis of 4'-pyridin-3-yl-1'-(pyridin-2-ylmethyl)-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one

Following the procedure as described in EXAMPLE 4, and making non-critical variations using 4'-bromo-1'-(pyridin-2-ylmethyl)-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one to replace 4'-bromo-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one, and pyridin-3-ylboronic acid to replace [6-(dimethylamino)pyridin-3-yl]boronic acid, the title compound was obtained (9%) as a colorless solid: mp >200 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.52 (d, 1H), 8.42 (d, 1H), 7.96 (s, 1H), 7.79 (t, 1H), 7.40 (d, 1H), 7.29 (t, 2H), 7.18-7.08 (m, 2H), 7.00 (d, 1H), 6.81 (d, 1H), 6.72 (s, 1H), 5.98 (s, 1H), 5.08 (ABq, 2H), 4.56-4.40 (m, 4H), 3.10-2.90 (m, 2H); MS (ES+) *m/z* 448.5 (M + 1).

EXAMPLE 4.12

Synthesis of 4'-(3-furyl)-1'-{[5-(trifluoromethyl)-2-furyl]methyl}-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one

Following the procedure as described in EXAMPLE 4, and making non-critical variations using 4'-bromo-1'-{[5-(trifluoromethyl)-2-furyl]methyl}-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one to replace 4'-bromo-1'-

pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one, and 3-furylboronic acid to replace [6-(dimethylamino)pyridin-3-yl]boronic acid, the title compound was obtained (27%) as a colorless solid: mp 167-169 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.34-7.29 (m, 2H), 7.01 (dd, 1H), 6.95 (dd, 1H), 6.77 (dd, 1H), 6.74 (dd, 1H), 6.51 (s, 1H), 6.41 (d, 1H), 6.34 (s, 1H), 6.00 (dd, 1H), 4.97 (ABq, 2H), 4.67 (ABq, 2H), 4.56 (t, 2H), 3.01 (t, 2H); MS (ES+) *m/z* 494.4 (*M* + 1).

EXAMPLE 4.13

Synthesis of 4'-quinolin-3-yl-1'-[[5-(trifluoromethyl)-2-furyl]methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure as described in EXAMPLE 4, and making non-critical variations using 4'-bromo-1'-[[5-(trifluoromethyl)-2-furyl]methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 4'-bromo-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one, quinolin-3-ylboronic acid to replace [6-(dimethylamino)pyridin-3-yl]boronic acid, the title compound was obtained (50%) as a colorless solid: ¹H NMR (300 MHz, CDCl₃) δ 8.52 (d, 1H), 8.09 (d, 1H), 7.74-7.68 (m, 1H), 7.56-7.50 (m, 1H), 7.42-7.39 (m, 2H), 7.32 (s, 1H), 7.09 (d, 1H), 7.01 (d, 1H), 6.78-6.77 (m, 1H), 6.45 (d, 1H), 6.26 (s, 1H), 5.94 (d, 1H), 5.91 (s, 1H), 5.89 (d, 1H), 5.03 (ABq, 2H), 4.52 (ABq, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 177.4, 156.0, 151.8, 150.0, 149.3, 147.0, 142.4, 141.8, 136.8, 135.8, 131.1, 130.2, 129.9, 129.3, 129.0, 128.8, 128.0, 127.1, 127.0, 126.4, 126.0, 120.4, 112.7, 109.5, 108.8, 102.5, 101.7, 93.7, 78.3, 58.5, 37.1; MS (ES+) *m/z* 557.4 (*M* + 1).

EXAMPLE 4.14

Synthesis of 4'-pyrimidin-5-yl-1'-[[5-(trifluoromethyl)-2-furyl]methyl]-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one

A mixture of 4'-bromo-1'-[[5-(trifluoromethyl)-2-furyl]methyl]-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one (0.11 g, 0.21 mmol), pyrimidine-5-boronic acid (0.04 g, 0.33 mmol), tetrakis(triphenylphosphine)palladium(0) (0.03 g, 0.02 mmol), 2.00 M sodium carbonate (1.00 mL) and 1,2-dimethoxyethane (10.0 mL) was heated at reflux for 16 h under nitrogen. After the organic solvent was evaporated *in vacuo*, the black residue was extracted with ethyl acetate (3 x 35.0 mL). The combined organic layers was dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo*. The residue was subjected to column chromatography eluting with ethyl acetate:hexane (35%) to afford the title compound

(0.03 g, 26%): mp 263-266 °C; ¹H NMR (300 MHz, CDCl₃) δ 9.10 (s, 1H), 8.14 (s, 2H), 7.39 (t, 1H), 7.10, (d, 1H), 6.87 (d, 1H), 6.76 (s, 1H), 6.51 (s, 1H), 6.46 (s, 1H), 6.07 (s, 1H), 5.03 (ABq, 2H), 4.62-4.48 (m, 2H), 4.58 (ABq, 2H), 3.01 (t, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 177.3, 162.5, 161.0, 157.4, 155.9, 151.6, 142.2, 141.7, 132.8, 132.3, 131.3, 129.3, 125.7, 120.6, 120.2, 118.3, 117.0, 112.7, 109.7, 109.4, 93.5, 78.9, 72.5, 57.7, 37.1, 28.9; MS (ES+) *m/z* 506.5 (M + 1).

EXAMPLE 4.15

Synthesis of *tert*-butyl 4-[(2'-oxo-4'-pyrimidin-5-ylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]piperidine-1-carboxylate

Following the procedure as described in EXAMPLE 4.14, and making non-critical variations using *tert*-butyl 4-[(4'-bromo-2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]piperidine-1-carboxylate to replace 4'-bromo-1'-[5-(trifluoromethyl)-2-furyl]methyl]-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one, the title compound was obtained (91%) as a colorless solid: ¹H NMR (300 MHz, CDCl₃) δ 9.13 (s, 1H), 8.23 (s, 2H), 8.24-7.37 (m, 5H), 7.01 (d, 1H), 6.85 (d, 1H), 6.14 (dd2H), 5.91 (d, 2H), 4.55 (ABq, 2H), 4.15 (d, 2H), 3.84-3.58 (m, 3H), 2.69 (t, 2H), 1.44 (s, 9H); MS (ES+) *m/z* 557.5 (M + 1).

EXAMPLE 4.16

Synthesis of 1'-methyl-4'-pyrimidin-5-ylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure as described in EXAMPLE 4.14, and making non-critical variations using 4'-bromo-1'-methylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 4'-bromo-1'-[5-(trifluoromethyl)-2-furyl]methyl]-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one, the title compound was obtained (22%) as a colorless solid: ¹H NMR (300 MHz, CDCl₃) δ 9.10 (s, 1H), 8.18 (s, 2H), 7.41 (t, 1H), 7.00 (d, 1H), 6.85 (d, 1H), 6.20 (s, 1H), 6.12 (s, 1H), 5.87 (d, 2H), 4.54 (ABq, 2H), 3.32 (s, 1H); MS (ES+) *m/z* 374.5 (M + 1).

EXAMPLE 4.17

Synthesis of 4'-(3-furyl)-1'-methylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure as described in EXAMPLE 4.14, and making non-critical variations using 4'-bromo-1'-methylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 4'-bromo-1'-[5-(trifluoromethyl)-2-furyl]methyl]-5,6-

dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(*1'H*)-one, and 3-furanboronic acid to replace pyrimidine-5-boronic acid, the title compound was obtained (81%) as a colorless solid: ¹H NMR (300 MHz, CDCl₃) δ 7.40-7.28 (m, 2H), 7.05-6.95 (m, 1H), 6.90-6.78 (m, 2H), 6.45-6.38 (m, 1H), 6.23-6.16 (m, 1H), 6.07-5.97 (m, 1H), 5.97-5.80 (m, 2H), 4.75-4.50 (m, 2H), 3.30-3.22 (m, 3H); MS (ES+) *m/z* 362.4 (M + 1).

EXAMPLE 4.18

Synthesis of 4'-(6-fluoropyridin-3-yl)-1'-methylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one

Following the procedure as described in EXAMPLE 4.14, and making non-critical variations using 4'-bromo-1'-methylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one to replace 4'-bromo-1'-[[5-(trifluoromethyl)-2-furyl]methyl]-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(*1'H*)-one, and (6-fluoropyridin-3-yl)boronic acid to replace pyrimidine-5-boronic acid, the title compound was obtained (100%) as a colorless solid: ¹H NMR (300 MHz, CDCl₃) δ 7.75-7.65 (m, 1H), 7.42-7.30 (m, 1H), 7.19-7.05 (m, 1H), 7.00-6.90 (m, 1H), 6.90-6.80 (m, 1H), 6.78-6.64 (m, 1H), 6.24-6.12 (m, 2H), 5.92-5.79 (m, 2H), 4.74-4.63 (m, 1H), 4.40-4.29 (m, 1H), 3.34-3.26 (m, 3H); MS (ES+) *m/z* 391.4 (M + 1).

EXAMPLE 4.19

Synthesis of 1'-(2-cyclopropylethyl)-4'-quinolin-3-ylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one

Following the procedure as described in EXAMPLE 4, and making non-critical variations using 4'-bromo-1'-(2-cyclopropylethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one to replace 4'-bromo-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one, and quinolin-3-ylboronic acid to replace [6-(dimethylamino)pyridin-3-yl]boronic acid, the title compound was obtained: MS (ES+) *m/z* 477.5 (M + 1)

EXAMPLE 4.20

Synthesis of *N*-(2-fluorophenyl)-2-(2'-oxo-4'-pyrimidin-5-yl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(*2'H*)-yl)acetamide

Following the procedure as described in EXAMPLE 4, and making non-critical variations using 2-(4'-bromo-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(*2'H*)-yl)-*N*-(2-fluorophenyl)acetamide to replace 4'-bromo-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one, and pyrimidine-5-boronic acid to replace [6-(dimethylamino)pyridin-3-yl]boronic acid, the title compound

was obtained (53%) as a colorless solid: mp 229-230 °C; ¹H NMR (300 MHz, CDCl₃) δ 9.10 (s, 1H), 8.26-8.15 (m, 3H), 7.98 (s, 1H), 7.41 (t, 1H), 7.15-7.05 (m, 4H), 6.89 (d, 1H), 6.68 (s, 1H), 6.06 (s, 1H), 4.81-4.76 (m, 2H), 4.59-4.42 (m, 4H), 3.00 (t, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 178.2, 164.4, 162.5, 161.0, 157.0, 155.8, 141.8, 132.6, 131.1, 129.4, 125.8, 125.5, 125.4, 125.2, 125.1, 124.7, 121.9, 120.6, 119.9, 118.7, 115.1, 114.8, 109.5, 93.4, 79.0, 72.4, 57.8, 44.9, 28.9; MS (ES+) *m/z* 509.5 (M + 1).

EXAMPLE 5

Synthesis of 4'-[(6-methoxypyridin-3-yl)amino]-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

To an oven-dried 2-neck 25 mL round bottom flask equipped with a condenser was charged with 4'-bromo-1'-pentylspiro-(6,7-dihydrofuro-[2,3-*f*][1,3]benzodioxole-7,3'-indole)-2'-(1'*H*)-one (50.5 mg, 0.12 mmol), 5-amino-2-methoxypyridine (22.3 mg, 0.18 mmol), Pd₂(dba)₃ (10 mole%), BINAP (10 mole%) and sodium methoxide (12.9 mg, 0.24 mmol). The flask was flushed with nitrogen for 5 min followed by the addition of degassed toluene (5.00 mL). The reaction mixture was heated at reflux for 16 h. After cooling to ambient temperature, the reaction mixture was diluted with ethyl acetate (20.0 mL) and washed with saturated ammonium chloride (10.0 mL), brine (10.0 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The brown residue was subjected to column chromatography eluting with ethyl acetate-hexane (20% to 50%) to yield the title compound (30.0 mg) in 54% yield: MS (ES+), *m/z* 474.3 (M + 1).

EXAMPLE 5.1

The compounds listed in the following table were synthesized using similar conditions as described in EXAMPLE 5. As previously noted, the compound numbers listed below do not correspond to the compound numbers provided in the general Reaction Schemes above.

Compound Number	Name	MS (<i>m/z</i> , M + 1)
198	4'-[(3,5-difluorophenyl)amino]-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	479.1
199	4'-[(4,6-dimethylpyridin-2-yl)amino]-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	473.3 (M+2)

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
200	4'-[(4-methyl-1,3-thiazol-2-yl)amino]-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	464.1

EXAMPLE 5.2

Synthesis of 4'-bromo-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

- A mixture of 4'-bromo-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one (0.05 g, 0.12 mmol), 3-(trifluoromethyl)aniline (0.03 g, 0.17 mmol), Pd₂(dba)₃ (0.02 g, 0.01 mmol), xanthphos (0.007 g, 0.01 mmol), and sodium *tert*-butoxide (0.02 g, 0.17 mmol) in toluene (5.00 mL) was heated at 110 °C for 4 days. After cooling down to ambient temperature, the mixture was extracted with ethyl acetate. The organic phase was dried over anhydrous sodium sulfate and filtered.
- The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography eluting with ethyl acetate/hexane to give the title compound (0.06 g, 71%) as a solid: MS (ES+) *m/z* 511.5 (*M* + 1).

EXAMPLE 5.3

- The compounds listed in the following table were synthesized using similar conditions as described in EXAMPLE 5.2. As previously noted, the compound numbers listed below do not correspond to the compound numbers provided in the general Reaction Schemes above.

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
201	4'-morpholino-1'-pentyl-6 <i>H</i> -spiro[benzofuro[6,5- <i>d</i>][1,3]dioxole-7,3'-indolin]-2'-one	437.5
202	4'-(4-methylpiperazin-1-yl)-1'-pentyl-6 <i>H</i> -spiro[benzofuro[6,5- <i>d</i>][1,3]dioxole-7,3'-indolin]-2'-one	450.5
203	1'-pentyl-4'-(pyrimidin-4-ylamino)-6 <i>H</i> -spiro[benzofuro[6,5- <i>d</i>][1,3]dioxole-7,3'-indolin]-2'-one	445.5
204	1'-pentyl-4'-(pyridin-3-ylamino)-6 <i>H</i> -spiro[benzofuro[6,5- <i>d</i>][1,3]dioxole-7,3'-indolin]-2'-one	444.5
205	4'-(4-chloro-2-(trifluoromethyl)phenylamino)-1'-pentyl-6 <i>H</i> -spiro[benzofuro[6,5- <i>d</i>][1,3]dioxole-7,3'-indolin]-2'-one	545.5

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
206	1'-pentyl-4'-(pyrimidin-2-ylamino)-6 <i>H</i> -spiro[benzofuro[6,5- <i>d</i>][1,3]dioxole-7,3'-indolin]-2'-one	444.5
207	4'-(benzo[<i>d</i>][1,3]dioxol-5-ylamino)-1'-pentyl-6 <i>H</i> -spiro[benzofuro[6,5- <i>d</i>][1,3]dioxole-7,3'-indolin]-2'-one	487.5
208	4'-(3-fluorophenylamino)-1'-pentyl-6 <i>H</i> -spiro[benzofuro[6,5- <i>d</i>][1,3]dioxole-7,3'-indolin]-2'-one	461.5
209	4'-(naphthalen-2-ylamino)-1'-pentyl-6 <i>H</i> -spiro[benzofuro[6,5- <i>d</i>][1,3]dioxole-7,3'-indolin]-2'-one	493.5
210	4'-(2-methoxyphenylamino)-1'-pentyl-6 <i>H</i> -spiro[benzofuro[6,5- <i>d</i>][1,3]dioxole-7,3'-indolin]-2'-one	473.2
211	4'-(4-methylthiazol-2-ylamino)-1'-pentyl-6 <i>H</i> -spiro[benzofuro[6,5- <i>d</i>][1,3]dioxole-7,3'-indolin]-2'-one	464.1
212	4'-(4,6-dimethylpyridin-2-ylamino)-1'-pentyl-6 <i>H</i> -spiro[benzofuro[6,5- <i>d</i>][1,3]dioxole-7,3'-indolin]-2'-one	473.3
213	4'-(3,5-difluorophenylamino)-1'-pentyl-6 <i>H</i> -spiro[benzofuro[6,5- <i>d</i>][1,3]dioxole-7,3'-indolin]-2'-one	479.1
214	4'-(6-methoxypyridin-3-ylamino)-1'-pentyl-6 <i>H</i> -spiro[benzofuro[6,5- <i>d</i>][1,3]dioxole-7,3'-indolin]-2'-one	474.3

EXAMPLE 6

Synthesis of 2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzoic acid

- 5 To a solution of methyl 2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzoate (7.56 g, 17.6 mmol) in a mixture of THF/water (2/1 v/v, 180 mL) was added lithium hydroxide monohydrate (1.48 g, 35.2 mmol). The resulting mixture was stirred at ambient temperature overnight and concentrated *in vacuo* followed by the addition of water (150 mL). The mixture was extracted with of ethyl
- 10 acetate/hexanes, 1/3 v/v, 50.0 mL). The water layer was acidified with 1 N HCl solution until the pH value reached 2. The precipitate was filtered and dried to give the title compound (7.30 g, 100%) as a white solid: mp > 250 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 13.25 (s, 1H), 7.95 (dd, 1H), 7.49 (dt, 1H), 7.37 (t, 1H), 7.24-7.16 (m, 2H), 7.11-

6.98 (m, 2H), 6.80 (d, 1H), 6.68 (s, 1H), 6.36 (s, 1H), 5.91 (s, 2H), 5.37-5.19 (m, 2H), 4.88-4.68 (m, 2H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 177.6, 168.8, 156.0, 148.8, 143.0, 142.3, 137.6, 133.1, 132.1, 131.5, 129.9, 129.4, 127.7, 126.5, 124.2, 123.6, 120.1, 109.8, 103.8, 101.9, 93.8, 80.5, 58.0, 42.6.

5

EXAMPLE 7

Synthesis of *N*-[2-(4-chlorophenyl)ethyl]-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide

A. Preparation of stock solution of 2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzoyl chloride

10

A solution of 2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzoic acid (0.21 g, 0.50 mmol), oxalyl chloride (0.09 mL, 1.00 mmol) and one drop of DMF in toluene (10.0 mL) was stirred at ambient temperature overnight. The mixture was concentrated under vacuum to afford a solid, which was dissolved in dichloromethane (5.00 mL) to form an acid chloride stock solution (0.10 mmol/mL) for use.

15

B. Synthesis of *N*-[2-(4-chlorophenyl)ethyl]-2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide

20

The acid chloride stock solution obtained above (1.00 mL, 0.10 mmol) was added to a mixture of 2-(4-chlorophenyl)ethylamine (0.02 g, 0.13 mmol), triethylamine (0.14 mL, 1.00 mmol) in dichloromethane (1.00 mL). The resulting mixture was stirred at ambient temperature overnight and diluted with dichloromethane (5.00 mL). The mixture was washed with 1 N HCl, saturated sodium bicarbonate solution, dried over sodium sulfate and filtered. The filtrate was concentrated under vacuum to dryness to give the title compound as a white powder: ¹H NMR (300 MHz, CDCl₃) δ 7.70-7.13 (m, 10H), 7.10-6.96 (m, 2H), 6.65-6.54 (br, 1H), 6.50 (s, 1H), 6.11 (s, 1H), 5.89-5.82 (m, 2H), 5.09-4.88 (m, 3H), 4.68 (d, 1H), 3.79-3.66 (m, 2H), 2.93 (t, 2H); MS (ES+), *m/z* 553.3 (*M* + 1), 575.3 (*M* + 23).

25

EXAMPLE 7.1

The compounds listed in the following table were synthesized using similar conditions as described in EXAMPLE 7. As previously noted, the compound numbers listed below do not correspond to the compound numbers provided in the general Reaction Schemes above.

30

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
215	<i>N</i> -(3-methylbutyl)-2-[(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	485.3
216	2-[(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -phenylbenzamide	491.2
217	<i>N,N</i> -diisopropyl-2-[(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	499.4
218	<i>N</i> -(3-fluorophenyl)-2-[(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	509.3
219	<i>N</i> -(4-chlorobenzyl)-2-[(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	539.3
220	<i>N</i> -butyl-2-[(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	471.3
221	2-[(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -pentylbenzamide	485.3
222	<i>N</i> -hexyl-2-[(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	499.4
223	2-[(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -propylbenzamide	457.3
224	<i>N</i> -isopropyl-2-[(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	457.3
225	<i>N</i> -cyclohexyl-2-[(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	497.3
226	<i>N</i> -cyclopentyl-2-[(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	483.3
227	<i>N</i> -heptyl-2-[(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	513.4
228	<i>N</i> -(4-fluorophenyl)-2-[(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	509.1

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
229	<i>N</i> -(3-fluorobenzyl)-2-[(2'-oxospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)- yl)methyl]benzamide	523.1
230	<i>N</i> -(3-chlorophenyl)-2-[(2'-oxospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)- yl)methyl]benzamide	525.0
231	<i>N</i> -(2-fluorophenyl)-2-[(2'-oxospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)- yl)methyl]benzamide	509.1
232	<i>N</i> -(2-ethylphenyl)-2-[(2'-oxospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)- yl)methyl]benzamide	519.1
233	<i>N</i> -(4-ethylphenyl)-2-[(2'-oxospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)- yl)methyl]benzamide	519.2
234	<i>N</i> -(3-methylphenyl)-2-[(2'-oxospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)- yl)methyl]benzamide	505.2
235	<i>N</i> -(2,3-dimethylphenyl)-2-[(2'-oxospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)- yl)methyl]benzamide	519.2
236	<i>N</i> -(3,5-dimethylphenyl)-2-[(2'-oxospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)- yl)methyl]benzamide	519.1
237	1'-[2-(piperidin-1-ylcarbonyl)benzyl]spiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	483.1
238	<i>N</i> -isobutyl-2-[(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'- indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	471.2
239	<i>N</i> -(2-chlorobenzyl)-2-[(2'-oxospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)- yl)methyl]benzamide	539.1
240	<i>N</i> -(2,6-dimethylphenyl)-2-[(2'-oxospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)- yl)methyl]benzamide	519.1

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
241	<i>N</i> -(2-methoxyphenyl)-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	521.1
242	<i>N</i> -(3-methoxypropyl)-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	487.2
243	<i>N</i> -[2-(4-methylphenyl)ethyl]-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	533.2
244	2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -(tetrahydrofuran-2-ylmethyl)benzamide	499.2
245	<i>N,N</i> -dibenzyl-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	595.2
246	2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -(3-phenylpropyl)benzamide	533.2
247	<i>N</i> -[2-(3-chlorophenyl)ethyl]-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	553.1
248	<i>N</i> -[2-(4-fluorophenyl)ethyl]-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	537.1
249	<i>N</i> -(4-fluorobenzyl)-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	523.1
250	<i>N</i> -(3-ethoxypropyl)-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	501.1
251	<i>N</i> -hexyl- <i>N</i> -methyl-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	513.2
252	<i>N</i> -(3-isopropoxypropyl)-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	515.2

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
253	<i>N</i> -(4-methoxybenzyl)-2-[(2'-oxospiro[furo[2,3- f[1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)- yl)methyl]benzamide	535.2
254	<i>N</i> -(cyclopropylmethyl)-2-[(2'-oxospiro[furo[2,3- f[1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)- yl)methyl]benzamide	469.1
255	<i>N</i> -(2-ethoxyethyl)-2-[(2'-oxospiro[furo[2,3- f[1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)- yl)methyl]benzamide	487.2
256	<i>N</i> -(cyclohexylmethyl)-2-[(2'-oxospiro[furo[2,3- f[1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)- yl)methyl]benzamide	511.2
257	<i>N</i> -(2-furylmethyl)-2-[(2'-oxospiro[furo[2,3- f[1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)- yl)methyl]benzamide	495.0
258	<i>N</i> -(2,4-dimethylphenyl)-2-[(2'-oxospiro[furo[2,3- f[1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)- yl)methyl]benzamide	519.2
259	<i>N</i> -(4-cyanophenyl)-2-[(2'-oxospiro[furo[2,3- f[1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)- yl)methyl]benzamide	516.2
260	<i>N</i> -(3,5-dichlorophenyl)-2-[(2'-oxospiro[furo[2,3- f[1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)- yl)methyl]benzamide	559.0
261	<i>N</i> -(3-fluoro-2-methylphenyl)-2-[(2'-oxospiro[furo[2,3- f[1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)- yl)methyl]benzamide	523.1
262	<i>N</i> -(4-methoxyphenyl)-2-[(2'-oxospiro[furo[2,3- f[1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)- yl)methyl]benzamide	521.1
263	<i>N</i> -(5-chloro-2-methylphenyl)-2-[(2'-oxospiro[furo[2,3- f[1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)- yl)methyl]benzamide	539.1

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
264	2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -[3-(trifluoromethyl)phenyl]benzamide	559.1
265	2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -(pyridin-4-ylmethyl)benzamide	506.1
266	<i>N</i> -cyclobutyl-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	469.1
267	<i>N</i> -methyl-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	429.1
268	<i>N</i> -ethyl-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	443.1
269	2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -(2,2,2-trifluoroethyl)benzamide	497.1
270	<i>N</i> -(2,2-diphenylethyl)-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	595.2
271	<i>N</i> -[2-(diethylamino)ethyl]-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	514.2
272	<i>N</i> -(3,3-dimethylbutyl)-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	499.2
273	<i>N</i> -(2-ethylbutyl)-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	499.2
274	2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -(2-pyrrolidin-1-ylethyl)benzamide	512.4
275	<i>N</i> -[(1-ethylpyrrolidin-2-yl)methyl]-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	526.4
276	2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -(2-piperidin-1-ylethyl)benzamide	526.5

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
277	<i>N</i> -(2-morpholin-4-ylethyl)-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	528.4
278	<i>N</i> -[(1 <i>S</i>)-1-cyclohexylethyl]-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	525.5
279	<i>N</i> -(2-fluoro-5-methylphenyl)-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	523.4
280	<i>N</i> -(2,4-difluorophenyl)-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	527.3
281	2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -(4-propylphenyl)benzamide	533.4
282	<i>N</i> -(3,3-diphenylpropyl)-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	609.4
283	<i>N</i> -(2-methoxyethyl)-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	473.4
284	<i>N</i> -(2,5-difluorobenzyl)-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	541.3
285	2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -(2-thienylmethyl)benzamide	511.4
286	<i>N</i> -[4-chloro-2-(trifluoromethyl)phenyl]-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	593.3
287	<i>N</i> -[2-(4-methoxyphenyl)ethyl]-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	549.4
288	<i>N</i> -(3,5-dichlorobenzyl)-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	573.2

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
289	<i>N</i> -(3-chlorobenzyl)-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	539.3
290	2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -[2-(2-thienyl)ethyl]benzamide	525.4
291	<i>N</i> -(2,3-dihydro-1 <i>H</i> -inden-1-yl)-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	531.4
292	2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -[4-(trifluoromethyl)benzyl]benzamide	573.3
293	<i>N</i> -[4-fluoro-2-(trifluoromethyl)phenyl]-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	577.5
294	2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -(pyridin-3-ylmethyl)benzamide	506.4
295	2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -[2-(trifluoromethyl)benzyl]benzamide	573.3
296	<i>N</i> -(3-methylpyridin-2-yl)-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	506.4
297	<i>N</i> -(1-benzylpiperidin-4-yl)-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	588.4
298	2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -[2-(trifluoromethyl)phenyl]benzamide	559.4
299	<i>N</i> -[(1 <i>R</i>)-1-cyclohexylethyl]-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	525.5
300	<i>N</i> -(2-cyanoethyl)-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	468.3

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
301	<i>N</i> -(6-methoxypyridin-3-yl)-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	522.4
302	2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -1,3-thiazol-2-ylbenzamide	498.3
303	2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -1,3,4-thiadiazol-2-ylbenzamide	499.3
304	<i>N</i> -(4,6-dimethylpyridin-2-yl)-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	520.3
305	<i>N</i> -(2,3-dihydro-1 <i>H</i> -inden-5-yl)-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	531.4
306	1'-{2-[(4-pyrimidin-2-yl)piperazin-1-yl]carbonyl}benzyl}spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	562.4
307	1'-{2-[[4-(1,3-benzodioxol-5-ylmethyl)piperazin-1-yl]carbonyl}benzyl}spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	618.4
308	<i>N</i> -2-adamantyl-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	549.5
309	<i>N</i> -1-adamantyl-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	549.5
310	<i>N</i> -1-naphthyl-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	541.4
311	<i>N</i> -(3,5-difluorophenyl)-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	527.3
312	1'-[2-(morpholin-4-ylcarbonyl)benzyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	485.4
313	<i>N</i> -[3-(dimethylamino)propyl]- <i>N</i> -methyl-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	514.4

EXAMPLE 8

Synthesis of 3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)methyl]benzoic acid

Following the procedure described in EXAMPLE 6, and making non-critical variations using methyl 3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)methyl]benzoate to replace methyl 2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)methyl]benzoate, the title compound was obtained (100%): ¹H NMR (300 MHz, CDCl₃) δ 13.03 (s, 1H), 7.86-7.80 (m, 2H), 7.59-7.57 (m, 1H), 7.48-7.44 (m, 1H), 7.25-7.16 (m, 2H), 7.03-6.95 (m, 2H), 6.68 (s, 1H), 6.18 (s, 1H), 5.90 (s, 2H), 5.05 (ABq, 2H), 4.75 (ABq, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 177.4, 167.5, 155.9, 148.9, 142.5, 142.3, 137.3, 132.2, 131.7, 129.6, 129.4, 128.8, 128.1, 124.3, 123.7, 120.1, 109.9, 103.3, 101.9, 93.9, 80.3, 58.0, 43.2; MS (ES+) *m/z* 416.2 (M + 1).

EXAMPLE 9

Synthesis of *N*-[2-(3-chlorophenyl)ethyl]-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)methyl]benzamide

A. Preparation of stock solution of 3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)methyl]benzoyl chloride

To a stirred slurry of 3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)methyl]benzoic acid (2.08 g, 5.00 mmol) in dry chloroform (50.0 mL) was added oxalyl chloride (0.95 g, 7.5 mmol) at ambient temperature followed by 1 drop of DMF. The mixture was stirred at ambient temperature overnight and evaporated to dryness *in vacuo*. The residue was dissolved in dry dichloromethane (60.0 mL) to form an acid chloride stock solution for use.

B. Synthesis of *N*-[2-(3-Chlorophenyl)ethyl]-3-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)methyl]benzamide

To a solution of 2-(3-chlorophenyl)ethylamine (0.02 mL, 0.24 mmol) in dry dichloromethane (2.00 mL) and triethylamine (0.05 mL, 0.32 mmol) was added the acid chloride stock solution (2.0 mL, 0.081 M in dichloromethane) obtained above at ambient temperature. The mixture was stirred for 2 h, washed with 15% HCl solution and water. The organic layer was separated, dried over Na₂SO₄ and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was dissolved in ethyl acetate, and the product was precipitated by the addition of hexane. The white solid was filtered and collected to yield the title compound (0.06 g) in 65% yield: ¹H NMR (300 MHz, CDCl₃) δ 7.97-7.95 (m, 2H), 7.53-7.50 (m, 1H), 7.45-7.40 (m, 1H), 7.21-7.15

(m, 2H), 7.04-6.99 (m, 1H), 6.73-6.71 (m, 1H), 6.52 (s, 1H), 6.20 (s, 1H), 5.86 (s, 1H), 5.18 (d, 1H), 4.72 (d, 1H), 4.80 (d, 1H), 4.69 (d, 1H), 3.89 (s, 1H); MS (ES+) m/z 554.0 (M + 1).

EXAMPLE 9.1

- 5 The compounds listed in the following table were synthesized using the similar procedure as described in EXAMPLE 9. As previously noted, the compound numbers listed below do not correspond to the compound numbers provided in the general Reaction Schemes above.

Compound Number	Name	MS (m/z , M + 1)
314	<i>N</i> -(3-methylbutyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	485.5
315	3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -phenylbenzamide	491.5
316	<i>N,N</i> -diisopropyl-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	499.6
317	<i>N</i> -(3-fluorophenyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	509.5
318	<i>N</i> -(4-chlorobenzyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	540.0
319	<i>N</i> -butyl-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	471.5
320	<i>N</i> -(3-fluorobenzyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	523.5
321	<i>N</i> -(3-chlorophenyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	526.0
322	<i>N</i> -(2-fluorophenyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	509.5

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
323	<i>N</i> -(2-ethylphenyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	519.6
324	<i>N</i> -(4-ethylphenyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	519.6
325	<i>N</i> -(3-methylphenyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	505.5
326	<i>N</i> -(2,3-dimethylphenyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	519.6
327	<i>N</i> -(3,5-dimethylphenyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	519.6
328	3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -pentylbenzamide	485.5
329	3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -propylbenzamide	457.5
330	<i>N</i> -isopropyl-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	457.5
331	1'-[3-(piperidin-1-ylcarbonyl)benzyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	483.5
332	<i>N</i> -isobutyl-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	471.5
333	<i>N</i> -hexyl-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	499.6
334	<i>N</i> -cyclohexyl-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	497.6
335	<i>N</i> -cyclopentyl-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	483.5

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
336	<i>N</i> -heptyl-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	513.6
337	<i>N</i> -(2-methoxybenzyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	535.6
338	<i>N</i> -(2-methoxyphenyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	521.5
339	<i>N</i> -cyclopropyl-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	455.5
340	<i>N</i> -(3-methoxypropyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	487.5
341	<i>N</i> -(2,4-dimethylphenyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	519.6
342	3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -(tetrahydrofuran-2-ylmethyl)benzamide	499.5
343	<i>N,N</i> -dibenzyl-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	595.7
344	<i>N</i> -[2-(diethylamino)ethyl]-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	514.6
345	<i>N</i> -methyl-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	429.4
346	3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -[3-(trifluoromethyl)phenyl]benzamide	559.5
347	<i>N</i> -ethyl-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	443.5

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
348	<i>N</i> -(3-ethoxypropyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	501.5
349	<i>N</i> -(4-methoxybenzyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	535.6
350	<i>N</i> -(3,5-dichlorophenyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	560.4
351	3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -pyridin-3-ylbenzamide	492.5
352	3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -(pyridin-4-ylmethyl)benzamide	506.5
353	<i>N</i> -(2-furylmethyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	495.5
354	<i>N</i> -(3-fluoro-2-methylphenyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	523.5
355	<i>N</i> -hexyl- <i>N</i> -methyl-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	513.6
356	<i>N</i> -(3-isopropoxypropyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	515.6
357	<i>N</i> -(2-ethoxyethyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	487.5
358	<i>N</i> -(cyclopropylmethyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	469.5
359	<i>N</i> -(4-methoxyphenyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	521.5

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
360	<i>N</i> -cyclobutyl-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	469.5
361	<i>N</i> -[2-(4-fluorophenyl)ethyl]-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	537.5
362	<i>N</i> -(cyclohexylmethyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	511.6
363	<i>N</i> -[2-(4-methylphenyl)ethyl]-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	533.6
364	<i>N</i> -(2-ethylbutyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	499.6
365	<i>N</i> -benzyl-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	505.5
366	<i>N</i> -(2-methoxyethyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	473.5
367	1'-[3-(morpholin-4-ylcarbonyl)benzyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	485.5
368	<i>N</i> -(1-benzylpiperidin-4-yl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	588.7
369	<i>N</i> -[2-(4-methoxyphenyl)ethyl]-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	549.6
370	3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -(2-piperidin-1-ylethyl)benzamide	526.6
371	<i>N</i> -(1-cyclohexylethyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	525.6

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
372	3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -(2-thienylmethyl)benzamide	511.6
373	3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -(4-propylphenyl)benzamide	533.6
374	<i>N</i> -(2,4-difluorobenzyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	541.5
375	<i>N</i> -(3,5-difluorophenyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	527.5
376	<i>N</i> -(2,3-dihydro-1 <i>H</i> -inden-5-yl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	531.6
377	3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -[4-(trifluoromethyl)benzyl]benzamide	573.5
378	3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -[2-(2-thienyl)ethyl]benzamide	525.6
379	3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -(pyridin-3-ylmethyl)benzamide	506.5
380	3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -[2-(trifluoromethyl)benzyl]benzamide	573.5
381	<i>N</i> -[2-(4-chlorophenyl)ethyl]-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	554.0
382	3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -(2-pyrrolidin-1-ylethyl)benzamide	512.6
383	<i>N</i> -(3-methylpyridin-2-yl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	506.5

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
384	<i>N</i> -1,3-benzodioxol-5-yl-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	535.5
385	<i>N</i> -(2-morpholin-4-ylethyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	528.6
386	1'-{3-[(4-pyrimidin-2-ylpiperazin-1-yl)carbonyl]benzyl}spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	562.6
387	3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -1,3-thiazol-2-ylbenzamide	498.5
388	<i>N</i> -(6-methoxypyridin-3-yl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	522.5
389	<i>N</i> -(3,5-dichlorobenzyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	574.4
390	<i>N</i> -1-naphthyl-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	541.6
391	<i>N</i> -(4,6-dimethylpyridin-2-yl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	520.5
392	3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -pyrimidin-4-ylbenzamide	493.5
393	<i>N</i> -(5-methyl-1,3-thiazol-2-yl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	512.5
394	<i>N</i> -(4-methylbenzyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	519.6
395	<i>N</i> -[3-(1 <i>H</i> -imidazol-1-yl)propyl]-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	523.6

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
396	1'-{3-[(4-methylpiperazin-1-yl)carbonyl]benzyl}spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	498.5
397	<i>N</i> -(5-cyclopropyl-1,3,4-thiadiazol-2-yl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	539.6
398	3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -1,3,4-thiadiazol-2-ylbenzamide	499.5
399	<i>N</i> -(3,3-dimethylbutyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	499.6
400	<i>N</i> -(4-morpholin-4-ylphenyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	576.6
401	<i>N</i> -[(1-ethylpyrrolidin-2-yl)methyl]-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	526.6
402	<i>N</i> -(2-cyanoethyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	
403	<i>N</i> -(2,2-diphenylethyl)-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	595.4

EXAMPLE 10

Synthesis of 1'-(4-fluorobenzyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

To a solution of spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one (0.16 g, 0.57 mmol) in ethylmethylketone (5.00 mL) was added Cs₂CO₃ (0.40 g, 1.20 mmol).
 5 The reaction mixture was stirred at ambient temperature for 15 min followed by the addition of 4-fluorobenzyl bromide (0.20 g, 1.0 mmol). The reaction mixture was refluxed for 4 h. After the completion of the reaction, the mixture was filtered and the solvent was removed under reduced pressure. The residue was recrystallized from
 10 EtOAc/Hexane to yield the title compound (0.111 g) as a white solid in 50% yield: MS

(ES+) m/z 390.3 ($M + 1$).

EXAMPLE 10.1

The compounds listed in the following table were synthesized using the similar procedure as described in EXAMPLE 10. As previously noted, the compound numbers listed below do not correspond to the compound numbers provided in the general Reaction Schemes above.

Compound Number	Name	MS (m/z , $M + 1$)
404	1'-{[1-(2,6-difluorobenzyl)-1 <i>H</i> -1,2,3-triazol-4-yl)methyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	489.3
405	1'-prop-2-yn-1-ylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	320.3
406	1'-benzylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	372.2
407	1'-{[6-(trifluoromethyl)pyridin-3-yl)methyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	441.2
408	1'-(3,5-difluorobenzyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	408.3
409	1'-(3-nitrobenzyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	417.2
410	1'-{[6-chloropyridin-3-yl)methyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	407.2
411	1'-(tetrahydro-2 <i>H</i> -pyran-2-ylmethyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	380.2
412	1'-(3-fluorobenzyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	390.3
413	1'-(tetrahydrofuran-2-ylmethyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	365.2
414	3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzonitrile	397.2
415	1'-(2,3-dihydro-1,4-benzodioxin-2-ylmethyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	430.3

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
416	1'-(2-ethoxyethyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	354.2
417	1'-[(2 <i>E</i>)-pent-2-en-1-yl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	350.2
418	1'-hex-5-en-1-ylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	364.3
419	1'-(cyclobutylmethyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	350.2
420	1'-pent-2-yn-1-ylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	348.2
421	1'-(5-chloropentyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	386.2
422	1'-[4-(1 <i>H</i> -pyrazol-1-yl)benzyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	438.3
423	1'-[(7-methoxy-2-oxo-2 <i>H</i> -1,4-benzoxazin-3-yl)methyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	471.3
424	1'-(4-fluorobutyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	356.2
425	1'-(5-methylhexyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	380.3
426	1'-[(3 <i>Z</i>)-4-methylhex-3-en-1-yl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	378.2
427	1'-[(5-methyl-2-phenyl-2 <i>H</i> -1,2,3-triazol-4-yl)methyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	453.2
428	1'-[[5-(trifluoromethyl)-2-furyl]methyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	430.2
429	1'-(3,4-dihydro-2 <i>H</i> -1,5-benzodioxepin-7-ylmethyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	444.3
430	1'-(biphenyl-4-ylmethyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	448.2
431	4'-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]biphenyl-2-carbonitrile	473.3

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
432	1'-(2-bromoethyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	389.1
433	1'-(1 <i>H</i> -1,2,3-triazol-4-ylmethyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	363.2
434	1'-(biphenyl-2-ylmethyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	448.3
435	1'-(diphenylmethyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	448.3
436	5-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)pentanenitrile	363.2
437	1'-[2-(2-methoxyethoxy)ethyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	384.2
438	1'-(cyclopropylmethyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	336.2
439	1'-(4,4,4-trifluorobutyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	392.2
440	ethyl 1-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]-1 <i>H</i> -1,2,3-triazole-5-carboxylate	449.3
441	ethyl 1-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]-1 <i>H</i> -1,2,3-triazole-4-carboxylate	449.3
442	diethyl [2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]phosphonate	446.1
443	1'-(1,3-thiazol-4-ylmethyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	379.3
444	1'-[(5-chloro-1-benzothien-3-yl)methyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	462.1
445	1'-(pyridin-2-ylmethyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	373.1
446	1'-(pyridin-4-ylmethyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	373.1
447	1'-(pyridin-3-ylmethyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	373.1

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
448	1'-[2-(1 <i>H</i> -pyrrol-1-yl)ethyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	375.2
449	1'-{[4-chloro-2-(trifluoromethyl)quinolin-6-yl)methyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	525.1
450	1'-(4-fluoro-3-methylbenzyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	404.3
451	1'-(5-fluoro-2-methylbenzyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	404.3
452	1'-[(2-methyl-1,3-thiazol-4-yl)methyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	393.2
453	1'-(1,3-benzothiazol-2-ylmethyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	329.3
454	1'-(2,5-difluorobenzyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	408.2
455	1'-[4-(1 <i>H</i> -pyrrol-1-yl)benzyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	437.3
456	1'-[3-(1 <i>H</i> -pyrrol-1-yl)benzyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	437.3
457	1'-(2,1,3-benzothiadiazol-4-ylmethyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	430.3
458	1'-(2,1,3-benzothiadiazol-5-ylmethyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	430.3
459	1'-[(1-methyl-1 <i>H</i> -1,2,3-benzotriazol-5-yl)methyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	427.2
460	1'-[(4-chlorophenoxy)methyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	422.2
461	1'-[2-fluoro-3-(trifluoromethyl)benzyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	458.1
462	1'-[2-fluoro-6-(trifluoromethyl)benzyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	458.1
463	1'-[3-fluoro-4-(trifluoromethyl)benzyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	458.1

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
464	1'-[4-fluoro-3-(trifluoromethyl)benzyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	458.1
465	1'-[2-fluoro-5-(trifluoromethyl)benzyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	458.1
466	1'-[4-fluoro-2-(trifluoromethyl)benzyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	458.1
467	1'-[5-fluoro-2-(trifluoromethyl)benzyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	458.1
468	1'-[2-fluoro-4-(trifluoromethyl)benzyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	458.1
469	1'-[3-(1 <i>H</i> -pyrrol-1-yl)propyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	389.2
470	1'-[(2,2,3,3-tetrafluorocyclobutyl)methyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	422.1
471	1'-[(3-methyl-5-phenylisoxazol-4-yl)methyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	453.3
472	1'-[2-(diethylamino)ethyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	381.2
473	1'-(2,3-difluorobenzyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	408.1
474	1'-[(1-bromo-2-naphthyl)methyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	501.2
475	1'-[(7-methoxy-2-oxo-2 <i>H</i> -chromen-4-yl)methyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	470.3
476	1'-[(benzyloxy)methyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	402.3
477	1'-[2-(2,5,5-trimethyl-1,3-dioxan-2-yl)ethyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	438.2

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
478	1'-[(6-fluoro-4 <i>H</i> -1,3-benzodioxin-8-yl)methyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	448.2
479	1'-allylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	322.3
480	1'-(1-naphthylmethyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	423.3
481	1'-[3-fluoro-5-(trifluoromethyl)benzyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	458.1
482	1'-(2,4-difluorobenzyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	408.1
483	1'-(2,6-difluorobenzyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	408.3
484	1'-[(5-phenyl-1,3-oxazol-4-yl)methyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	439.2
485	1'-(3,5,5-trimethylhexyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	408.3
486	1'-(2-ethylbutyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	366.3
487	1'-(4-methylpentyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	366.3
488	1'-(3-methoxybenzyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	402.3
489	1'-(3-methylbutyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	352.2
490	1'-(3-methylbut-2-en-1-yl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	350.2
491	1'-pent-4-en-1-ylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	350.2
492	4-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)butanenitrile	349.1
493	1'-[4-(1 <i>H</i> -1,2,4-triazol-1-yl)benzyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	439.2
494	1'-(1,3-benzodioxol-5-ylmethyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	416.2

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
495	1'-[4,4-bis(4-fluorophenyl)butyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	526.2
496	1'-[(2-methylcyclopropyl)methyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	350.4
497	1'-(3-cyclopropylpropyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	364.3
498	1'-hexylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	366.3
499	1'-[(2-cyclopropyl-6-hydroxypyrimidin-4-yl)methyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	430.3

EXAMPLE 10.2

Synthesis of 1'-(piperidin-4-ylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

- 5 Following the procedure as described in EXAMPLE 10, and making non-critical variations using *tert*-butyl 4-(bromomethyl)piperidine-1-carboxylate to replace 4-fluorobenzyl bromide, the title compound was obtained in 67% yield as a white solid upon acidification of the intermediate with 33% HBr: MS (ES+) *m/z* 379.3 (*M* + 1).

EXAMPLE 10.3

- 10 Synthesis of 1'-[(1-methylpiperidin-4-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one hydrochloride

- To a solution of 1'-(piperidin-4-ylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one (0.19 g, 0.50 mmol) in dichloroethane (5.00 mL) was added formaldehyde (0.10 mL, 33% solution, 0.03 g, 1.10 mmol) and sodium triacetoxyborohydride (0.30 g, 1.40 mmol). After stirring at ambient temperature for 20 hours, the reaction mixture was diluted with dichloromethane (20.0 mL) and washed with water (2 x 20.0 mL). The organic layer was dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography and the product was dissolved in dichloromethane (5.00 mL) and excess of HCl in ether was added. The precipitate was filtered to give the title compound in 20% yield: MS (ES+) *m/z* 393.3 (*M* + 1).
- 15
- 20

EXAMPLE 10.4

Synthesis of 1'-[(1-ethylpiperidin-4-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one hydrochloride

Following the procedure as described in EXAMPLE 10.3, and making non-critical variations using acetaldehyde to replace formalin, the title compound was obtained in 20% yield as a white solid: MS (ES+) *m/z* 407.3 (*M* + 1).

EXAMPLE 10.5

Synthesis of 1'-[(1-cyclohexyllpiperidin-4-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one hydrochloride

Following the procedure as described in EXAMPLE 10.3, and making non-critical variations using cyclohexanone to replace formalin, the title compound was obtained 24% yield as a white solid: MS (ES+) *m/z* 461.5 (*M* + 1).

EXAMPLE 10.6

Synthesis of 1'-[[1-(cyclopropylmethyl)piperidin-4-yl]methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one hydrochloride

Following the procedure as described in EXAMPLE 10.3, and making non-critical variations using cyclopropanecarbaldehyde to replace formalin, the title compound was obtained in 14% yield as a white solid: MS (ES+) *m/z* 433.5 (*M* + 1).

EXAMPLE 10.7

Synthesis of 1'-[(1-cyclopentylpiperidin-4-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one hydrochloride

Following the procedure as described in EXAMPLE 10.3, and making non-critical variations using cyclopentanone to replace formalin, the title compound was obtained in 37% yield as a white solid: MS (ES+) *m/z* 447.3 (*M* + 1).

EXAMPLE 10.8

Synthesis of 1'-[[1-(pyridine-3-ylmethyl)piperidin-4-yl]methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one hydrochloride

Following the procedure as described in EXAMPLE 10.3, and making non-critical variations using nicotinaldehyde to replace formalin, the title compound was obtained in 11% yield as a white solid: MS (ES+) *m/z* 470.4 (*M* + 1).

EXAMPLE 10.9

Synthesis of 1'-{[1-(3-methylbutyl)piperidin-4-yl]methyl}spiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-2'(1'H)-one hydrochloride

Following the procedure as described in EXAMPLE 10.3, and making non-critical variations using 3-methylbutanal to replace formalin, the title compound was
5 obtained in 15% yield as a white solid: MS (ES+) m/z 449.5 (M + 1).

EXAMPLE 10.10

Synthesis of 1'-{[1-(1-ethylpropyl)piperidin-4-yl]methyl}spiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-2'(1'H)-one hydrochloride

Following the procedure as described in EXAMPLE 10.3, and making non-critical variations using pentan-3-one to replace formalin, the title compound was
10 obtained in 17% yield as a white solid: MS (ES+) m/z 449.4 (M + 1).

EXAMPLE 10.11

Synthesis of 1'-{[1-(1-cyclobutyl)piperidin-4-yl]methyl}spiro[furo[2,3-f][1,3]benzodioxole-
15 7,3'-indol]-2'(1'H)-one hydrochloride

Following the procedure as described in EXAMPLE 10.3, and making non-critical variations using cyclobutanone to replace formalin, the title compound was obtained in 31% yield as a white solid: MS (ES+) m/z 433.4 (M + 1).

EXAMPLE 10.12

Synthesis of 1'-{[1-(1-isopropyl)piperidin-4-yl]methyl}spiro[furo[2,3-f][1,3]benzodioxole-
20 7,3'-indol]-2'(1'H)-one hydrochloride

Following the procedure as described in Example 10.3, and making non-critical variations using acetone to replace formalin, the title compound was obtained in 31% yield as a white solid: ^1H NMR (300 MHz, DMSO- d_6) δ 10.36 (s, 1H), 7.79-6.87 (m, 4H), 6.82-6.48 (m, 1H), 6.38-6.15 (m, 1H), 5.89 (s, 2H), 4.67 (ABq, 2H), 4.12 (s, 1H),
25 3.79-0.60 (m, 16H); MS (ES+) m/z 421.4 (M + 1).

EXAMPLE 10.13

Synthesis of 1'-{[1-(pyridin-2-ylmethyl)piperidin-4-yl]methyl}spiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-2'(1'H)-one hydrochloride

Following the procedure as described in EXAMPLE 10.3, and making non-critical variations using picolinaldehyde to replace formalin, the title compound was
30 obtained in 15% yield as a white solid: MS (ES+) m/z 470.4 (M + 1).

EXAMPLE 10.14

Synthesis of 1'-{[1-(2-thienylmethyl)piperidin-4-yl]methyl}spiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-2'(1'H)-one hydrochloride

Following the procedure as described in EXAMPLE 10.3, and making non-critical variations using thiophene-2-carbaldehyde to replace formalin, the title compound was obtained in 21% yield as a white solid: MS (ES+) m/z 475.3 (M + 1).

EXAMPLE 10.15

Synthesis of 1'-{[1-[3-(methylthio)propyl]piperidin-4-yl]methyl}spiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-2'(1'H)-one hydrochloride

Following the procedure as described in EXAMPLE 10.3, and making non-critical variations using 3-(methylthio)propanal to replace formalin, the title compound was obtained in 7% yield as a white solid: MS (ES+) m/z 467.5 (M + 1).

EXAMPLE 10.16

Synthesis of 1'-{[1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl]methyl}spiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-2'(1'H)-one hydrochloride

Following the procedure as described in EXAMPLE 10.3, and making non-critical variations using tetrahydro-4H-pyran-4-one to replace formalin, the title compound was obtained in 33% yield as a white solid: MS (ES+) m/z 463.4 (M + 1).

EXAMPLE 10.17

Synthesis of 1'-{[1-(3,3-dimethylbutyl)piperidin-4-yl]methyl}spiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-2'(1'H)-one hydrochloride

Following the procedure as described in EXAMPLE 10.3, and making non-critical variations using 3,3-dimethylbutanal to replace formalin, the title compound was obtained in 19% yield as a white solid: MS (ES+) m/z 463.5 (M + 1).

EXAMPLE 10.18

Synthesis of *tert*-butyl 4-[(5,5-dimethyl-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'H)-yl)methyl]piperidine-1-carboxylate

Following the procedure as described in EXAMPLE 10, and making non-critical variations using 5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'H)-one to replace spiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]-2'(1'H)-one, and *tert*-butyl 4-(tosyloxymethyl)piperidine-1-carboxylate to replace 4-fluorobenzyl bromide, the title compound was obtained in 70% yield: mp 65-75 °C; ¹H NMR (300 MHz, CDCl₃) δ

7.30 (td, 1H), 7.18 (d, 1H), 7.05 (t, 1H), 6.89 (d, 1H), 6.38 (s, 1H), 6.28 (s, 1H), 4.88 (d, 1H), 4.64 (d, 1H), 4.18 (s, 2H), 4.17-4.01 (br, 2H), 3.74-3.53 (m, 2H), 2.74-2.59 (m, 2H), 2.11-1.92 (m, 1H), 1.70-1.59 (m, 2H), 1.43 (s, 9H), 1.37-1.19 (m, 2H), 1.17 (s, 3H), 1.14 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 178.0, 161.3, 161.0, 154.7, 142.8, 132.6, 129.9, 128.7, 124.2, 123.3, 120.3, 116.2, 108.5, 93.4, 85.4, 80.6, 79.5, 57.7, 45.7, 41.3, 35.0, 30.0, 28.4, 27.8, 27.5; MS (ES+) *m/z* 527.5 (M + 23).

EXAMPLE 10.19

Synthesis of 5,5-dimethyl-1'-(piperidin-4-ylmethyl)-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one hydrochloride

To a stirred solution of *tert*-butyl 4-[(5,5-dimethyl-2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(2'*H*)-yl)methyl]piperidine-1-carboxylate (80 mg, 0.16 mmol) in 10.0 mL dichloromethane was added hydrobromic acid (0.50 mL of hydrobromic acid ≥33% in glacial acetic acid, 1.60 mmol) slowly at 0 °C. The mixture was stirred at ambient temperature for one hour and concentrated *in vacuo* to dryness. The residue was treated with 10.0 mL of 2 N sodium hydroxide solution and extracted with dichloromethane (3 x 30.0 mL). The combined organic layers was washed with brine (100 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography (2% methanol in ethyl acetate) to give 5,5-dimethyl-1'-(piperidin-4-ylmethyl)-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one (0.03 g, 46%), which was treated with 2.0 M HCl in diethyl ether to give the title compound: ¹H NMR (300 MHz, CD₃OD) δ 7.41 (td, 1H), 7.25-7.12 (m, 3H), 6.43 (s, 1H), 6.37 (s, 1H), 4.87 (d, 1H), 4.72 (d, 1H), 4.23 (s, 2H), 3.80 (d, 2H), 3.51-3.38 (m, 2H), 3.11-2.94 (m, 2H), 2.39-2.19 (m, 1H), 2.06-1.94 (m, 2H), 1.67-1.49 (m, 2H), 1.22 (s, 3H), 1.19 (s, 3H); ¹³C NMR (75 MHz, CD₃OD) δ 181.4, 163.9, 163.4, 144.7, 134.7, 132.3, 131.0, 125.9, 125.8, 122.6, 118.4, 111.3, 94.9, 87.4, 82.6, 60.2, 46.7, 45.7, 45.6, 43.3, 34.6, 28.8, 28.7, 28.6; MS (ES+) *m/z* 405.4 (M + 1).

EXAMPLE 10.20

Synthesis of 7'-fluoro-1'-[(1-isopropylpiperidin-4-yl)methyl]spiro[furo[2,3-*f'*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one hydrochloride

A. Following the procedure as described in EXAMPLES 10.18 and 10.19, and making non-critical variations using 7'-fluorospiro[furo[2,3-*f'*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-

3,3'-indol]-2'(1'*H*)-one, 7'-fluoro-1'-(piperidin-4-ylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one was obtained and used in the next step.

- B. To a stirred solution of 7'-fluoro-1'-(piperidin-4-ylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one (120 mg, 0.28 mmol) and triethylamine (3.9 μ L, 0.028 mmol) in 5.00 mL dichloromethane was added acetone (4.1 μ L, 0.56 mmol) followed with sodium triacetoxyborohydride (124 mg, 0.56 mmol) at ambient temperature. The mixture was stirred at ambient temperature overnight, quenched with water (10.0 mL). The mixture was extracted with dichloromethane (3 x 30.0 mL). The combined organic layers was dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo*. The residue was subjected to column chromatography (2% methanol in ethyl acetate/hexane) to give 7'-fluoro-1'-[(1-isopropylpiperidin-4-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one (85 mg, 69%) as a white solid, which was treated with 2.0 M HCl in diethyl ether to give the title compound: mp 157-160 °C; ¹H NMR (300 MHz, CD₃OD) δ 7.22-7.05 (m, 2H), 7.05-6.98 (m, 1H), 6.52 (s, 1H), 6.21 (s, 1H), 5.86 (s, 2H), 4.83 (d, 1H), 4.68 (d, 1H), 3.95-3.77 (m, 2H), 3.55-3.42 (m, 3H), 3.12-2.96 (m, 2H), 2.30-2.10 (m, 1H), 2.10-1.97 (m, 2H), 1.76-1.52 (m, 2H), 1.34 (d, 6H); ¹³C NMR (75 MHz, CD₃OD) δ 179.7, 157.6, 150.6, 150.4, 147.1, 143.9, 136.6, 125.8, 121.2, 120.3, 118.0, 103.9, 103.0, 94.3, 81.8, 60.1, 59.7, 47.6, 35.33, 35.30, 28.6, 28.5, 16.98, 16.96; MS (ES+) *m/z* 439.27 (M + 1).

EXAMPLE 10.21

Synthesis of 5,5-dimethyl-1'-{[5-(trifluoromethyl)-2-furyl]methyl}-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one

- To a solution of 5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one (0.09 g, 0.29 mmol) in 2-butanone (10.0 mL) was added 2-bromomethyl-5-(trifluoromethyl)furan (0.08 g, 0.35 mmol) followed by cesium carbonate (0.19 g, 0.58 mmol) at 0 °C. The mixture was stirred at ambient temperature overnight. The reaction mixture was filtered and the filtrate was concentrated *in vacuo*. The residue was subjected to column chromatography (ethyl acetate/hexane, 1/5) to give the title compound (0.06 g, 45%): mp 155-160 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.29 (t, 1H), 7.19 (d, 1H), 7.07 (t, 1H), 6.97 (d, 1H), 6.73 (t, 1H), 6.42-6.37 (m, 2H), 6.30 (s, 1H), 5.08 (d, 1H), 4.94-4.84 (m, 2H), 4.65 (d, 1H), 4.18 (s, 2H), 1.19 (s, 3H), 1.14 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 177.5, 161.2, 161.0, 152.0, 141.4, 132.5, 130.1, 128.8, 124.2, 123.8, 120.1, 116.4, 112.6, 109.3, 108.7, 93.4, 85.5, 80.6, 57.7, 41.4,

36.9, 27.6, 27.5; MS (ES+) m/z 456.5 ($M + 1$).

EXAMPLE 10.22

Synthesis of 5,5-dimethyl-1'-(pyridin-3-ylmethyl)-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one hydrochloride

5 To a solution of 5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one (0.08 g, 0.26 mmol) in DMF (10 mL) was added sodium hydride (0.03 g, 0.78 mmol) slowly at 0 °C. After 30 min, 3-(bromomethyl)-pyridine hydrobromide (0.10 g, 0.39 mmol) was added. The mixture was stirred at ambient temperature overnight, quenched with saturated ammonium chloride (10.0 mL). The
10 mixture was extracted with ethyl acetate (3 x 20.0 mL). The combined organic layers was dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo*. The residue was subjected to column chromatography (ethyl acetate/hexane, 2/1) to give 5,5-dimethyl-1'-(pyridin-3-ylmethyl)-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one as a white solid (0.05 g, 48%), which was treated with
15 2.0 M HCl in diethyl ether to give the title compound: mp 124-126 °C; ¹H NMR (300 MHz, CD₃OD) δ 8.96 (br, 1H), 8.82 (br, 1H), 8.62 (d, 1H), 7.3 (t, 1H), 7.32 (td, 1H), 7.23-7.17 (m, 1H), 7.16-7.08 (m, 2H), 6.42 (s, 1H), 6.32 (s, 1H), 5.35-5.14 (m, 2H), 4.93-4.84 (m, 1H), 4.74 (d, 1H), 4.18 (s, 2H), 1.18 (s, 3H), 1.14 (s, 3H); ¹³C NMR (75 MHz, CD₃OD) δ 178.9, 161.6, 161.1, 145.4, 141.3, 141.1, 132.5, 130.1, 128.8, 124.0,
20 123.9, 120.1, 116.2, 108.8, 92.6, 85.1, 80.2, 57.8, 41.0, 40.5, 26.5, 26.4; MS (ES+) m/z 399.5 ($M + 1$).

EXAMPLE 10.23

Synthesis of 5,5-dimethyl-1'-(pyridin-2-ylmethyl)-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one hydrochloride

25 Following the procedure as described in EXAMPLE 10.22, and making non-critical variations using 2-(bromomethyl)-pyridine hydrobromide to replace 3-(bromomethyl)-pyridine hydrobromide, the title compound was obtained (45%): mp 145-147 °C; ¹H NMR (300 MHz, CD₃OD) δ 8.86 (dd, 1H), 8.56 (td, 1H), 8.05-7.97 (m, 2H), 7.37 (td, 1H), 7.31-7.25 (m, 1H), 7.24-7.16 (m, 1H), 7.11 (d, 1H), 6.55 (s, 1H),
30 6.37 (s, 1H), 5.52 (d, 1H), 5.38 (d, 1H), 4.97 (d, 1H), 4.79 (d, 1H), 4.23 (s, 2H), 1.24 (s, 3H), 1.20 (s, 3H); ¹³C NMR (75 MHz, CD₃OD) δ 177.4, 160.0, 159.6, 150.3, 144.7, 141.0, 139.7, 131.0, 128.6, 127.2, 124.3, 123.7, 122.6, 122.4, 118.5, 114.8, 107.2, 91.0, 83.6, 78.7, 56.3, 40.1, 39.4, 24.9, 24.8; MS (ES+) m/z 399.5 ($M + 1$).

EXAMPLE 10.24

Synthesis of 1'-[(6-methylpyridin-3-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one hydrochloride

Following the procedure as described in EXAMPLE 10.21, and making non-critical variations using (6-methylpyridin-3-yl)methyl 4-methylbenzenesulfonate to replace 2-bromomethyl-5-(trifloromethyl)furan, and spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one, 1'-[(6-methylpyridin-3-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one was obtained (56%), which was treated with 2.0 M HCl in diethyl ether to give the title compound: ¹H NMR (300 MHz, CD₃OD) δ 8.77 (s, 1H), 8.46 (dd, 1H), 7.91 (d, 1H), 7.33 (t, 1H), 7.24-7.09 (m, 3H), 6.52 (s, 1H), 6.14 (s, 1H), 5.86 (s, 2H), 5.18 (s, 2H), 4.93-4.85 (m, 1H), 4.71 (d, 1H), 2.77 (s, 3H); ¹³C NMR (75 MHz, CD₃OD) δ 180.0, 157.6, 155.1, 150.6, 146.6, 143.8, 142.7, 141.2, 135.7, 133.5, 130.3, 129.5, 125.3, 125.2, 120.5, 110.3, 103.8, 103.0, 94.3, 81.5, 59.7, 41.5, 19.5; MS (ES+) *m/z* 387.4 (M + 1).

EXAMPLE 10.25

Synthesis of 1'-[(6-methoxypyridin-3-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure as described in EXAMPLE 10.21, and making non-critical variations using (6-methoxypyridin-3-yl)methyl 4-methylbenzenesulfonate to replace 2-bromomethyl-5-(trifloromethyl)furan, and spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one, the title compound was obtained (45%): ¹H NMR (300 MHz, CDCl₃) δ 8.19 (d, 1H), 7.59 (dd, 1H), 7.26-7.12 (m, 2H), 7.02 (t, 1H), 6.83 (d, 1H), 6.74 (d, 1H), 6.50 (s, 1H), 6.07 (s, 1H), 5.89-5.82 (m, 2H), 5.00-4.90 (m, 2H), 4.76 (d, 1H), 4.65 (d, 1H), 3.93 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 177.6, 163.7, 155.9, 149.0, 145.3, 142.4, 141.6, 138.9, 132.2, 129.0, 124.4, 124.1, 123.7, 119.2, 111.7, 109.0, 102.9, 101.5, 93.7, 80.4, 58.2, 53.9, 41.1; MS (ES+) *m/z* 403.2 (M + 1).

EXAMPLE 10.26

Synthesis of 1'-[(6-chloropyridin-3-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure described in EXAMPLE 10.21, and making non-critical variations using 2-chloro-5-(chloromethyl)pyridine to replace 2-bromomethyl-5-

(trifloromethyl)furan, and spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one, the title compound was obtained (69%): ¹H NMR (300 MHz, CDCl₃) δ 8.42 (d, 1H), 7.63 (dd, 1H), 7.34-7.14 (m, 3H), 7.05 (t, 1H), 6.77 (d, 1H), 6.51 (s, 1H), 6.06 (s, 1H), 5.89-5.84 (m, 2H), 5.07-4.78 (m, 3H), 4.66 (d, 1H); MS (ES+) *m/z* 407.3 (M + 1).

EXAMPLE 10.27

Synthesis of 1'-{[6-(dimethylamino)pyridin-3-yl]methyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one hydrochloride

To a seal tube was added 1'-((6-chloropyridin-3-yl)methyl)-6*H*-spiro[benzofuro[6,5-*d*][1,3]dioxole-7,3'-indolin]-2'-one (0.10 g, 0.25 mmol) and dimethylamine (2.00 mL of 2 M THF solution, 4.00 mmol). The mixture was stirred at 130 °C overnight. After cooling down to ambient temperature, the mixture was concentrated *in vacuo*. The residue was subjected to column chromatography (ethyl acetate/hexane, 1/2) to give 1'-{[6-(dimethylamino)pyridin-3-yl]methyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one as a white solid (50 mg, 48%), which was treated with 2.0 M HCl in diethyl ether to give the title compound: mp 146-150 °C; ¹H NMR (300 MHz, CD₃OD) δ 8.03 (d, 1H), 7.95 (dd, 1H), 7.36 (td, 1H), 7.25-7.12 (m, 4H), 6.57 (s, 1H), 6.09 (s, 1H), 5.90 (s, 2H), 5.07-4.87 (m, 3H), 4.72 (d, 1H), 3.27 (s, 6H); ¹³C NMR (75 MHz, CD₃OD) δ 179.9, 157.6, 154.6, 150.5, 143.8, 143.4, 142.9, 137.7, 133.5, 130.2, 125.1, 121.8, 120.6, 113.2, 110.4, 103.7, 103.0, 94.3, 81.4, 59.7, 41.1, 39.5; MS (ES+) *m/z* 416.5 (M + 1).

EXAMPLE 10.28

Synthesis of 1'-{[6-morpholin-4-ylpyridin-3-yl]methyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one hydrochloride

Following the procedure as described in EXAMPLE 10.27, and making non-critical variations using morpholine to replace dimethylamine solution, the title compound was obtained (52%): mp 185-200 °C; ¹H NMR (300 MHz, CD₃OD) δ 8.13-8.04 (m, 2H), 7.45 (d, 1H), 7.37 (t, 1H), 7.26-7.14 (m, 3H), 6.56 (s, 1H), 6.10 (s, 1H), 5.89 (s, 2H), 5.10-4.87 (m, 3H), 4.72 (d, 1H), 3.91-3.84 (m, 4H), 3.73-3.67 (m, 4H); ¹³C NMR (75 MHz, CD₃OD) δ 180.0, 157.6, 153.7, 150.5, 145.1, 143.8, 142.8, 136.3, 133.5, 130.3, 125.2, 125.1, 123.6, 120.6, 114.6, 110.4, 103.7, 103.0, 94.3, 81.5, 66.7, 59.7, 47.2, 40.9; MS (ES+) *m/z* 458.5 (M + 1).

EXAMPLE 10.29

Synthesis of 1'-[(6-pyrrolidin-1-ylpyridin-3-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one hydrochloride

Following the procedure as described in EXAMPLE 10.27, and making non-critical variations using pyrrolidine to replace dimethylamine solution, the title compound was obtained (45%): mp 160-165 °C; ¹H NMR (300 MHz, CD₃OD) δ 7.99-7.91 (m, 2H), 7.33 (td, 1H), 7.22-7.06 (m, 4H), 6.53 (s, 1H), 6.05 (s, 1H), 5.86 (s, 2H), 5.04-4.82 (m, 3H), 4.68 (d, 1H), 3.57 (t, 4H), 2.13 (t, 4H); ¹³C NMR (75 MHz, CD₃OD) δ 177.0, 154.6, 148.0, 147.6, 141.1, 140.8, 139.9, 132.5, 130.5, 127.3, 122.2, 118.8, 117.6, 112.0, 107.4, 100.7, 100.0, 91.3, 78.5, 56.7, 38.0, 23.2; MS (ES+) *m/z* 442.2 (M + 1).

EXAMPLE 10.30

Synthesis of 1'-(2-chloro-4-fluorobenzyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure described in EXAMPLE 10.21, and making non-critical variations using spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one, and 1-(bromomethyl)-2-chloro-4-fluorobenzene to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound was obtained (54%) as a white solid: mp 174-175 °C; MS (ES+) *m/z* 424.2 (M + 1).

EXAMPLE 10.31

Synthesis of 1'-[(2-methylcyclopropyl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure described in EXAMPLE 10.21, and making non-critical variations using spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one, and 1-(bromomethyl)-2-methylcyclopropane to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound was obtained (37%) as a white solid: MS (ES+) *m/z* 350.3 (M + 1).

EXAMPLE 10.32

Synthesis of 1'-(3-cyclopropylpropyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure described in EXAMPLE 10.21, and making non-critical

variations using spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one, and (3-bromopropyl)cyclopropane to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound was obtained (51%) as a white solid: mp 111-113 °C; MS (ES+) *m/z* 364.3 (M + 1).

EXAMPLE 10.33

Synthesis of 1'-butylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure described in EXAMPLE 10.21, and making non-critical variations using spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one, and 1-bromobutane to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound was obtained (62%) as a white solid: mp 119-120 °C; MS (ES+) *m/z* 338.3 (M + 1).

EXAMPLE 10.34

Synthesis of 1'-[(5-methylisoxazol-4-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure described in EXAMPLE 10.21, and making non-critical variations using spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one, and 4-(bromomethyl)-5-methylisoxazole to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound was obtained (25%) as a white solid: mp 159-161 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.39-6.91 (m, 4H), 6.50 (s, 1H), 6.11 (s, 1H), 5.94 (d, 1H), 5.85 (ABq, 2H), 4.95 (ABq, 2H), 4.78 (ABq, 2H), 2.37 (s, 3H); MS (ES+) *m/z* 377.3 (M + 1).

EXAMPLE 10.35

Synthesis of 1'-(tetrahydro-2*H*-pyran-4-ylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure described in EXAMPLE 10.21, and making non-critical variations using spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one, and 4-(bromomethyl)tetrahydro-2*H*-pyran to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound was obtained (25%) as a white solid: mp 142-144 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.34-6.85 (m, 4H), 6.50 (s, 1H), 6.08 (s, 1H), 5.85 (ABq, 2H), 4.76 (ABq, 2H), 4.18-3.86 (m, 2H), 3.63 (ddd, 2H), 3.34 (t, 2H), 2.38-1.92 (m, 1H), 1.70-1.36 (m, 4H); MS (ES+) *m/z* 380.3 (M + 1).

EXAMPLE 10.36

Synthesis of 1'[2-(trifluoromethoxy)benzyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure described in EXAMPLE 10.21, and making non-critical variations using spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one, and 1-(bromomethyl)-2-(trifluoromethoxy)benzene to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound was obtained (77%) as a white solid: mp 130-135 °C; MS (ES+) *m/z* 456.3 (M + 1).

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EXAMPLE 10.37

Synthesis of 1'[3-(trifluoromethoxy)benzyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure described in EXAMPLE 10.21, and making non-critical variations using spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one, and 1-(bromomethyl)-3-(trifluoromethoxy)benzene to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound was obtained (65%) as a white solid: mp 88-91 °C; MS (ES+) *m/z* 456.3 (M + 1).

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EXAMPLE 10.38

20 Synthesis of 1'[4-(trifluoromethoxy)benzyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure described in EXAMPLE 10.21, and making non-critical variations using spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one, and 1-(bromomethyl)-4-(trifluoromethoxy)benzene to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound was obtained (50%) as a white solid: mp 99-101 °C; MS (ES+) *m/z* 456.3 (M + 1).

25

EXAMPLE 10.39

Synthesis of 1'-methylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

30 Following the procedure described in EXAMPLE 10.21, and making non-critical variations using spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(1'*H*)-one, and iodomethane to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound

was obtained (72%) as a white solid: mp 142-144 °C; MS (ES+) *m/z* 296.2 (*M* + 1).

EXAMPLE 10.40

Synthesis of 1'-Propylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one

Following the procedure described in EXAMPLE 10.21, and making non-critical variations using spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one to replace 5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(*1'H*)-one, and 1-bromopropane to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound was obtained (64%) as a white solid: mp 158-160 °C; MS (ES+) *m/z* 324.4 (*M* + 1).

EXAMPLE 10.41

10 Synthesis of 1'-(2,1,3-benzoxadiazol-5-ylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one

Following the procedure described in EXAMPLE 10.21, and making non-critical variations using spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one to replace 5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(*1'H*)-one, and 5-(bromomethyl)benzo[*c*][1,2,5]oxadiazole to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound was obtained (17%) as a white solid: mp 163-165 °C; MS (ES+) *m/z* 414.4 (*M* + 1).

EXAMPLE 10.42

20 Synthesis of 1'[(1-methyl-1*H*-benzotriazol-6-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one

Following the procedure described in EXAMPLE 10.21, and making non-critical variations using spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one to replace 5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(*1'H*)-one, and 6-(bromomethyl)-1-methyl-1*H*-benzotriazole to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound was obtained (17%) as a white solid: mp 230-235 °C; MS (ES+) *m/z* 427.3 (*M* + 1).

EXAMPLE 10.43

Synthesis of *tert*-butyl 4-[(2'-oxo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-1'(*2'H*)-yl)methyl]piperidine 1-carboxylate

30 Following the procedure described in EXAMPLE 10.21, and making non-critical variations using 5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(*1'H*)-one to replace 5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(*1'H*)-one,

and *tert*-butyl 4-(bromomethyl)peridine-1-carboxylate to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound was obtained (58%) as a white solid: mp 96-98 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.84-6.85 (m, 4H), 6.40 (s, 1H), 6.37 (s, 1H), 4.68 (ABq, 2H), 4.46 (t, 2H), 4.06-3.73 (m, 2H), 3.68-3.45 (m, 2H), 2.92 (t, 2H), 2.63 (s, 2H), 2.04-1.82 (m, 1H), 1.76-0.66 (m, 13H); MS (ES+) *m/z* 477.4 (M + 1).

EXAMPLE 10.44

Synthesis of 1'-(2,3-difluorobenzyl)-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(*1'H*)-one

Following the procedure described in EXAMPLE 10.21, and making non-critical variations using 5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(*1'H*)-one to replace 5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(*1'H*)-one, and 1-(bromomethyl)-2,3-difluorobenzene to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound was obtained (67%) as a white solid: mp 156-158 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.50-6.85 (m, 7H), 6.43 (s, 1H), 6.39 (s, 1H), 5.01 (q, 2H), 4.75 (dd, 2H), 4.46 (t, 2H), 2.92 (t, 2H); MS (ES+) *m/z* 406.2 (M + 1).

EXAMPLE 10.45

Synthesis of 1'-(pyridin-2-ylmethyl)-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(*1'H*)-one hydrochloride

Following the procedure described in EXAMPLE 10.21, and making non-critical variations using 5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(*1'H*)-one to replace 5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(*1'H*)-one, and 2-(bromomethyl)pyridine hydrobromide to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, 1'-(pyridin-2-ylmethyl)-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(*1'H*)-one was obtained (27%) as a white solid, which was treated in CH₂Cl₂ with excess of HCl in ether to give the title compound: mp 208-210 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.78-8.53 (m, 1H), 8.05 (t, 1H), 7.64-7.47 (m, 2H), 7.30-6.92 (m, 4H), 6.59 (s, 1H), 6.38 (s, 1H), 5.24-5.06 (m, 2H), 4.78 (ABq, 2H), 4.46 (t, 2H), 2.94 (t, 2H); MS (ES+) *m/z* 371.4 (M + 1).

EXAMPLE 10.46

Synthesis of 1'-(4-methoxybenzyl)-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(*1'H*)-one

Following the procedure described in EXAMPLE 10.21, and making non-critical variations using 5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(*1'H*)-one to

replace 5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(*1'H*)-one, and 1-(chloromethyl)-4-methoxybenzene to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound was obtained (56%) as a white solid: mp 120-121 °C; MS (ES+) *m/z* 400.2 (*M* + 1).

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EXAMPLE 10.47

Synthesis of 4'-bromo-1'-[[5-(trifluoromethyl)-2-furyl]methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one

To a solution of 4'-bromospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one (0.48 g, 1.33 mmol) in *N,N*-dimethylformamide (5.00 mL) was added sodium hydride (0.08 g, 1.98 mmol, 60% dispersion in mineral oil) in one portion at 0 °C. The reaction mixture was stirred for 0.5 h followed by the addition of a solution of 2-(bromomethyl)-5-trifluoromethylfuran in *N,N*-dimethylformamide (1.00 mL). The reaction mixture was stirred at ambient temperature for 16 h and quenched by slow addition of water (5.00 mL). The reaction mixture was extracted with ethyl acetate (3 x 20.0 mL), washed with brine, dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography eluting with ethyl acetate:hexane (35%) to afford the title compound (0.46 g, 69%) as a colorless solid: ¹H NMR (300 MHz, CDCl₃) δ 7.22-7.14 (m, 2H), 6.94 (dd, 1H), 6.73 (d, 1H), 6.46 (s, 1H), 6.39 (d, 1H), 6.04 (s, 1H), 5.86 (dd, 2H), 4.94 (ABq, 2H), 4.92 (ABq, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 177.0, 157.2, 151.6, 151.5, 149.3, 143.4, 142.2, 130.5, 127.8, 129.6, 120.1, 116.0, 112.7, 109.5, 107.9, 102.5, 101.6, 93.3, 77.1, 59.6, 37.1; MS (ES+) *m/z* 508.2 (*M* + 2).

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EXAMPLE 10.48

Synthesis of 4'-bromo-1'-[[5-(trifluoromethyl)-2-furyl]methyl]-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(*1'H*)-one

Following the procedure described in EXAMPLE 10.47, and making non-critical variations using 4'-bromo-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(*1'H*)-one to replace 4'-bromospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one, the title compound was obtained (76%) as a colorless solid: mp 182-184 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.21-7.11 (m, 2H), 6.92 (dd, 1H), 6.74 (d, 1H), 6.41 (d, 1H), 6.38 (s, 1H), 6.37 (s, 1H), 5.10 (d, 1H), 5.02 (d, 1H), 4.87 (d, 1H), 4.81 (d, 1H), 4.53 (t, 2H), 2.98 (t, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 177.3, 162.4, 162.2, 151.5, 143.4, 130.2, 127.7, 120.5, 120.0, 119.7, 118.4, 117.0, 112.7, 112.6, 109.5, 107.8, 92.9, 77.1, 72.4, 59.1,

30

37.0, 28.9; MS (ES+) m/z 506.3 ($M + 1$).

EXAMPLE 10.49

Synthesis of 4'-bromo-1'-methylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one

Following the procedure described in EXAMPLE 10.47, and making non-critical
5 variations using iodomethane to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the
title compound was obtained (79%) as a colorless solid: mp 155-157 °C; ¹H NMR (300
MHz, CDCl₃) δ 7.19 (d, 1H), 7.17 (s, 1H), 6.84 (dd, 1H), 6.46 (s, 1H), 6.08 (s, 1H), 5.86
(dd, 2H), 4.90 (ABq, 2H), 3.25 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 177.3, 157.2,
149.2, 145.1, 142.0, 130.4, 129.9, 127.3, 119.9, 116.3, 107.3, 102.7, 101.5, 93.3, 77.3,
10 59.7, 26.9; MS (ES+) m/z 376.4 ($M + 2$).

EXAMPLE 10.50

Synthesis of *tert*-butyl 4-[(4'-bromo-2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-
1'(*2'H*)-yl)methyl]piperidine-1-carboxylate

Following the procedure described in EXAMPLE 10.47, and making non-critical
15 variations using *tert*-butyl 4-([[(4-methylphenyl)sulfonyl]oxy)methyl]piperidine-1-
carboxylate to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound
was obtained (43%) as a colorless solid: ¹H NMR (300 MHz, CDCl₃) δ 7.17 (d, 2H),
6.83 (t, 1H), 6.46 (s, 1H), 6.04 (s, 1H), 5.87 (d, 2H), 4.89 (ABq, 2H), 4.11 (d, 2H), 3.73-
3.42 (m, 3H), 2.66 (t, 2H), 2.03-1.90 (m, 1H), 1.43 (s, 9H); ¹³C NMR (75 MHz, CDCl₃) δ
20 177.6, 157.3, 154.7, 149.2, 144.8, 142.1, 130.3, 129.8, 127.3, 120.2, 116.3, 107.6,
102.4, 101.6, 93.4, 79.6, 77.2, 59.6, 46.1, 43.4, 34.9, 28.4; MS (ES+) m/z 581.4 ($M +$
23), 579.4 ($M + 23$), 503.3 ($M - 57$), 501.3 ($M - 57$).

EXAMPLE 10.51

Synthesis of 1'-[(3,5-dimethylisoxazol-4-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-
25 7,3'-indol]-2'(*1'H*)-one

Following the procedure described in EXAMPLE 10.47, and making non-critical
variations using spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one to replace 4'-
bromospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one, and 4-(chloromethyl)-
3,5-dimethylisoxazole to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title
30 compound was obtained (35%) as a colorless solid: mp 165-167 °C; ¹H NMR (300
MHz, CDCl₃) δ 7.24 (t, 1H), 7.16 (d, 1H), 7.05 (t, 1H), 6.72 (d, 1H), 6.50 (s, 1H), 6.05
(s, 1H), 5.85 (d, 2H), 4.75 (ABq, 2H), 4.67 (ABq, 2H), 2.46 (s, 3H), 2.22 (s, 3H); ¹³C

NMR (75 MHz, CDCl₃) δ 177.5, 167.1, 159.1, 156.1, 149.1, 142.4, 141.7, 131.8, 129.0, 124.3, 123.8, 118.9, 108.8, 108.6, 102.9, 101.6, 93.8, 80.6, 58.2, 33.3, 11.5, 10.7; MS (ES+) m/z 391.3 (M + 1).

EXAMPLE 10.52

- 5 Synthesis of 1'-(2-furylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one
- Following the procedure described in EXAMPLE 10.47, and making non-critical variations using spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 4'-bromospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one, and 2-chloromethylfuran to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title
- 10 compound (40%) as a colorless solid: mp 110-112 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.35-7.33 (m, 1H), 7.29-7.23 (m, 1H), 7.15 (d, 1H), 7.06-7.00 (m, 2H), 6.50 (s, 1H), 6.34-6.31 (m, 2H), 6.10 (s, 1H), 5.85 (dd, 2H), 4.92 (ABq, 2H), 4.79 (ABq, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 177.1, 155.9, 149.0, 148.9, 142.6, 142.3, 141.8, 132.2, 128.9, 123.8, 123.5, 119.5, 110.6, 109.3, 108.7, 103.1, 101.5, 93.6, 80.4, 58.2, 37.1; MS
- 15 (ES+) m/z 362.5 (M + 1).

EXAMPLE 10.53

Synthesis of ethyl 5-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)pentanoate

- Following the procedure described in EXAMPLE 10.47, and making non-critical
- 20 variations using spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 4'-bromospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one, and ethyl 5-bromovalerate to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound was obtained (62%) as a gummy material: ¹H NMR (300 MHz, CDCl₃) δ 7.28 (t, 1H), 7.14 (d, 1H), 7.03 (t, 1H), 6.88 (d, 1H), 6.48 (s, 1H), 6.13 (s, 1H), 5.84 (d, 2H), 4.76
- 25 (ABq, 2H), 4.07 (q, 2H), 3.87-3.65 (m, 2H), 2.35 (t, 2H), 1.80-1.64 (m, 4H), 1.20 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 177.4, 173.1, 155.9, 148.8, 142.3, 142.2, 132.5, 128.9, 124.04, 123.3, 119.5, 108.6, 103.0, 101.5, 93.6, 80.5, 60.4, 58.2, 39.9, 33.7, 26.8, 22.2, 14.2; MS (ES+) m/z 432.09 (M + 23).

EXAMPLE 10.54

- 30 Synthesis of ethyl 4-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)butanoate

Following the procedure described in EXAMPLE 10.47, and making non-critical

variations using spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 4'-bromospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one, and ethyl 4-bromobutyrate to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound was obtained (80%) as a gummy material: ¹H NMR (300 MHz, CDCl₃) δ 7.29 (t, 1H), 7.14 (d, 1H), 7.04 (d, 1H), 6.99 (d, 1H), 6.48 (s, 1H), 6.18 (s, 1H), 5.84 (d, 2H), 4.76 (ABq, 2H), 4.11 (q, 2H), 3.88-3.71 (m, 2H), 2.40 (t, 2H), 2.03 (t, 2H), 1.21 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 177.4, 172.8, 156.0, 148.9, 142.4, 142.2, 132.4, 129.0, 124.0, 123.3, 119.4, 108.7, 103.0, 101.5, 93.6, 80.5, 60.7, 58.2, 39.6, 31.2, 22.6, 14.3; MS (ES+) *m/z* 418.08 (M + 23), 396.1 (M + 1).

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EXAMPLE 10.55

Synthesis of 1'-[(1,2,4-oxadiazol-3-ylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure described in EXAMPLE 10.47, and making non-critical variations using spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 4'-bromospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one, and 3-(chloromethyl)-1,2,4-oxadiazole to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound was obtained (36%)) as a colorless solid: mp 160-162 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.39 (dt, 1H), 7.20-7.13 (m, 3H), 7.05 (d, 1H), 6.50 (s, 1H), 6.12 (s, 1H), 5.86 (dd, 2H), 4.78 (ABq, 2H), 4.68 (s, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 176.7, 156.0, 149.3, 142.5, 139.6, 131.6, 129.4, 124.8, 124.5, 118.4, 113.6, 108.7, 103.0, 101.7, 93.7, 80.3, 58.2, 29.7, 28.0; MS (ES+) *m/z* 365.2 (M + 1).

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EXAMPLE 10.56

Synthesis of 1'-[[5-(3-chlorophenyl)-2-furyl]methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure described in EXAMPLE 10.47, and making non-critical variations using spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 4'-bromospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one, and 2-(chloromethyl)-5-[3-chlorophenyl]furan to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound was obtained (22%) as a colorless solid: mp 205-207 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.55 (t, 1H), 7.46 (dt, 1H), 7.28 (d, 2H), 7.21-7.14 (m, 2H), 7.09-7.04 (m, 2H), 6.59 (d, 1H), 6.50 (s, 1H), 6.40 (d, 1H), 6.10 (s, 1H), 5.84 (dd, 2H), 4.98 (ABq, 2H), 4.80 (ABq, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 177.2, 155.9, 152.5, 149.2, 148.9, 142.4, 141.7, 134.8, 132.1, 132.0, 130.1, 128.9, 127.5, 124.0, 123.7, 123.6, 121.7,

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119.4, 110.8, 109.2, 106.9, 103.0, 101.5, 93.6, 80.4, 58.2, 37.3; MS (ES+) m/z 472.2 ($M + 1$).

EXAMPLE 10.57

Synthesis of 1'-(3-chloropropyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

5 Following the procedure described in EXAMPLE 10.47, and making non-critical variations using spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 4'-bromospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one, and 1-bromo-3-chloropropane to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound was obtained (22%) as a colorless solid: mp 144-146 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.31 (dt, 1H), 7.14-7.12 (m, 2H), 7.01(t, 1H), 6.65 (s, 1H), 6.23 (s, 1H), 5.89 (s, 2H), 10 4.68 (ABq, 2H), 3.85-3.79 (m, 2H), 3.67 (t, 2H), 2.06 (t, 1H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 177.2, 155.8, 148.7, 142.9, 142.2, 132.4, 129.3, 124.1, 123.3, 120.3, 109.3, 103.6, 101.7, 80.3, 57.8, 43.4, 30.6; MS(ES+) m/z 358.2 ($M + 1$).

EXAMPLE 10.58

15 Synthesis of 1'-[(2-isopropyl-1,3-oxazol-4-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

 Following the procedure described in EXAMPLE 10.47, and making non-critical variations using spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 4'-bromospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one, and 4-chloromethyl-2-20 isopropylloxazole to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound was obtained (22%) as a colorless solid: mp 118-120 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.97 (s, 1H), 7.24 (t, 1H), 7.13 (d, 1H), 7.05 (d, 1H), 6.98 (t, 1H), 6.65 (s, 1H), 6.26 (s, 1H), 5.88 (d, 2H), 4.85 (d, 1H), 4.77 (d, 1H), 4.71-4.66 (m, 2H), 3.04-2.95 (m, 1H), 1.18 (dd, 6H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 176.9, 169.1, 155.6, 25 148.7, 142.4, 142.2, 136.8, 135.2, 132.4, 129.2, 123.9, 123.4, 120.5, 109.9, 103.6, 101.9, 93.7, 79.9, 57.9, 36.2, 28.1, 20.7, 20.6; MS (ES+) m/z 405.2 ($M + 1$).

EXAMPLE 10.59

Synthesis of 1'-[(1-methyl-1*H*-benzimidazol-2-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

30 Following the procedure described in EXAMPLE 10.47, and making non-critical variations using spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 4'-bromospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one, and 2-(bromomethyl)-1-methyl-1*H*-benzimidazole to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the

title compound was obtained (22%) as a colorless solid: mp >250 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.71 (d, 1H), 7.65 (d, 1H), 7.54 (t, 1H), 7.39 (t, 1H), 7.30-7.24 (m, 1H), 7.16 (d, 1H), 7.05 (d, 2H), 6.63 (s, 1H), 6.49 (s, 1H), 6.44 (d, 1H), 6.11 (s, 1H), 5.83 (d, 2H), 4.99 (ABq, 2H), 4.80 (ABq, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 177.2, 155.9, 150.6, 149.6, 148.9, 142.3, 141.7, 132.1, 131.8, 129.8, 128.9, 127.9, 126.8, 126.7, 126.6, 123.9, 123.6, 119.4, 111.0, 110.9, 110.6, 109.3, 103.1, 101.5, 93.6, 80.4, 58.2, 37.3; MS (ES+) *m/z* 506.3 (*M* + 1).

EXAMPLE 10.60

Synthesis of 1'-[(2-oxo-1,3-benzothiazol-3(2*H*)-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure described in EXAMPLE 10.47, and making non-critical variations using spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 4'-bromospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one, and 3-(bromomethyl)-benzo[*d*]thiazol-2(3*H*)-one to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound was obtained (31%) as a colorless solid: ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.67 (d, 1H), 7.41 (d, 1H), 7.35-7.29 (m, 3H), 7.23-7.14 (m, 2H), 7.05 (t, 1H), 6.68 (s, 1H), 5.94-5.85 (m, 5H), 4.69 (td, 1H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 178.1, 170.6, 155.9, 148.9, 142.2, 141.0, 136.1, 131.8, 129.6, 127.3, 124.5, 124.4, 124.3, 123.7, 121.5, 119.8, 112.1, 110.0, 103.4, 101.9, 93.8, 80.3, 58.3, 47.9; MS (ES+) *m/z* 467.2 (*M* + 23).

EXAMPLE 10.61

Synthesis of 1'-[(5-chloro-2-thienyl)methyl]-5'-fluorospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure described in EXAMPLE 10.47, and making non-critical variations using 5'-fluorospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 4'-bromospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one, and 5-chloro-2-(chloromethyl)thiophene to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound was obtained (76%) as a colorless solid: mp 142-144 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.22-7.17 (m, 1H), 7.14-7.13 (m, 1H), 7.12-7.10 (m, 2H), 6.96 (d, 1H), 6.68 (s, 1H), 6.13 (s, 1H), 5.91 (d, 2H), 5.02 (ABq, 2H), 4.73 (ABq, 2H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 176.9, 161.0, 157.8, 156.0, 149.0, 142.2, 138.3, 138.2 (d, ⁴*J*_{CF} = 7.0 Hz) 133.6 (d, ³*J*_{CF} = 33 Hz), 128.3, 127.8, 127.1, 119.5, 115.6 (d, ¹*J*_{CF} = 93 Hz), 112.5 (d, ¹*J*_{CF} = 100 Hz), 110.8 (d, ³*J*_{CF} = 32 Hz), 103.2, 102.0, 93.9, 79.8, 58.2 (d, ⁴*J*_{CF}

= 7.0 Hz), 39.0; MS (ES+) m/z 430.1 ($M + 1$).

EXAMPLE 10.62

Synthesis of 1'-[(5-chloro-2-furyl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one

5 To an ice-cooled solution of (5-chloro-2-furyl)methanol (2.03 g, 15.3 mmol) in anhydrous dichloromethane (50.0 mL) was added triethylamine (4.64 g, 45.9 mmol) followed by thionyl chloride (3.64 g, 30.6 mmol). The reaction mixture was stirred at 0 °C for 30 min and quenched with saturated ammonium chloride (25.0 mL). After the aqueous layer was separated, the organic layer was washed with 10% aqueous HCl
10 (20.0 mL), brine (20 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness to give 5-chloro-2-chloromethylfuran as a yellow oil. A solution of this oil in anhydrous *N,N*-dimethylformamide (3.00 mL) was added directly without any further purification to a mixture of spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one (0.84 g, 3.00 mmol) and sodium hydroxide
15 (0.48 g, 12.0 mmol) in anhydrous *N,N*-dimethylformamide (9.00 mL). The reaction mixture was heated at 70 °C for 16 h, cooled to ambient temperature followed by the addition of saturated ammonium chloride (5.0). *N,N*-Dimethylformamide was removed under high vacuum. The residue was diluted with ethyl acetate (100 mL), washed with 10% aqueous HCl (25.0 mL), brine (25.0 mL), dried over anhydrous sodium sulfate
20 and filtered. The filtrate was concentrated *in vacuo* to dryness. The brown residue was subjected to column chromatography eluting with ethyl acetate/hexane (35%) to afford the title compound (0.74 g, 62%) as a colorless solid: mp 148-150 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.29 (t, 1H), 7.15-7.12 (m, 2H), 7.01 (d, 1H), 6.67 (s, 1H), 6.60 (d, 1H), 6.39 (d, 1H), 6.10 (s, 1H), 5.89 (d, 2H), 4.89 (ABq, 2H), 4.72 (ABq, 2H); ¹³C
25 NMR (75 MHz, DMSO-*d*₆) δ 176.9 155.8 149.7, 148.8, 142.2, 142.1, 134.8, 132.1, 129.3 124.1, 123.7 120.2, 112.0, 109.9, 108.2 103.2, 101.9, 93.8, 80.0, 57.9 37.0; MS (ES+) m/z 396 ($M + 1$).

EXAMPLE 10.63

Synthesis of 1'-[(4-hydroxy-1,2,2,6,6-pentamethylpiperidin-4-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one

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Following the procedure described in EXAMPLE 10.62, and making non-critical variations using 5,5,6,7,7-pentamethyl-1-oxa-6-azaspiro[2.5]octane to replace (5-chloro-2-furyl)methanol, the title compound was obtained (70%) as a colorless solid:

mp 210-214 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.29 (d, 1H), 7.24 (t, 1H), 7.10 (d, 1H), 7.01 (t, 1H), 6.66 (s, 1H), 6.45 (s, 1H), 5.90 (d, 2H), 5.20 (br, 1H), 4.70 (ABq, 2H), 3.57 (q, 2H), 3.30 (s, 3H), 2.01-1.83 (m, 4H), 1.45 (s, 6H), 1.34 (s, 6H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 178.5, 156.0, 148.7, 144.5, 142.2, 132.3, 128.9, 123.8, 123.2, 120.3, 110.9, 104.1, 101.9, 93.7, 80.9, 71.6, 65.3, 57.8, 52.6, 30.2, 28.7, 22.1; MS (ES+) *m/z* 465.4 (M + 1).

EXAMPLE 10.64

Synthesis of 1'-[[5-(2-chlorophenyl)-2-furyl]methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure described in EXAMPLE 10.62, and making non-critical variations using [5-(2-chlorophenyl)-2-furyl]methanol to replace (5-chloro-2-furyl)methanol, the title compound was obtained (48%) as a colorless solid: mp 148-150 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.74 (d, 1H), 7.39 (d, 1H), 7.29 (d, 1H), 7.24 (d, 1H), 7.19-7.15 (m, 2H), 7.08-7.04 (m, 3H), 6.51 (s, 1H), 6.45 (d, 1H), 6.12 (s, 1H), 6.84 (s, 2H), 4.99 (ABq, 2H), 4.78 (ABq, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 177.2, 155.9, 150.3, 149.0, 148.6, 142.4, 141.8, 132.1, 130.8, 130.0, 128.9, 128.7, 128.2, 127.7, 126.9, 123.9, 123.6, 119.4, 111.8, 110.7, 109.2, 103.1, 101.5, 93.6, 80.4, 58.2, 37.3; MS (ES+) *m/z* 472.2 (M + 1).

EXAMPLE 10.65

Synthesis of 1'-[(5-methyl-2-furyl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure described in EXAMPLE 10.62, and making non-critical variations using (5-methyl-2-furyl)methanol to replace (5-chloro-2-furyl)methanol, the title compound was obtained (70%) as a colorless solid: mp 117-119 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.26 (t, 1H), 7.12 (t, 2H), 6.99 (t, 1H), 6.67 (s, 1H), 6.32 (d, 1H), 6.07 (s, 1H), 5.97 (d, 1H), 5.89 (d, 2H), 4.84 (ABq, 2H), 4.72 (ABq, 2H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 176.8, 155.7, 151.9, 148.8, 147.7, 142.3, 142.2, 132.1, 129.2, 124.0, 123.5, 120.4, 110.1, 110.0, 107.0, 103.2, 101.9, 93.8, 79.9, 57.9, 37.2, 13.7; MS (ES+) *m/z* 376 (M + 1).

EXAMPLE 10.66

Synthesis of 1'-[(5-bromo-2-furyl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure described in EXAMPLE 10.62, and making non-critical variations using (5-bromo-2-furyl)methanol to replace (5-chloro-2-furyl)methanol, the title compound was obtained (76%) as colorless solid: ¹H NMR (300 MHz, DMSO-*d*₆) δ 9.29 (s, 1H), 7.69 (dt, 1H), 7.32-7.26 (m, 2H), 7.04 (d, 1H), 6.99 (d, 1H), 6.71 (d, 1H), 6.02 (s, 1H), 4.91 (ABq, 2H), 4.47 (t, 2H), 3.08 (t, 2H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 176.9, 160.4, 156.3, 153.8, 149.7, 146.1, 137.5, 130.9, 130.8, 126.5, 125.8, 123.1, 121.5, 118.8, 116.4, 108.3, 96.7, 76.6, 71.9, 45.7, 29.1; MS (ES+) *m/z* 440.1 (M + 1), 442.1 (M + 1).

EXAMPLE 10.67

Synthesis of 1'-[(5-chloro-2-thienyl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure described in EXAMPLE 10.62, and making non-critical variations using (5-chloro-2-thienyl)methanol to replace (5-chloro-2-furyl)methanol, the title compound was obtained (77%) as a colorless solid: mp 145-146 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.28 (t, 1H), 7.20-7.14 (m, 2H), 7.10 (d, 1H), 7.01 (t, 1H), 6.95 (d, 1H), 6.67 (s, 1H), 6.09 (s, 1H), 5.89 (d, 2H), 5.02 (ABq, 2H), 4.71 (ABq, 2H); MS (ES+) *m/z* 411.9 (M + 1).

EXAMPLE 10.68

Synthesis of 1'-{[3-hydroxy-5-(trifluoromethyl)-2-thienyl]methyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure described in EXAMPLE 10.62, and making non-critical variations using 2-(hydroxymethyl)-5-(trifluoromethyl)thiophene-3-ol to replace (5-chloro-2-furyl)methanol, the title compound was obtained (48%) as a colorless solid: mp 225-227 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 10.4 (s, 1H), 7.29 (dt, 1H), 7.16-7.10 (m, 3H), 7.01 (dt, 1H), 6.68 (s, 1H), 6.09 (s, 1H), 5.89 (d, 2H), 4.94 (ABq, 2H), 4.70 (ABq, 2H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 176.9, 155.8, 152.3, 148.9, 142.2, 141.9, 132.1, 129.4, 125.9, 125.4, 124.5, 124.2, 123.8, 122.6, 120.9, 120.0, 116.5, 109.5, 103.3, 101.9, 93.8, 80.2, 57.9, 34.9; MS (ES+) *m/z* 460.38 (M - 1).

EXAMPLE 10.69

Synthesis of 1'-{[5-(2-trifluoromethylphenyl)-2-furyl]methyl}-4*H*-spiro[furo[2,3-
g][1,3]benzodioxine-8,3'-indol]-2'(1'*H*)-one

Following the procedure described in EXAMPLE 10.62, and making non-critical
5 variations using {5-[2-(trifluoromethyl)phenyl]-2-furyl}methanol to replace (5-chloro-2-
furyl)methanol, the title compound was obtained (28%) as a colorless solid: mp 124-
126 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.71 (d, 1H), 7.65 (d, 1H), 7.54 (t, 1H), 7.39 (t,
1H), 7.30-7.24 (m, 1H), 7.16 (d, 1H), 7.05 (d, 2H), 6.63 (s, 1H), 6.49 (s, 1H), 6.44 (d,
1H), 6.11 (s, 1H), 5.83 (d, 2H), 4.99 (ABq, 2H), 4.80 (ABq, 2H); ¹³C NMR (75 MHz,
10 CDCl₃) δ 177.2, 155.9, 150.6, 149.6, 148.9, 142.3, 141.7, 132.1, 131.8, 129.8, 128.9,
127.9, 126.8, 126.7, 126.6, 123.9, 123.6, 119.4, 111.0, 110.9, 110.6, 109.3, 103.1,
101.5, 93.6, 80.4, 58.2, 37.3; MS (ES+) *m/z* 506.27 (M + 1).

EXAMPLE 10.70

Synthesis of 1'[(2-chloro-1,3-thiazol-5-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-
15 indol]-2'(1'*H*)-one

To a solution of (2-chloro-1,3-thiazol-5-yl)methanol (0.30 g, 2.00 mmol) in
anhydrous CH₂Cl₂ (20.0 mL) was added thionyl chloride (0.50 g, 4.20 mmol) followed
by triethylamine (0.40 g, 4.00 mmol) at 0 °C. After stirring at 0 °C for one hour and
ambient temperature for one hour, the reaction mixture was diluted with CH₂Cl₂ (50.0
20 mL) and extracted with water (2 x 20 mL). The organic phase was dried over Na₂SO₄
and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was
dissolved in methyl-ethyl ketone (10.0 mL) followed by the additions of spiro[furo[2,3-
f][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one (0.36 g, 2.00 mmol) and cesium carbonate
(1.95 g, 6.00 mmol). The reaction mixture was heated at 70 °C overnight, cooled,
25 filtered and the filtrate was concentrated *in vacuo* to dryness. The residue was
subjected to column chromatography to yield the title compound (0.032 g, 3.4%) as a
colorless solid: mp 195-198 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.81 (s, 1H), 7.39-
6.93 (m, 5H), 6.66 (s, 1H), 6.15-6.12 (m, 1H), 5.89 (d, 2H), 5.10 (s, 2H), 4.70 (dd, 2H);
MS (ES+) *m/z* 413.1 (M + 1).

30

EXAMPLE 10.71

Synthesis of 1'-{[5-(trifluoromethyl)-2-furyl]methyl}-6,7-dihydrospiro[benzo[1,2-*b*:4,5-
b']difuran-3,3'-indol]-2'(1'*H*)-one

Following the procedure as described in EXAMPLE 10.21, and making non-

critical variations using 6,7-dihydrospiro[benzo[1,2-*b*:4,5-*b'*]difuran-3,3'-indol]-2'(*1'H*)-one to replace 5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(*1'H*)-one, the title compound was obtained (19%) as a white solid: mp 174-177 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.33-6.95 (m, 5H), 6.84 (s, 1H), 6.71 (d, 1H), 5.88 (s, 1H), 5.03 (ABq, 2H), 4.70 (ABq, 2H), 4.46-4.31 (m, 2H), 3.07 (t, 2H); MS (ES+) *m/z* 428.0 (M + 1).

EXAMPLE 10.72

Synthesis of 1'-[[5-(trifluoromethyl)-2-furyl]methyl]5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]2'(*1'H*)-one

Following the procedure described in EXAMPLE 10.21, and making non-critical variations using 5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]2'(*1'H*)-one to replace 5,5-dimethyl-5,6-dihydrospiro[benzo[1,2-*b*:5,4-*b'*]difuran-3,3'-indol]-2'(*1'H*)-one, the title compound was obtained (71%) as a white solid: mp 173-176 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.50-6.90 (m, 5H), 6.73 (d, 1H), 6.38 (s, 1H), 6.32 (s, 1H), 5.04 (ABq, 2H), 4.75 (ABq, 2H), 4.55-4.36 (m, 2H), 2.88 (t, 2H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 177.2, 161.7, 161.0, 153.5, 142.0, 140.3, 139.7, 139.2, 132.6, 129.1, 124.1, 123.8, 121.2, 121.0, 120.3, 119.1, 117.7, 114.6, 114.5, 110.4, 109.6, 93.0, 80.0, 72.5, 57.3, 36.8, 28.7; MS (ES+) *m/z* 428.2 (M + 1).

EXAMPLE 10.73

Synthesis of 1'-[[5-(trifluoromethyl)-2-thienyl]methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one

To a solution of 1'-[[3-hydroxy-5-(trifluoromethyl)-2-thienyl]methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one (0.75 g, 1.62 mmol) in anhydrous dichloromethane (12.0 mL) was added triethylamine (0.49 g, 0.70 mL, 4.85 mmol) and trifluoromethanesulfonic anhydride (0.91 g, 0.50 mL, 3.24 mmol) at 0 °C under nitrogen. The reaction mixture was stirred for 30 min and quenched with saturated ammonium chloride (15.0 mL). After the aqueous layer was separated, the organic layer was washed with 10% HCl (10.0 mL), brine (10.0 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography to provide brown gummy material as the triflate. A mixture of this triflate (15.3 mmol), tetrakis(triphenylphosphine)palladium(0) (0.19 g, 0.17 mmol), triethylamine (1.66 g, 2.30 mL, 16.5 mmol), and formic acid (0.76 mg, 0.60 mL, 16.5 mmol) in anhydrous

dioxane (24 mL) was heated at reflux for 16 h. After the reaction mixture was cooled down to ambient temperature, the solvent was removed under reduced pressure. The black residue was diluted with ethyl acetate (50.0 mL), washed with 10% HCl (20.0 mL), saturated ammonium chloride (20.0 mL), brine (20.0 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography eluting with ethyl acetate:hexane (35%) to afford the title compound (0.65 g, 89%) as a colorless solid: mp 127-130 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.58-7.56 (m, 1H), 7.32-7.27 (m, 2H), 7.22 (s, 1H), 7.18 (d, 1H), 7.16 (s, 1H), 7.09 (dt, 1H), 6.68 (s, 1H), 6.10 (s, 1H), 5.89 (d, 2H), 5.17 (ABq, 2H), 4.72 (ABq, 2H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 177.0, 155.9, 148.9, 144.7, 142.2, 141.8, 132.1, 130.6, 130.5, 129.3, 128.7, 128.0, 124.3, 123.9, 120.0, 109.8, 103.3, 102.0, 93.9, 80.2, 57.8, 38.7; MS (ES+) *m/z* 446.1 (M + 1).

EXAMPLE 10.74

Synthesis of 1'-{[3-methoxy-5-(trifluoromethyl)-2-thienyl]methyl}spiro[furo[2,3-
f][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

A mixture of 1'-{[3-hydroxy-5-(trifluoromethyl)-2-thienyl]methyl}spiro[furo[2,3-
f][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one (0.18 g, 0.39 mmol), NaOH (0.08 g, 1.96 mmol) and iodomethane (0.17 g, 1.18 mmol) in anhydrous *N,N*-dimethylformamide (2.00 mL) was stirred at ambient temperature for 16 h. The reaction was quenched by addition of saturated ammonium chloride (10.0 mL) and extracted with ethyl acetate (3 x 50.0 mL). The combined organic layers was washed with water (3 x 20.0 mL), brine (20.0 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The colorless solid was triturated with ether to give the title compound (0.15 g, 81%): mp 178-180 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.71 (s, 1H), 7.30 (dt, 1H), 7.15 (d, 1H), 7.07-7.02 (m, 2H), 6.68 (s, 1H), 6.08 (s, 1H), 5.89 (d, 2H), 4.95 (ABq, 2H), 4.70 (ABq, 2H), 3.90 (s, 3H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 177.0, 155.8, 154.9, 148.9, 142.2, 141.8, 132.1, 129.4, 125.7, 124.3, 123.8, 120.4, 120.3, 120.0, 119.5, 109.4, 103.2, 102.0, 93.9, 80.1, 59.9, 57.9, 34.9; MS (ES+) *m/z* 476.3 (M + 1).

EXAMPLE 10.75

Synthesis of 4'-methyl-1'-{[5-(trifluoromethyl)-2-furyl]methyl}spiro[furo[2,3-
f][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

A mixture of 4'-bromo-1'-{[(5-(trifluoromethyl)furan-2-yl)methyl]-6*H*-

spiro[benzofuro[6,5-*d*][1,3]dioxole-7,3'-indolin]-2'-one (0.51 g, 1.00 mmol), lithium chloride (0.09 mg, 2.00 mmol), Pd₂(dba)₃ (0.09 mg, 10 mole%) was flushed with nitrogen. To the above mixture was added anhydrous 1-methyl-2-pyrrolidinone (5.00 mL) and tetramethyltin (0.27 mg, 0.20 mL, 1.50 mmol). The reaction mixture was heated at 60 °C for 16 h and quenched with saturated ammonium chloride (10.0 mL). The reaction mixture was extracted with ethyl acetate (3 x 10.0 mL). The combined organic layers was dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography eluting with ethyl acetate:hexane (20%) to afford the title compound (0.07 g, 16%) as a colorless solid: mp 117-119 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.18 (t, 1H), 6.82 (t, 2H), 6.72 (d, 1H), 6.47 (s, 1H), 6.37 (d, 1H), 6.09 (s, 1H), 5.86 (d, 2H), 4.95 (ABq, 2H), 4.83 (ABq, 2H), 2.03 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 177.6, 156.2, 152.0, 149.1, 142.3, 141.3, 135.6, 129.4, 128.9, 126.0, 120.6, 117.2, 112.7, 112.6, 109.2, 106.5, 102.9, 101.6, 93.3, 78.4, 58.3, 37.0, 17.1; MS (ES+) *m/z* 444.1 (M + 1).

EXAMPLE 10.76

Synthesis of 5'-methyl-1'-{[5-(trifluoromethyl)-2-furyl]methyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure described in EXAMPLE 10.47, and making non-critical variations using 5'-methylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 4'-bromospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one, the title compound was obtained (77%): mp 96-98 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.09 (d, 1H), 7.00 (s, 1H), 6.87 (d, 1H), 6.74 (d, 1H), 6.52 (s, 1H), 6.38 (d, 1H), 6.11 (s, 1H), 5.88 (d, 2H), 4.96 (ABq, 2H), 4.80 (ABq, 2H), 2.29 (s, 3H); MS (ES+) *m/z* 444.2 (M + 1).

EXAMPLE 10.77

Synthesis of 1'-{[5-[4-(trifluoromethyl)phenyl]-1,2,4-oxadiazol-3-yl]methyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure described in EXAMPLE 10.47, and making non-critical variations using spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 4'-bromospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one, and 3-chloromethyl-5-[4-(trifluoromethyl)phenyl]-1,2,4-oxadiazole to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound was obtained (44%): ¹H NMR (300 MHz,

CDCl₃) δ 8.22 (d, 2H), 7.76 (d, 2H), 7.30-7.18 (m, 2H), 7.06 (t, 1H), 6.91 (d, 1H), 6.51 (s, 1H), 6.40 (s, 1H), 5.88 (s, 2H), 5.17 (ABq, 2H), 4.86 (ABq, 2H); MS (ES+) m/z 508.1 (M + 1).

EXAMPLE 10.78

5 Synthesis of 1'-(2-thienylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one

Following the procedure described in EXAMPLE 10.62, and making non-critical variations using 2-thiophenemethanol to replace (5-chloro-2-furyl)methanol, the title compound was obtained (37%) as a colorless solid: ¹H NMR (300 MHz, CDCl₃) δ 7.26-7.20 (m, 2H), 7.18-7.13 (m, 1H), 7.10-6.98 (m, 2H), 6.97-6.90 (m, 2H), 6.50 (s, 1H), 10 6.12 (s, 1H), 5.85 (d, 2H), 5.10 (ABq, 2H), 4.79 (ABq, 2H); MS (ES+) m/z 378.19 (M + 1).

EXAMPLE 10.79

15 Synthesis of 5-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)methyl]thiophene-2-carbonitrile

A mixture of 1'-[(5-bromo-2-thienyl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one (0.23 g, 0.49 mmol), zinc cyanide (0.07 g, 0.59 mmol), tris(dibenzylideneacetone)dipalladium(0) (0.10 g, 0.11 mmol), 1,1'-bis(diphenylphosphino)ferrocene (0.06 g, 0.11 mmol), *N,N*-dimethylformamide (6.00 mL) and a catalytic amount of water (2 drops) was heated at 120 °C for 24 hours. After cooling down to ambient temperature, the organic solvent was evaporated *in vacuo*. The residue was extracted with ethyl acetate (5 x 15.0 mL) and the combined organic solution was passed through a bed of celite. The filtrate was successively washed with saturated aqueous ammonium chloride (25.0 mL), water (2 x 35.0 mL) and brine (40.0 mL). The organic layer was dried over sodium sulfate and filtered. The filtrate was 25 concentrated *in vacuo* to dryness. The residue was subjected to column chromatography eluted with 20-35% ethyl acetate in hexanes to afford solid which was further purified by preparative thin layer chromatography, eluted with 20% ethyl acetate in hexanes to afford the title compound (0.09 g, 44%): ¹H NMR (300 MHz, CDCl₃) δ 30 7.50 (d, 1H), 7.32-7.16 (m, 2H), 7.12-7.04 (m, 2H), 6.86 (d, 1H), 6.51 (s, 1H), 6.08 (s, 1H), 5.87 (d, 2H), 5.10 (ABq, 2H), 4.78 (ABq, 2H); MS (ES+) m/z 403.0 (M + 1).

EXAMPLE 10.80

Synthesis of 5-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]-2-furonitrile

Following the procedure described in EXAMPLE 10.79, and making non-critical variations using 1'-[(5-bromo-2-furyl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 1'-[(5-bromo-2-thienyl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one, the title compound was obtained (44%) as a colorless solid: mp 167-169 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.34-7.27 (m, 1H), 7.21-7.17 (m, 1H), 7.12-7.08 (m, 1H), 7.07-7.03 (m, 1H), 6.95 (d, 1H), 6.51 (s, 1H), 6.44 (d, 1H), 6.08 (s, 1H), 5.86 (q, 2H), 4.96 (ABq, 2H), 4.78 (ABq, 2H); MS (ES+) *m/z* 387.2 (M + 1).

EXAMPLE 10.81

Synthesis of 1'-[[5-(methylsulfonyl)-2-furyl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

A mixture of 1'-[(5-bromo-2-furyl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one (0.70 g, 1.59 mmol), sodium methanesulfinate (85%, 0.23 g, 1.91 mmol), copper (I) iodide (0.04 g, 0.22 mmol), L-proline (0.04 g, 0.35 mmol) and dimethyl sulfoxide (4.00 mL) was heated at 100 °C. After 3 days, the reaction mixture was cooled down to ambient temperature, quenched with water (50.0 mL) and extracted with ethyl acetate (3 x 40.0 mL). The combined organic layers was washed with brine (2 x 50.0 mL), dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography eluting with ethyl acetate:hexane (30-50%) to afford the title compound (0.50 g, 71%): mp 177-179 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.29 (t, 1H), 7.19 (d, 1H), 7.12-7.04 (m, 2H), 6.94 (d, 1H), 6.50 (s, 1H), 6.42 (d, 1H), 6.11 (s, 1H), 5.86 (s, 2H), 5.00 (ABq, 2H), 4.79 (ABq, 2H), 3.11 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 177.3, 155.9, 154.5, 149.1, 149.1, 142.4, 141.1, 131.9, 129.1, 124.2, 124.1, 119.0, 118.4, 109.9, 108.7, 102.9, 101.6, 93.7, 80.3, 58.2, 43.4, 37.2; MS (ES+) *m/z* 440.0 (M + 1).

EXAMPLE 10.82

Synthesis of 1'-[(6-oxo-1,6-dihydropyridin-3-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

To a mixture of 1'-[(6-methoxypyridin-3-yl)methyl]spiro[furo[2,3-

f[1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one (0.23 g, 0.57 mmol), sodium iodide (0.28 g, 1.87 mmol), water (2 drops) in anhydrous acetonitrile (5.00 mL) was added chlorotrimethylsilane (0.19 g, 1.78 mmol) at 0 °C. The reaction mixture was stirred at ambient temperature for 16 h and quenched with sodium bisulfite (0.20 g). The
 5 reaction mixture was diluted with ethyl acetate (100 mL) and washed with brine (2 x 25.0 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was triturated with ether (2 x 10.0 mL) to give the title compound (0.16 g, 72%) as a light yellow solid: mp 247-250 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 11.50 (br, 1H), 7.50 (bd, 1H), 7.36-7.24 (m, 2H), 7.17-
 10 7.12 (m, 2H), 7.01 (dt, 1H), 6.67 (s, 1H), 6.28 (d, 1H), 6.09 (s, 1H), 5.91- 5.88 (m, 2H), 4.78 (d, 1H), 4.67- 4.62 (m, 3H); MS (ES+) *m/z* 389.15 (M + 1).

EXAMPLE 10.83

Synthesis of 1'-[(1-methyl-6-oxo-1, 6-dihydropyridin-3-yl)methyl]spiro[furo[2,3-
f[1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

15 Following the procedure described in PREPARATION 1A, and making non-critical variations using 1'-[(6-oxo-1,6-dihydropyridin-3-yl)methyl]spiro[furo[2,3-
f[1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 4-bromoindole, and methyl iodide to replace 1-bromopentane, the title compound was obtained (78%): mp 115-118 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.39-7.23 (m, 3H), 7.18 (d, 1H), 7.06 (t, 1H), 6.87 (d, 1H),
 20 6.57-6.48 (m, 2H), 6.02 (s, 1H), 5.87-5.83 (m, 2H), 4.90 (d, 1H), 4.75-4.52 (m, 3H), 3.51 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 177.8, 162.5, 155.9, 149.1, 142.4, 141.6, 139.7, 137.6, 132.1, 129.1, 124.4, 123.9, 121.3, 119.1, 114.0, 108.6, 102.8, 101.6, 93.7, 80.3, 58.2, 40.8, 38.0; MS (ES+) *m/z* 403.3 (M + 1).

EXAMPLE 10.84

25 Synthesis of 5-bromo-1'-[(5-chloro-2-thienyl)methyl]spiro[1-benzofuran-3,3'-indol]-
 2'(1'*H*)-one

Following the procedure described in EXAMPLE 10, and making non-critical variations using 5-bromospiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one to replace spiro[furo[2,3-*f*[1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one, and 2-chloro-5-
 30 (chloromethyl)thiophene to replace 4-fluorobenzyl bromide, the title compound was obtained (95%) as a white solid: mp 140-142 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.33-7.26 (m, 2H), 7.16-7.02 (m, 2H), 6.94 (d, 1H), 6.97-6.75 (m, 4H), 5.07-4.91 (m, 3H), 4.68 (d, 1H); MS (ES+) *m/z* 446.7 (M + 1), 448.7 (M + 1).

EXAMPLE 10.85

Synthesis of 1'-[(5-chloro-1,3,4-thiadiazol-2-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one

To a solution of spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one (0.56 g, 1.99 mmol) and (5-chloro-1,3,4-thiadiazol-2-yl)methanol (0.30 g, 1.99 mmol) in anhydrous tetrahydrofuran (12.0 mL) was added tributylphosphine (0.60 g, 2.99 mmol) at 0 °C. The reaction mixture was stirred for 15 min followed by the addition of *N,N,N',N'*-tetramethylazodicarboxamide (0.51 g, 2.99 mmol). The reaction mixture was stirred at ambient temperature overnight, quenched with aqueous ammonium chloride (10.0 mL) and diluted with ethyl acetate (350 mL). The organic layer was washed with aqueous saturated sodium chloride (2 x 25.0 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography (ethyl acetate/hexane, 1/2) to give the title compound (0.20 g, 24%) as a yellowish solid: mp 194-197 °C; ¹H NMR (300 MHz, DMSO-*d*₆) δ 7.30 (dt, 1H), 7.20-7.12 (m, 2H), 7.05 (dt, 1H), 6.67 (s, 1H), 6.28 (s, 1H), 5.90 (s, 2H), 5.43 (d, 1H), 5.34 (d, 1H), 4.78 (d, 1H), 4.67 (d, 1H); ¹³C NMR (75 MHz, DMSO-*d*₆) δ 177.2, 168.3, 155.8, 155.4, 148.9, 142.2, 141.9, 132.2, 129.4, 124.2, 124.0, 120.1, 109.8, 103.7, 101.9, 93.8, 80.1, 67.5, 57.9, 25.6; MS (ES+) *m/z* 414.2 (M + 1), 416.2 (M + 1).

EXAMPLE 10.86

Synthesis of 1'-[(1-pyridin-2-yl)piperidin-4-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one

A mixture of 1'-(piperidin-4-ylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one hydrobromide (0.20 g, 0.44 mmol), 2-bromopyridine (0.16 mL, 0.65 mmol), tetrabutyl ammonium iodide (0.05 g) and DBU (0.16 mL, 1.09 mmol) in DMF (5.00 mL) was heated at 120 °C for 15 hrs. After cooling down to ambient temperature, water (30.0 mL) was added. The above mixture was extracted twice with ethyl acetate (50.0 mL), the combined organic phase was dried over Na₂SO₄ and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to flash chromatography eluting with 30% ethyl acetate in hexane to give a white solid (0.05 g, 27%): mp 95-97 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.17 (d, 1H), 7.47 (td, 1H), 7.31 (t, 1H), 7.18 (d, 1H), 7.06 (t, 1H), 6.92 (d, 1H), 6.66 (d, 1H), 6.59 (dd, 1H), 6.52 (s, 1H), 6.12 (s, 1H), 5.91-5.84 (m, 2H), 4.91 (d, 1H), 4.66 (d, 1H), 4.42-4.27 (m, 2H), 3.82-3.53 (m, 2H), 2.85 (t, 2H), 2.22-2.05 (m, 1H), 1.85-1.70 (m, 2H), 1.53-1.35 (m,

2H); ^{13}C NMR(75 MHz, CDCl_3) δ 177.9, 158.8, 156.1, 149.0, 147.4, 142.8, 142.5, 138.0, 132.4, 129.1, 124.2, 123.5, 119.5, 112.9, 108.8, 107.7, 103.1, 101.7, 93.8, 80.7, 58.3, 46.0, 45.5, 45.4, 35.2, 29.8, 29.7; MS (ES+) m/z 456 ($M + 1$).

EXAMPLE 10.87

5 Synthesis of 1'-[(1-phenyl-2-ylpiperidin-4-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

A mixture of 1'-(piperidin-4-ylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one hydrobromide (0.20 g, 0.44 mmol), 2-bromobenzene(0.07 mL, 0.65 mmol), $\text{Pd}_2(\text{dba})_3$ (0.03 g, 0.03 mmol), BINAP (0.06 g, 0.10 mmol) and NaOBu^t (0.13 g, 1.30 mmol) in toluene was heated at 100 °C for 15 hrs under nitrogen. After cooling down to ambient temperature, water (30.0 mL) was added. The above mixture was extracted twice with ethyl acetate (50.0 mL), the combined organic phase was dried over Na_2SO_4 and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to flash chromatography eluting 30 % ethyl acetate in hexane to give a white solid (0.10 g, 48%): mp 76-78 °C; ^1H NMR (300 MHz, CDCl_3) δ 7.37-7.16 (m, 4H), 7.12-6.80 (m, 5H), 6.53 (s, 1H), 6.14 (s, 1H), 5.87 (dd, 2H), 4.92 (d, 1H), 4.66 (d, 1H), 3.87-3.55 (m, 4H), 2.72 (t, 2H), 2.12-1.94 (m, 1H), 1.89-1.73 (m, 2H), 1.71-1.45 (m, 2H); ^{13}C NMR(75 MHz, CDCl_3) δ 177.9, 156.1, 149.0, 142.9, 142.5, 132.4, 129.2, 129.1, 124.2, 123.4, 119.9, 119.5, 116.9, 108.8, 103.1, 101.6, 93.8, 80.8, 60.5, 58.3, 49.8, 46.1, 34.8, 30.1, 30.0; MS (ES+) m/z 455 ($M + 1$).

EXAMPLE 10.88

Synthesis of 1'-(pyridin-2-ylmethyl)-6-(trifluoromethoxy)spiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one hydrochloride

Following the procedure described in EXAMPLE 10.47, and making non-critical variations using 6-(trifluoromethoxy)spiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one to replace 4'-bromospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one, and 2-(bromomethyl)pyridine hydrobromide to replace 2-(bromomethyl)-2-(trifluoromethyl)furan, 1'-(pyridin-2-ylmethyl)-6-(trifluoromethoxy)spiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one was obtained, which was treated with 4.0 M HCl in dioxane to give the title compound (39%): mp 150-152 °C; ^1H NMR (300 MHz, CD_3OD) δ 8.89-8.78 (m, 1 H), 8.62-8.47 (m, 1H), 8.07-7.00 (m, 2H), 7.42-6.70 (m, 7H), 5.52-5.31 (m, 2H), 5.05 (d, 1H), 4.89 (d, 1H); ^{13}C NMR(75 MHz, CD_3OD) δ 179.4, 163.5, 153.1, 152.7, 148.2, 143.8, 142.8, 133.1, 130.6, 129.3, 127.4, 126.8, 125.7, 125.6, 125.4,

114.9, 110.4, 104.9, 82.0, 58.9, 43.0; MS (ES+) m/z 413 ($M + 1$).

EXAMPLE 10.89

Synthesis of 1'-(pyridin-3-ylmethyl)-6-(trifluoromethoxy)spiro[1-benzofuran-3,3'-indol]-2'($1'H$)-one hydrochloride

5 Following the procedure described in EXAMPLE 10.47, and making non-critical variations using 6-(trifluoromethoxy)spiro[1-benzofuran-3,3'-indol]-2'($1'H$)-one to replace 4'-bromospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'($1'H$)-one, and 3-(bromomethyl)pyridine hydrobromide to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, 1'-(pyridin-3-ylmethyl)-6-(trifluoromethoxy)spiro[1-benzofuran-3,3'-indol]-2'($1'H$)-one was obtained, which was treated with 4.0 M HCl in dioxane to give the title compound (70%) as a white solid: mp 151-153 °C; ^1H NMR (300 MHz, CD_3OD) δ 9.07-8.61 (m, 3 H), 8.19-8.04 (m, 1H), 7.42-6.71 (m, 7H), 5.28 (s, 2H), 5.05 (d, 1H), 4.86 (d, 1H); ^{13}C NMR (75 MHz, CD_3OD) δ 179.43, 163.5, 151.8, 147.0, 142.9, 142.4, 142.2, 133.0, 130.6, 129.3, 128.9, 125.5, 125.4, 125.3, 114.9, 110.5, 104.9, 82.0, 58.9, 42.0; MS (ES+) m/z 413 ($M + 1$).

EXAMPLE 10.90

Synthesis of 6-(trifluoromethoxy)-1'-[[5-(trifluoromethyl)-2-furyl]methyl]spiro[1-benzofuran-3,3'-indol]-2'($1'H$)-one

20 Following the procedure described in EXAMPLE 10.47, and making non-critical variations using 6-(trifluoromethoxy)spiro[1-benzofuran-3,3'-indol]-2'($1'H$)-one to replace 4'-bromospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'($1'H$)-one, the title compound was obtained (82%) as a white solid: mp 78-80 °C; ^1H NMR (300 MHz, CDCl_3) δ 7.33 (td, 1H), 7.21-6.98 (m, 3H), 6.86-6.73 (m, 2H), 6.67 (s, 2H), 6.42 (d, 1H), 5.09 (d, 1H), 5.04 (d, 1H), 4.88 (d, 1H), 4.77 (d, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 176.7, 161.7, 151.9, 150.6, 141.5, 131.7, 129.5, 127.5, 124.2, 124.2, 124.0, 114.1, 112.8, 112.8, 109.6, 109.2, 104.3, 80.7, 57.6, 37.1; MS (ES+) m/z 470 ($M + 1$).

EXAMPLE 10.91

Synthesis of 1'-(4-methoxybenzyl)-6-(trifluoromethoxy)spiro[1-benzofuran-3,3'-indol]-2'($1'H$)-one

30 Following the procedure described in EXAMPLE 10.47, and making non-critical variations using 6-(trifluoromethoxy)spiro[1-benzofuran-3,3'-indol]-2'($1'H$)-one to replace 4'-bromospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'($1'H$)-one, and 4-

methoxybenzyl chloride to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound was obtained (91%) as a white solid: mp 82-84 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.32-6.80 (m, 9H), 6.68 (s, 2H), 5.06 (d, 1H), 5.03 (d, 1H), 4.80 (d, 1H), 4.77 (d, 1H), 3.80 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 171.1, 161.8, 159.4, 150.5, 142.3, 132.0, 129.2, 128.9, 127.7, 124.1, 124.0, 123.7, 122.2, 118.8, 114.4, 114.1, 109.7, 104.3, 80.9, 57.6, 55.4, 43.9; MS (ES+) *m/z* 442 (*M* + 1).

EXAMPLE 10.92

Synthesis of 1'-(cyclohexylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure described in EXAMPLE 10.47, and making non-critical variations using spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 4'-bromospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one, and bromomethyl cyclohexane to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound was obtained (74%) as a white solid: mp 153-154 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.30 (td, 1H), 7.16 (d, 1H), 7.04 (t, 1H), 6.90 (d, 1H), 6.51 (s, 1H), 6.14 (s, 1H), 5.90-5.84 (m, 2H), 4.91 (d, 1H), 4.65 (d, 1H), 3.72-3.44 (m, 2H), 1.94-1.60 (m, 6H), 1.32-0.99 (m, 5H); ¹³C NMR (75 MHz, CDCl₃) δ 177.8, 156.1, 148.9, 143.0, 142.4, 132.5, 128.9, 124.0, 123.2, 119.7, 109.0, 103.2, 101.6, 93.7, 80.8, 58.3, 46.8, 36.3, 31.1, 31.0, 26.4, 25.9, 25.8; MS (ES+) *m/z* 378 (*M* + 1), 400 (*M* + 23).

EXAMPLE 10.93

Synthesis of 1'-(methylsulfonyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

Following the procedure described in EXAMPLE 10.47, and making non-critical variations using spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one to replace 4'-bromospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one, and methanesulfonyl chloride to replace 2-(bromomethyl)-5-(trifluoromethyl)furan, the title compound was obtained (51%) as a white solid: mp 215-217 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.83 (d, 1H), 7.42-7.31 (m, 1H), 7.25-7.17 (m, 2H), 6.52 (s, 1H), 6.20 (s, 1H), 5.93-5.87 (m, 2H), 4.98 (d, 1H), 4.68 (d, 1H), 3.46 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 176.9, 155.8, 149.5, 142.7, 138.1, 130.5, 129.7, 125.9, 124.3, 118.5, 113.8, 102.9, 101.8, 93.8, 80.6, 58.8, 41.8; MS (ES+) *m/z* 360 (*M* + 1), 382 (*M* + 23).

EXAMPLE 10.94

Synthesis of 1'-(2-piperidin-1-ylethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one hydrochloride

A mixture of 1'-(2-aminoethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one (0.20 g, 0.62 mmol), 1,5-dibromopentane (0.08 mL, 0.62 mmol) and triethyl amine (0.17 mL, 1.23 mmol) in THF (10.0 mL) was refluxed for 15 hrs and concentrated *in vacuo* to dryness. The residue was subjected to flash chromatography eluting with 10% methanol in ethyl acetate to give 1'-(2-piperidin-1-ylethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one, which was treated with 4.0 M HCl in dioxane to give the title compound (28%): mp >240 °C; ¹H NMR (300 MHz, CD₃OD) δ 7.40 (t, 1H), 7.27-7.11 (m, 3H), 6.51 (s, 1H), 6.17 (s, 1H), 5.86 (s, 2H), 4.91 (d, 1H), 4.71 (d, 1H), 4.40-4.13 (m, 2H), 3.95-3.84 (m, 1H), 3.66-3.37 (m, 3H), 3.14-2.96 (m, 2H), 2.06-1.45 (m, 6H); ¹³C NMR (75 MHz, CD₃OD) δ 180.4, 157.5, 150.5, 143.8, 142.5, 133.9, 130.3, 125.3, 125.1, 120.6, 110.2, 103.9, 102.9, 94.2, 81.4, 59.7, 55.4, 54.9, 53.9, 36.4, 24.2, 22.6; MS (ES+) *m/z* 393 (M + 1).

EXAMPLE 10.95

Synthesis of 1'-[2-(pyridin-2-ylamino)ethyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one and 1'-[2-(dipyridin-2-ylamino)ethyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one

and

Following the procedure described in EXAMPLE 10.87, and making non-critical variations using 1'-(2-aminoethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one to replace 1'-(piperidin-4-ylmethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one, and 2-bromopyridine to replace 2-bromobenzene, 1'-(2-(pyridin-2-ylamino)ethyl)-spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one was obtained as the first fraction from the chromatography as a white solid (5%): mp 61-63 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.05 (d, 1H), 7.50-6.97 (m, 5H), 6.57 (dd, 1H), 6.50 (s, 1H), 6.38 (d, 1H), 6.03 (s, 1H), 5.85 (s, 1H), 5.84 (s, 1H), 4.84 (d, 1H), 4.79 (t, 1H), 4.60 (d, 1H), 4.15-3.94 (m, 2H), 3.81-3.64 (m, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 178.4, 158.2, 156.0, 149.0, 148.0, 142.4, 142.38, 137.4, 132.3, 129.1, 124.0, 123.5, 119.5, 113.3, 109.0, 108.3, 103.2, 101.6, 93.7, 80.5, 58.3, 40.1, 39.9; MS (ES+) *m/z* 402 (M + 1). 1'-(2-(dipyridin-2-ylamino)ethyl)-spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(*1'H*)-one was obtained as the second fraction from the chromatography (31%): mp 165-167 °C; ¹H

NMR (300 MHz, CDCl₃) δ 8.31 (dd, 2H), 7.48 (d, 2H), 7.23 (t, 1H), 7.09-6.83 (m, 7H), 6.47 (s, 1H), 5.95 (s, 1H), 5.88-5.81 (m, 2H), 4.73 (d, 1H), 4.67-4.49 (m, 2H), 4.46 (d, 1H), 4.20 (t, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 177.6, 157.0, 156.0, 148.8, 148.4, 143.1, 142.3, 137.4, 132.3, 128.9, 123.6, 123.1, 119.6, 117.5, 114.5, 109.3, 103.4, 101.6, 93.6, 80.7, 58.2, 45.9, 39.5; MS (ES+) *m/z* 479 (M + 1).

EXAMPLE 10.96

Synthesis of *tert*-butyl 4-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]piperidine-1-carboxylate

Following the procedure as described in EXAMPLE 10, and making non-critical variations using *tert*-butyl 4-(2-[(4-methylphenyl)sulfonyl]oxy)ethyl]piperidine-1-carboxylate to replace 4-fluorobenzyl bromide, the title compound was obtained in 95% yield: mp 173-175 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.31 (t, 1H), 7.17 (d, 1H), 7.06 (t, 1H), 6.88 (d, 1H), 6.51 (s, 1H), 6.10 (s, 1H), 5.90-5.84 (m, 2H), 4.90 (d, 1H), 4.65 (d, 1H), 4.0-3.64 (m, 4H), 2.75-2.58 (m, 2H), 1.85-1.09 (m, 16H); ¹³C NMR (75 MHz, CDCl₃) δ 177.5, 156.0, 155.0, 149.0, 142.4, 142.2, 132.6, 129.0, 124.2, 123.4, 119.5, 108.6, 103.0, 101.6, 93.8, 80.5, 79.5, 58.3, 38.0, 34.0, 33.9, 32.1, 31.9, 28.6; MS (ES+) *m/z* 515 (M + 23), 393 (M - 100).

EXAMPLE 10.97

Synthesis of 1'-(2-piperidin-4-ylethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one hydrochloride

To a solution of *tert*-butyl 4-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]piperidine-1-carboxylate (0.94 g, 1.91 mmol) in dioxane (5.00 mL) was added 4.0 M HCl in dioxane (2.00 mL, 8.00 mmol). The mixture was stirred at ambient temperature for 30 min followed by the addition of anhydrous ether (40.0 mL). The precipitated white solid was filtered, washed with ether and dried to give the title compound (0.75 g, 91%): ¹H NMR (300 MHz, CD₃OD) δ 7.37 (t, 1H), 7.20-7.07 (m, 3H), 6.52 (s, 1H), 6.10 (s, 1H), 5.86 (s, 2H), 4.83 (d, 1H), 4.67 (d, 1H), 3.97-3.75 (m, 2H), 3.45-3.33 (m, 2H), 3.01-2.85 (m, 2H), 2.15-2.01 (m, 2H), 1.82-1.37 (m, 5H); ¹³C NMR (75 MHz, CD₃OD) δ 179.8, 157.6, 150.4, 143.7, 143.4, 133.6, 130.3, 124.9, 124.8, 120.8, 110.3, 103.7, 102.9, 94.3, 81.4, 59.8, 45.2, 38.5, 34.4, 32.6, 29.8, 29.7; MS (ES+) *m/z* 393 (M + 1).

EXAMPLE 10.98

Synthesis of 1'-[2-(1-cyclopentylpiperidin-4-yl)ethyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one hydrochloride

To a solution of cyclopentanone (0.04 mL, 0.45 mmol) and triethyl amine (0.12 mL, 0.84 mmol) in dichloroethane (5.00 mL) was added 1'-(2-piperidin-4-ylethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one hydrochloride (0.12 g, 0.28 mmol) and sodium triacetoxyborohydride (0.10 g, 0.45 mmol). The reaction mixture was stirred for 16 hrs and concentrated *in vacuo* to dryness. The residue was subjected to flash chromatography eluting with ethyl acetate /methanol/ammonium hydroxide (15/1/0.1) to give 1'-[2-(1-cyclopentylpiperidin-4-yl)ethyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one as a white solid, which was treated with 4.0 M HCl in dioxane to give the title compound (0.05 g, 32% yield): mp 153-155 °C; ¹H NMR (300 MHz, CD₃OD) δ 7.37 (td, 1H), 7.21-7.08 (m, 3H), 6.53 (s, 1H), 6.11 (s, 1H), 5.88 (s, 1H), 5.87 (s, 1H), 4.83 (d, 1H), 4.69 (d, 1H), 3.98-3.75 (m, 2H), 3.68-3.38 (m, 3H), 3.01-2.83 (m, 2H), 2.25-2.08 (m, 4H), 1.92-1.37 (m, 11H); ¹³C NMR (75 MHz, CD₃OD) δ 179.8, 157.6, 150.4, 143.8, 143.4, 133.6, 130.3, 124.9, 124.8, 120.8, 110.3, 103.7, 103.0, 94.3, 81.4, 69.1, 59.8, 53.2, 38.6, 34.3, 32.5, 30.6, 30.5, 29.4, 24.7; MS (ES+) *m/z* 461 (M + 1).

EXAMPLE 10.99

Synthesis of 1'-[2-(1-isopropylpiperidin-4-yl)ethyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one hydrochloride

Following the procedure as described in EXAMPLE 10.98, and making non-critical variations using acetone to replace cyclopentanone, the title compound was obtained (42%) as a white solid: mp 155-156 °C; ¹H NMR (300 MHz, CD₃OD) δ 7.37 (t, 1H), 7.21-7.08 (m, 3H), 6.53 (s, 1H), 6.11 (s, 1H), 5.87 (s, 2H), 4.84 (d, 1H), 4.69 (d, 1H), 3.98-3.75 (m, 2H), 3.58-3.38 (m, 3H), 3.05-2.85 (m, 2H), 2.23-2.09 (m, 2H), 1.82-1.44 (m, 5H), 1.35 (d, 6H); ¹³C NMR (75 MHz, CD₃OD) δ 179.8, 157.6, 150.5, 143.8, 143.4, 133.6, 130.3, 125.0, 124.8, 120.8, 110.3, 103.7, 103.0, 94.3, 81.4, 59.8, 59.6, 38.6, 34.2, 32.7, 30.6, 30.5, 24.2, 16.9, 15.4; MS (ES+) *m/z* 435 (M + 1).

EXAMPLE 10.100

Synthesis of 1'-[2-(1-cyclobutylpiperidin-4-yl)ethyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one hydrochloride

Following the procedure as described in EXAMPLE 10.98, and making non-

critical variations using cyclobutanone to replace cyclopentanone, the title compound was obtained (81%) as a white solid: mp 158-160 °C; ¹H NMR (300 MHz, CD₃OD) δ 7.37 (t, 1H), 7.21-7.05 (m, 3H), 6.52 (s, 1H), 6.10 (s, 1H), 5.86 (s, 2H), 4.83 (d, 1H), 4.67 (d, 1H), 3.98-3.39 (m, 5H), 2.85-2.59 (m, 2H), 2.43-1.42 (m, 13H); ¹³C NMR (75 MHz, CD₃OD) δ 179.8, 157.6, 150.4, 143.7, 143.4, 133.6, 130.3, 124.9, 124.8, 120.8, 110.4, 103.8, 103.0, 94.2, 81.5, 60.5, 59.8, 50.8, 38.6, 34.4, 32.5, 30.1, 26.8, 14.4; MS (ES+) *m/z* 447 (M + 1).

EXAMPLE 10.101

Synthesis of 1'-{2-[1-(tetrahydro-2*H*-pyran-4-yl)piperidin-4-yl]ethyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one hydrochloride

Following the procedure as described in EXAMPLE 10.98, and making non-critical variations using tetrahydro-4*H*-pyran-4-one to replace cyclopentanone, the title compound was obtained (45%) as a white solid: mp 168-170 °C; ¹H NMR (300 MHz, CD₃OD) δ 7.37 (t, 1H), 7.21-7.06 (m, 3H), 6.52 (s, 1H), 6.11 (s, 1H), 5.86 (s, 2H), 4.83 (d, 1H), 4.67 (d, 1H), 4.12-3.31 (m, 9H), 3.05-2.85 (m, 2H), 2.25-1.45 (m, 11H); ¹³C NMR (75 MHz, CD₃OD) δ 179.8, 157.6, 150.4, 143.7, 143.4, 133.6, 130.3, 125.0, 124.8, 120.8, 110.3, 103.8, 102.9, 94.3, 81.4, 67.2, 64.1, 59.8, 50.7, 38.6, 34.2, 32.7, 30.6, 30.5, 28.7; MS (ES+) *m/z* 477 (M + 1).

EXAMPLE 11

Synthesis of 4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzoic acid

Following the procedure described in EXAMPLE 6, and making non-critical variations using methyl 4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzoate to replace methyl 2-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzoate, the title compound was obtained (100%): ¹H NMR (300 MHz, CDCl₃) δ 12.96 (s, 1H), 7.90 (d, 2H), 7.43 (d, 2H), 7.22 (t, 1H), 7.17 (d, 1H), 7.00 (t, 1H), 6.94 (d, 1H), 6.68 (s, 1H), 6.21 (s, 1H), 5.90 (s, 2H), 4.98 (s, 2H), 4.76 (ABq, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 177.4, 167.5, 156.0, 148.9, 142.6, 142.3, 141.8, 132.1, 130.5, 130.3, 129.3, 127.7, 124.2, 123.7, 120.1, 109.9, 103.5, 101.9, 93.8, 80.4, 58.0, 43.4.

EXAMPLE 12

Synthesis of *N*-(3-fluorophenyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide

A. Preparation of stock solution of 4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzoyl chloride

To a stirred slurry of 4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzoic acid (2.08 g, 5.00 mmol) in dry chloroform (50.0 mL) was added oxalyl chloride (0.95 g, 7.50 mmol) at ambient temperature followed by 1 drop of DMF. The mixture was stirred at ambient temperature for 2 h and evaporated to dryness *in vacuo*. The residue was dissolved in dry dichloromethane (60.0 mL) to form an acid chloride stock solution for use.

B. Synthesis of *N*-(3-fluorophenyl)-4-[(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)methyl]benzamide

To a solution of 3-fluorophenylamine (0.02 mL, 0.24 mmol) in dry dichloromethane (2.00 mL) and triethylamine (0.05 mL, 0.32 mmol) was added the acid chloride stock solution (2.0 mL, 0.081 M in dichloromethane) obtained above at ambient temperature. The mixture was stirred for 2 h, washed with 15% HCl solution and water. The organic layer was separated, dried over Na₂SO₄ and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was dissolved in ethyl acetate, and the product was precipitated by the addition of hexane. The white solid was filtered and collected to yield the title compound (0.06 g) in 70% yield: ¹H NMR (300 MHz, CDCl₃) δ 8.30 (s, 1H), 7.83 (d, 2H), 7.58 (ddd, 1H), 7.38 (d, 2H), 7.27-7.23 (m, 2H), 7.21-7.16 (m, 2H), 7.04 (dt, 1H), 6.85-6.78 (m, 1H), 6.74 (d, 1H), 6.46 (s, 1H), 6.10 (s, 1H), 5.77 (d, 1H), 5.68 (d, 1H), 4.97 (ABq, 2H), 4.76 (ABq, 2H); MS (ES⁺), *m/z* 509.1 (M + 1).

EXAMPLE 12.1

The compounds listed in the following table were prepared using the similar procedure as described in EXAMPLE 12. As previously noted, the compound numbers listed below do not correspond to the compound numbers provided in the general Reaction Schemes above.

Compound Number	Name	MS (<i>m/z</i> , M + 1)
500	<i>N</i> -butyl-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	471.2

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
501	<i>N</i> -(3-fluorobenzyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	523.1
502	1'-[4-(piperidin-1-ylcarbonyl)benzyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	483.2
503	<i>N,N</i> -diisopropyl-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	499.1
504	<i>N</i> -(4-chlorobenzyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	540.1
505	<i>N</i> -(3-chlorophenyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	526.1
506	<i>N</i> -(2-fluorophenyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	509.2
507	<i>N</i> -(2-ethylphenyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	519.2
508	<i>N</i> -(4-ethylphenyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	519.2
509	<i>N</i> -(4-methylphenyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	505.2
510	<i>N</i> -(3,5-dimethylphenyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	519.2
511	<i>N</i> -(2,3-dimethylphenyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	519.2
512	4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -pentylbenzamide	485.1

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
513	4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -propylbenzamide	457.1
514	<i>N</i> -isopropyl-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	457.1
515	<i>N</i> -isobutyl-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	471.1
516	<i>N</i> -hexyl-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	499.2
517	<i>N</i> -cyclohexyl-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	497.2
518	<i>N</i> -cyclopentyl-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	483.2
519	<i>N</i> -heptyl-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	513.2
520	<i>N</i> -(2-methoxybenzyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	535.2
521	<i>N</i> -(2,6-dimethylphenyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	519.2
522	<i>N</i> -(2-methoxyphenyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	521.2
523	<i>N</i> -cyclopropyl-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	455.1
524	<i>N</i> -(3-methoxypropyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	487.2
525	4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -phenylbenzamide	491.2

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
526	<i>N</i> -(2,4-dimethylphenyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	519.2
527	4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -(tetrahydrofuran-2-ylmethyl)benzamide	499.2
528	<i>N,N</i> -dibenzyl-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	595.2
529	<i>N</i> -[2-(diethylamino)ethyl]-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	514.2
530	<i>N</i> -methyl-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	429.2
531	4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -[3-(trifluoromethyl)phenyl]benzamide	559.1
532	<i>N</i> -ethyl-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	443.1
533	<i>N</i> -(3-ethoxypropyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	501.2
534	<i>N</i> -(4-methoxybenzyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	535.2
535	<i>N</i> -(3,5-dichlorophenyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	560.2
536	4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -pyridin-3-ylbenzamide	492.2
537	<i>N</i> -(4-cyanophenyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	516.2

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
538	<i>N</i> -(4-methylpentyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	499.2
539	4-[(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -(2,2,2-trifluoroethyl)benzamide	497.2
540	4-[(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -(pyridin-4-ylmethyl)benzamide	506.1
541	<i>N</i> -[2-(3-chlorophenyl)ethyl]-4-[(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	554
542	<i>N</i> -(2-furylmethyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	495.1
543	<i>N</i> -(3-fluoro-2-methylphenyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	523.1
544	<i>N</i> -hexyl- <i>N</i> -methyl-4-[(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	513.1
545	<i>N</i> -(3-isopropoxypropyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	515.2
546	<i>N</i> -(2-ethoxyethyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	487.2
547	<i>N</i> -(cyclopropylmethyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	469.1
548	<i>N</i> -(4-methoxyphenyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i> [1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	521.1

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
549	<i>N</i> -cyclobutyl-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	469.1
550	<i>N</i> -(2,2-diphenylethyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	595.2
551	<i>N</i> -[2-(4-fluorophenyl)ethyl]-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	537.2
552	<i>N</i> -(cyclohexylmethyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	511.2
553	<i>N</i> -(2-fluoro-4-methylphenyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	523.2
554	<i>N</i> -[2-(4-methylphenyl)ethyl]-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	533.2
555	<i>N</i> -(2-ethylbutyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	499.2
556	<i>N</i> -benzyl-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	505.1
557	<i>N</i> -(2-methoxyethyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	473.1
558	1'-[4-(morpholin-4-ylcarbonyl)benzyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	485.1
559	<i>N</i> -(1-benzylpiperidin-4-yl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	588.2
560	<i>N</i> -[2-(4-methoxyphenyl)ethyl]-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	549.2

Compound Number	Name	MS (m/z, M + 1)
561	4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -[2-(trifluoromethyl)phenyl]benzamide	559.1
562	<i>N</i> -[4-chloro-2-(trifluoromethyl)phenyl]-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	594.1
563	<i>N</i> -[4-fluoro-2-(trifluoromethyl)phenyl]-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	577.1
564	<i>N</i> -(2-cyanoethyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	468.1
565	<i>N</i> -[(1 <i>S</i>)-1-cyclohexylethyl]-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	525.2
566	<i>N</i> -[(1 <i>R</i>)-1-cyclohexylethyl]-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	525.2
567	<i>N</i> -(2,4-difluorophenyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	527.1
568	<i>N</i> -(2,3-dihydro-1 <i>H</i> -inden-1-yl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	531.2
569	4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -(2-thienylmethyl)benzamide	511.2
570	<i>N</i> -[(1-ethylpyrrolidin-2-yl)methyl]-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	526.2
571	4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -(4-propylphenyl)benzamide	533.2
572	<i>N</i> -(2,5-difluorobenzyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	541.1

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
573	<i>N</i> -(2,3-dihydro-1 <i>H</i> -inden-5-yl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	531.2
574	<i>N</i> -(2,5-difluorophenyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	527.1
575	4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -[4-(trifluoromethyl)benzyl]benzamide	573.1
576	4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -[2-(2-thienyl)ethyl]benzamide	525.1
577	4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -(pyridin-3-ylmethyl)benzamide	506.2
578	4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -[2-(trifluoromethyl)benzyl]benzamide	573.1
579	<i>N</i> -[2-(4-chlorophenyl)ethyl]-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	554
580	4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -(2-pyrrolidin-1-ylethyl)benzamide	512.2
581	<i>N</i> -(3-methylpyridin-2-yl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	506.1
582	<i>N</i> -[3-(dimethylamino)propyl]- <i>N</i> -methyl-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	514.2
583	<i>N</i> -1,3-benzodioxol-5-yl-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	535.1
584	<i>N</i> -(2-morpholin-4-ylethyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	528.2

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
585	1'-{4-[(4-pyrimidin-2-ylpiperazin-1-yl)carbonyl]benzyl}spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	562.2
586	4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -1,3-thiazol-2-ylbenzamide	498.1
587	<i>N</i> -(6-methoxypyridin-3-yl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	522.1
588	<i>N</i> -(3,5-dichlorobenzyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	574.1
589	<i>N</i> -1-naphthyl-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	541.2
590	1'-(4-{4-(1,3-benzodioxol-5-ylmethyl)piperazin-1-yl}carbonyl)benzyl}spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	618.2
591	<i>N</i> -(4,6-dimethylpyridin-2-yl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	520.2
592	4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]- <i>N</i> -pyrimidin-4-ylbenzamide	493.1
593	<i>N</i> -(5-methyl-1,3-thiazol-2-yl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	512.2
594	<i>N</i> -(2-cyano-6-fluorophenyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	534.1
595	<i>N</i> -(4-methylbenzyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	519.1
596	<i>N</i> -[3-(1 <i>H</i> -imidazol-1-yl)propyl]-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	523.1

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
597	<i>N</i> -(4-morpholin-4-ylphenyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	576.2
598	1'-{4-[(4-methylpiperazin-1-yl)carbonyl]benzyl}spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	498.2
599	<i>N</i> -(5-cyclopropyl-1,3,4-thiadiazol-2-yl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	539.2

EXAMPLE 13

Synthesis of 1'-(3-hydroxypropyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

- 5 A suspension of 1'-[3-(benzyloxy)propyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one (6.27 g, 14.5 mmol) and 10% Pd/C (0.5 g) in MeOH (150 mL) was hydrogenated under the normal pressure of hydrogen overnight and filtered through a pad of celite. The filtrate was concentrated *in vacuo* to dryness. The residue was crystallized from ether to yield the title compound (4.82 g) as a white solid in 98% yield:
- 10 ¹H NMR (300 MHz, CDCl₃) δ 7.38-6.93 (m, 4H), 6.49 (s, 1H), 6.10 (s, 1H), 4.87 (m, 1H), 4.63 (m, 1H), 4.01-3.81 (m, 2H), 3.62 (t, 2H), 2.89 (br, 1H), 1.99-1.91 (m, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 178.8, 156.0, 148.9, 142.4, 142.1, 132.3, 129.0, 128.9, 124.1, 123.9, 119.0, 108.6, 103.0, 101.5, 93.6, 80.4, 58.3, 37.8, 29.8; MS (ES+) *m/z* 340.2 (*M* + 1).

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EXAMPLE 14

Synthesis of 3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propanal

- To a solution of 1'-(3-hydroxypropyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one (4.82 g, 14.2 mmol) in dichloromethane (150 mL) was added 1,1,1-triacetoxy-1,1-dihydro-1,2-benzodioxol-3(1'*H*)-one (7.00 g, 16.7 mmol) at 0 °C. The resulting mixture was stirred at 0 °C for 4 h, diluted with ethyl acetate, washed sequentially with 10% Na₂S₂O₃ solution, saturated NaHCO₃ and brine, dried over
- 20

anhydrous Na₂SO₄ and filtered. The filtrate was concentrated *in vacuo* to dryness.

The residue was subjected to flash chromatography and the product was recrystallized from ethyl acetate/hexanes to afford the title compound (3.86 g) in 80% yield: ¹H NMR (300 MHz, CDCl₃) δ 9.83 (s, 1H), 7.33-6.92 (m, 4H), 6.48 (s, 1H), 6.08 (s, 1H), 4.86 (m, 1H), 4.61 (m, 1H), 4.15-3.98 (m, 2H), 2.97-2.84 (m, 2H); MS (ES+, *m/z*) 338.1 (*M* + 1).

EXAMPLE 15

Synthesis of 1'-{3-[(cyclopropylmethyl)amino]propyl}spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

To a solution of 3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propanal (0.07 g, 0.20 mmol) in THF (5.00 mL) was added (aminomethyl)cyclopropane (0.30 mmol) and MP-triacetoxyborohydride (0.26 g, 0.60 mmol). After overnight shaking, the polymer-bound 4-phenyloxybenzaldehyde (0.25 g, 0.18 mmol) was added. After another overnight shaking, the mixture was diluted with ether (10.0 mL) and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was recrystallized to give the title compound (0.05 g) in 62% yield as a white solid: ¹H NMR (300 MHz, CDCl₃) δ 7.32-6.92 (m, 4H), 6.49 (s, 1H), 6.12 (s, 1H), 5.83 (m, 2H), 4.86 (m, 1H), 4.64 (m, 1H), 3.97-3.77 (m, 2H), 2.87-2.80 (m, 2H), 2.66-2.56 (m, 2H), 1.02-0.94 (m, 1H), 0.56-0.47 (m, 2H), 0.25-0.18 (m, 2H); MS (ES+) *m/z* 393.3 (*M* + 1).

EXAMPLE 15.1

The compounds listed in the following table were prepared using the similar procedure as described in EXAMPLE 15. As previously noted, the compound numbers listed below do not correspond to the compound numbers provided in the general Reaction Schemes above.

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
600	1'-{3-[(4-fluorobenzyl)amino]propyl}spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	447.0
601	1'-{3-[(4-chlorophenyl)amino]propyl}spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	449.2
602	1'-[3-(pentylamino)propyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	409.1
603	1'-{3-[(2-ethoxyethyl)amino]propyl}spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	411.1

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
604	1'-{3-[(3-methoxypropyl)amino]propyl}spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	411.1
605	1'-{3-[(3-methylbutyl)amino]propyl}spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	409.6
606	1'-{3-[(3-ethoxypropyl)amino]propyl}spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	425.6
607	1'-{3-[(2,2-dimethylpropyl)amino]propyl}spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	409.1
608	3-{[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]amino}propanenitrile	392.4
609	1'-{3-[(2,2,2-trifluoroethyl)amino]propyl}spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	421.1
610	1'-[3-(cyclopropylamino)propyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	379.1
611	1'-[3-(cyclobutylamino)propyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	393.1
612	1'-{3-[(2-cyclopropylethyl)amino]propyl}spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	407.1
613	1'-[3-(isobutylamino)propyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	395.1
614	1'-[3-(hexylamino)propyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	423.5
615	1'-[3-(heptylamino)propyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	437.1
616	1'-[3-(isopropylamino)propyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	381.7
617	1'-{3-[(tetrahydrofuran-2-ylmethyl)amino]propyl}spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	423.1
618	1'-[3-(benzylamino)propyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	429.1
619	1'-{3-[(2-phenylethyl)amino]propyl}spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	443.1
620	1'-[3-(dibenzylamino)propyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	519.4

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
621	1'-[3-(propylamino)propyl]spiro[furo[2,3- η[1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	381.1
622	1'-{3-[[2-(3-fluorophenyl)ethyl]amino]propyl}spiro[furo[2,3- η[1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	461.5
623	1'-{3-[[3-phenylpropyl]amino]propyl}spiro[furo[2,3- η[1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	457.5
624	1'-{3-[[2,2-diphenylethyl]amino]propyl}spiro[furo[2,3- η[1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	519.4
625	1'-{3-[[2-(4-methylphenyl)ethyl]amino]propyl}spiro[furo[2,3- η[1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	457.5
626	1'-{3-[[2-(3-chlorophenyl)ethyl]amino]propyl}spiro[furo[2,3- η[1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	477.3
627	1'-{3-[[2-pyridin-4-ylethyl]amino]propyl}spiro[furo[2,3- η[1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	444.2
628	1'-{3-[[pyridin-4-ylmethyl]amino]propyl}spiro[furo[2,3- η[1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	430.5
629	1'-{3-[[2-(4-fluorophenyl)ethyl]amino]propyl}spiro[furo[2,3- η[1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	461.0
630	1'-{3-[[pyridin-2-ylmethyl]amino]propyl}spiro[furo[2,3- η[1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	430.2
631	1'-{3-[[1-(1 <i>R</i>)-1-cyclohexylethyl]amino]propyl}spiro[furo[2,3- η[1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	449.1
632	1'-{3-[[2-furylmethyl]amino]propyl}spiro[furo[2,3- η[1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	419.4
633	1'-{3-[[4-chlorobenzyl]amino]propyl}spiro[furo[2,3- η[1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	463.1
634	1'-{3-[[4-methoxybenzyl]amino]propyl}spiro[furo[2,3- η[1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	459.4
635	1'-{3-[[3-isopropoxypropyl]amino]propyl}spiro[furo[2,3- η[1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	439.1
636	1'-{3-[[2-(2-fluorophenyl)ethyl]amino]propyl}spiro[furo[2,3- η[1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	461.0

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
637	1'-{3-[(3,3-dimethylbutyl)amino]propyl}spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	423.5
638	1'-{3-[(cyclohexylmethyl)amino]propyl}spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	435.0
639	1'-{3-[(1 <i>S</i>)-1-cyclohexylethyl]amino}propyl}spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	436.5
640	1'-{3-[(2-piperidin-1-ylethyl)amino]propyl}spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	449.1
641	1'-{3-[(2-pyrrolidin-1-ylethyl)amino]propyl}spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	450.5
642	1'-{3-[(2-morpholin-4-ylethyl)amino]propyl}spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	452.4
643	1'-[3-(cyclohexylamino)propyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	421.5
644	1'-[3-(cyclopentylamino)propyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	407.3
645	1'-{3-[(2-chlorobenzyl)amino]propyl}spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	463.2
646	1'-{3-(pyrrolidin-1-ylpropyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	393.5
647	1'-[3-(dibutylamino)propyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	451.5
648	1'-{3-(piperidin-1-ylpropyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	407.0
649	1'-[3-(dipropylamino)propyl]spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	423.2
650	1'-{3-{[2-(dimethylamino)ethyl]amino}propyl}spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	410.5
651	1'-{3-{[2-(diethylamino)ethyl](methyl)amino}propyl}spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	452.1
652	1'-{3-{[2-(diisopropylamino)ethyl]amino}propyl}spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	466.1

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
653	1'-[3-(diisopropylamino)propyl]spiro[furo[2,3- <i>η</i> [1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	423.0
654	1'-[3-(methylamino)propyl]spiro[furo[2,3- <i>η</i> [1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	353.0
655	1'-[3-(ethylamino)propyl]spiro[furo[2,3- <i>η</i> [1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	367.0
656	1'-[3-[bis(2-methoxyethyl)amino]propyl]spiro[furo[2,3- <i>η</i> [1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	455.0
657	1'-[3-[(2-fluorobenzyl)amino]propyl]spiro[furo[2,3- <i>η</i> [1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	446.9
658	1'-[3-[(3,5-difluorobenzyl)amino]propyl]spiro[furo[2,3- <i>η</i> [1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	464.9
659	1'-[3-{[3-(dimethylamino)propyl]amino}propyl]spiro[furo[2,3- <i>η</i> [1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	424.0
660	1'-[3-(diethylamino)propyl]spiro[furo[2,3- <i>η</i> [1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	394.9
661	1'-[3-(octylamino)propyl]spiro[furo[2,3- <i>η</i> [1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	451.5
662	1'-[3-[(1-methylbutyl)amino]propyl]spiro[furo[2,3- <i>η</i> [1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	409.0
663	1'-[3-[butyl(methyl)amino]propyl]spiro[furo[2,3- <i>η</i> [1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	409.0
664	1'-[3-[(2-isopropoxyethyl)amino]propyl]spiro[furo[2,3- <i>η</i> [1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	425.0
665	1'-[3-[(2,4-difluorobenzyl)amino]propyl]spiro[furo[2,3- <i>η</i> [1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	464.9
666	1'-[3-[(2-methylbenzyl)amino]propyl]spiro[furo[2,3- <i>η</i> [1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	443.0
667	1'-[3-[(3-fluorobenzyl)amino]propyl]spiro[furo[2,3- <i>η</i> [1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	446.9
668	1'-[3-[(2,6-difluorobenzyl)amino]propyl]spiro[furo[2,3- <i>η</i> [1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	464.9
669	1'-[3-[(1,2-dimethylpropyl)amino]propyl]spiro[furo[2,3- <i>η</i> [1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	409.0

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
670	1'-(3-([2-(1-methylpyrrolidin-2-yl)ethyl]amino)propyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'-(1' <i>H</i>)-one	450.4
671	1'-(3-([2-(pyridin-3-ylethyl)amino]propyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'-(1' <i>H</i>)-one	444.5
672	1'-(3-([1-(1-methyl-2-phenylethyl)amino]propyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'-(1' <i>H</i>)-one	457.0
673	1'-(3-([2-(2-chlorophenyl)ethyl]amino)propyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'-(1' <i>H</i>)-one	476.9
674	1'-(3-([2-(cyclohexylethyl)amino]propyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'-(1' <i>H</i>)-one	448.1
675	1'-(3-([2-(pyridin-2-ylethyl)amino]propyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'-(1' <i>H</i>)-one	444.2
676	1'-(3-([2-(biphenyl-4-ylethyl)amino]propyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'-(1' <i>H</i>)-one	519.6
677	1'-(3-([3-(morpholin-4-yl)propyl]amino)propyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'-(1' <i>H</i>)-one	466.2
678	1'-(3-([5-methyl-2-furyl)methyl]amino)propyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'-(1' <i>H</i>)-one	433.3
679	1'-(3-([3-(methylbenzyl)amino]propyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'-(1' <i>H</i>)-one	443.4

EXAMPLE 16

Synthesis of 1'-(3-aminopropyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one

To a solution of 2-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)propyl]-1*H*-isoindole-1,3(2*H*)-dione (3.20 g, 6.80 mmol) in ethanol (70.0 mL) was added hydrazine monohydrate (1.87 g, 37.0 mmol). The mixture was stirred at ambient temperature for 4 h. The solvent was removed under reduced pressure and the residue was re-dissolved in ethyl acetate. The solution was washed with sodium bicarbonate and brine solution, dried over MgSO₄ and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was crystallized from hexane to yield the title compound (2.50 g) in 75% yield: ¹H NMR (300 MHz, CDCl₃) δ 7.31-7.24 (m,

1H), 7.16-7.14 (m, 1H), 7.06-7.01 (m, 1H), 6.94-6.91 (m, 1H), 6.48 (s, 1H), 6.10 (s, 1H), 5.82 (m, 2H), 4.90-4.87 (m, 1H), 4.61 (d, 1H), 3.98-3.71 (m, 2H), 2.77-2.73 (m, 2H), 1.97 (br, 2H), 1.84-1.81 (m, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 177.8, 155.9, 148.9, 142.3, 142.2, 132.4, 129.0, 124.0, 123.4, 119.4, 108.7, 103.0, 101.5, 93.6, 80.5, 58.2, 38.8, 37.5, 30.6; MS (ES+) *m/z* 339.3 (M + 1).

EXAMPLE 17

Synthesis of 3-chloro-*N*-[3-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)propyl]thiophene-2-carboxamide

To a solution of 1'-(3-aminopropyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one (0.05 g, 0.13 mmol) in dichloromethane (4.00 mL) was added triethylamine (0.03 g, 0.26 mmol) and 3-chlorothiophene-2-carbonyl chloride (0.02 g, 0.12 mmol) at 0 °C. The mixture was stirred for 2 h, washed with 15% HCl solution and water. The organic layer was dried over MgSO₄ and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was dissolved in ethyl acetate, and the product was precipitated with the addition of hexane. The white solid was collected by filtration and dried *in vacuo* to yield the title compound (0.04 g) in 67% yield: ¹H NMR (300 MHz, CDCl₃) δ 7.60 (t, 1H), 7.41 (d, 1H), 7.33-7.27- (m, 1H), 7.17 (d, 1H), 7.08-7.03- (m, 1H), 6.93 (t, 1H), 6.49 (s, 1H), 6.11 (s, 1H), 5.95 (m, 2H), 4.90 (d, 1H), 4.65 (d, 1H), 3.96-3.79- (m, 2H), 3.53-3.36- (m, 2H), 2.04-1.93- (m, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 178.3, 160.6, 156.0, 149.0, 142.4, 141.8, 132.5, 129.4, 129.2, 129.1, 124.2, 123.7, 123.6, 119.2, 108.5, 102.9, 101.6, 93.7, 80.5, 58.3, 37.4, 36.5, 27.3; MS (ES+) *m/z* 483 (M + 1).

EXAMPLE 17.1

The compounds listed in the following table were synthesized using the similar procedure as described in EXAMPLE 17. As previously noted, the compound numbers listed below do not correspond to the compound numbers provided in the general Reaction Schemes above.

Compound Number	Name	MS (m/z, M + 1)
680	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]cyclopropanecarboxamide	407.3

Compound Number	Name	MS (m/z, M + 1)
681	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]cyclobutanecarboxamide	421.3
682	2-chloro- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]nicotinamide	478.3
683	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]cyclopentanecarboxamide	435.3
684	2,2-dimethyl- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]propanamide	423.3
685	2-(4-methoxyphenyl)- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]acetamide	487.3
686	4-tert-butyl- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]benzamide	499.2
687	3,3-dimethyl- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]butanamide	437.3
688	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]biphenyl-4-carboxamide	519.3
689	3-methyl- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]-1-benzofuran-2-carboxamide	497.2
690	2-(benzyloxy)- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]acetamide	487.3
691	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]-2-furamide	433.3
692	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]-1,3-benzodioxole-5-carboxamide	487.3
693	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]quinoline-2-carboxamide	494.3
694	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]-2-phenylacetamide	457.4

Compound Number	Name	MS (m/z, M + 1)
695	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]piperidine-1-carboxamide	450.3
696	2-methoxy- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]acetamide	411.2
697	4-(dimethylamino)- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]benzamide	486.3
698	4-ethoxy- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]benzamide	487.3
699	2-methyl- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]butanamide	423.3
700	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]-2-phenoxyacetamide	473.2
701	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]quinoxaline-2-carboxamide	495.0
702	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]cyclohexanecarboxamide	449.3
703	4-fluoro- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]benzamide	461.3
704	2-ethyl- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]butanamide	437.3
705	2-(4-fluorophenyl)- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]acetamide	475.3
706	6-chloro- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]nicotinamide	478.0
707	2-fluoro- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]benzamide	461.4
708	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]-2-phenylcyclopropanecarboxamide	482.8

Compound Number	Name	MS (m/z, M + 1)
709	4-methyl- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]benzamide	457.7
710	1-(4-fluorophenyl)-5-methyl- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]-1 <i>H</i> -pyrazole-4-carboxamide	541.2
711	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]-1-benzofuran-5-carboxamide	483.1
712	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]-2,1,3-benzoxadiazole-5-carboxamide	485.4
713	2,4-dichloro- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]benzamide	513.1
714	1-methyl- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]-1 <i>H</i> -1,2,3-benzotriazole-5-carboxamide	498.4
715	5-fluoro-2-methyl- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]benzamide	475.1
716	2-chloro- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]isonicotinamide	478.1
717	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]-2,3-dihydro-1,4-benzodioxine-6-carboxamide	501.1
718	5-methyl- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]isoxazole-3-carboxamide	448.2
719	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]-1-benzofuran-2-carboxamide	483.1
720	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]-1-benzothiophene-2-carboxamide	499.1
721	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]-2,3-dihydro-1,4-benzodioxine-2-carboxamide	501.1

Compound Number	Name	MS (m/z, M + 1)
722	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]-4-(1 <i>H</i> -pyrazol-1-yl)benzamide	509.1
723	1,3-dimethyl- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]-1 <i>H</i> -pyrazole-5-carboxamide	461.2
724	4-methyl- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]-3,4-dihydro-2 <i>H</i> -1,4-benzoxazine-7-carboxamide	514.2
725	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]quinoxaline-6-carboxamide	495.2
726	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]-2,3-dihydro-1-benzofuran-2-carboxamide	485.2
727	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]-2,3-dihydro-1-benzothiophene-5-carboxamide	499.1
728	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]-2-(trifluoromethoxy)benzamide	526.9
729	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]pentanamide	445.2
730	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]heptanamide	473.2
731	3-cyclopentyl- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]propanamide	463.0
732	9-oxo- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]-9 <i>H</i> -fluorene-4-carboxamide	545.0
733	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]-4-(trifluoromethyl)benzamide	511.4
734	2,5-difluoro- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]benzamide	479.3

Compound Number	Name	MS (m/z, M + 1)
735	2,5-dimethyl- <i>N</i> -[3-(2'-oxospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]-3- furanamide	461.4
736	<i>N</i> -[3-(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]- 1'(2' <i>H</i>)-yl)propyl]-4-phenoxybutanamide	523.3
737	4-fluoro- <i>N</i> -[3-(2'-oxospiro[furo[2,3-f][1,3]benzodioxole- 7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]-2- (trifluoromethyl)benzamide	529.0
738	<i>N</i> -[3-(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]- 1'(2' <i>H</i>)-yl)propyl]-2-(2-thienyl)acetamide	463.3
739	2-chloro-5-fluoro- <i>N</i> -[3-(2'-oxospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)- yl)propyl]benzamide	495.0
740	<i>N</i> -[3-(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]- 1'(2' <i>H</i>)-yl)propyl]-2-naphthamide	493.0
741	2-(4-chlorophenoxy)- <i>N</i> -[3-(2'-oxospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)- yl)propyl]acetamide	507.3
742	2,4-dimethoxy- <i>N</i> -[3-(2'-oxospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)- yl)propyl]benzamide	503.4
743	2-nitro- <i>N</i> -[3-(2'-oxospiro[furo[2,3-f][1,3]benzodioxole- 7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]benzamide	488.4
744	2-(4-chlorophenyl)-3-methyl- <i>N</i> -[3-(2'-oxospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)- yl)propyl]butanamide	533.4
745	4-amino- <i>N</i> -[3-(2'-oxospiro[furo[2,3-f][1,3]benzodioxole- 7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]benzamide	458.4
746	3,4-dimethoxy- <i>N</i> -[3-(2'-oxospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)- yl)propyl]benzamide	503.3
747	<i>N</i> -[3-(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]- 1'(2' <i>H</i>)-yl)propyl]-5 <i>H</i> -dibenzo[<i>b,f</i>]azepine-5- carboxamide	558.4

Compound Number	Name	MS (m/z, M + 1)
748	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]adamantane-1-carboxamide	501.5
749	2-[(2-isopropyl-5-methylcyclohexyl)oxy]- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]acetamide	535.5
750	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]-3,5-bis(trifluoromethyl)benzamide	579.3
751	2-(2,5-dimethoxyphenyl)- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]acetamide	517.4
752	2-chloro- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]benzamide	477.3
753	3-chloro- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]benzamide	477.3
754	4-chloro- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]benzamide	477.3
755	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]hexanamide	437.4
756	2,6-difluoro- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]benzamide	479.4
757	2-chloro- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]acetamide	415.3
758	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]-2,5-bis(trifluoromethyl)benzamide	579.4
759	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]pyrrolidine-1-carboxamide	436.4
760	2-bromo-2,2-difluoro- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]acetamide	497.3
761	2,3,5-trifluoro- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]benzamide	497.3

Compound Number	Name	MS (m/z, M + 1)
762	5-fluoro- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]-2-(trifluoromethyl)benzamide	529.4
763	5-chloro- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]-2-(trifluoromethyl)benzamide	545.3
764	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]thiophene-2-carboxamide	449.3
765	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]morpholine-4-carboxamide	452.4
766	2-(1-naphthyl)- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]acetamide	507.4
767	2-methyl- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]propanamide	409.4
768	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]- <i>N</i> -propionylpropanamide	451.4
769	<i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]-4-pentylbenzamide	513.3
770	4,7,7-trimethyl-3-oxo- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]-2-oxabicyclo[2.2.1]heptane-1-carboxamide	519.4
771	2-bromo- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]benzamide	523.2
772	3-cyano- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]benzamide	468.3
773	4-cyano- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]benzamide	468.3

EXAMPLE 18

Synthesis of 1'-(2-aminoethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

To a suspension of 2-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]-1*H*-isoindole-1,3(2*H*)-dione (20.0 g, 44.0 mmol) in methanol (400 mL)

was added hydrazine (8.00 mL). The mixture was stirred at ambient temperature for 48 h and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to flash chromatography eluting with ethyl acetate/methanol/ammonia (10/1/0.2) to afford the crude product which was recrystallized from ethyl acetate to yield the title compound (8.0 g) in 56% yield as a white solid: ¹H NMR (300 MHz, CDCl₃) δ 7.34 (m, 1H), 7.17 (dd, 1H), 7.06 (dd, 1H), 6.95 (d, 1H), 6.51 (s, 1H), 6.18 (s, 1H), 5.89-5.82- (ABq, 2H), 4.93 (d, 1H), 4.66 (d, 1H), 3.95-3.74- (m, 2H), 3.06 (t, 2H), 1.59-1.35- (br, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 178.0, 155.9, 148.8, 142.3, 132.4, 128.9, 124.0, 123.4, 119.5, 108.6, 103.1, 101.5, 93.6, 80.5, 58.2, 43.4, 39.8; MS (ES+) *m/z* 325 (M + 1), 308 (M - 16).

EXAMPLE 19

Synthesis of 1-(4-fluorophenyl)-3-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)ethyl]urea

To a mixture of 1'-(2-aminoethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one (0.15 mmol) and triethylamine (0.01 mmol) in anhydrous dichloromethane was added 1-fluoro-4-isocyanatobenzene (0.14 mmol) at ambient temperature. The mixture was stirred for 16 h, diluted with of dichloromethane (5.00 mL), washed with 10% HCl solution and brine, dried over Na₂SO₄ and filtered. The filtrate was concentrated *in vacuo* to dryness to give the title compound (0.05 g) in 82% yield: ¹H NMR (300 MHz, DMSO-*d*₆) δ 8.54 (s, 1H), 7.35-7.25 (m, 3H), 7.19 (d, 1H), 7.11 (d, 1H), 7.06-6.91 (m, 3H), 6.67 (s, 1H), 6.52 (t, 1H), 5.94-5.84 (ABq, 2H), 4.74 (d, 1H), 4.61 (d, 1H), 3.91-3.69 (m, 2H), 3.49-3.34 (m, 2H); MS (ES+) *m/z* 462 (M + 1), 484 (M + 23).

EXAMPLE 19.1

The compounds listed in the following table were synthesized using the similar procedure as described in EXAMPLE 19. As previously noted, the compound numbers listed below do not correspond to the compound numbers provided in the general Reaction Schemes above.

Compound Number	Name	MS (<i>m/z</i> , M + 1)
774	1-benzyl-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	458

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
775	1-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]-3-(4-phenoxyphenyl)urea	536
776	1-butyl-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	424
777	1-cyclohexyl-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	450
778	1-ethyl-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	396
779	1-isopropyl-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	410
780	1-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]-3-propylurea	410
781	1- <i>tert</i> -butyl-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	424
782	1-cyclopentyl-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	436
783	1-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]-3-pentylurea	438
784	1-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]-3-phenylurea	444
785	1-(2-furylmethyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	448
786	1-hexyl-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	452
787	ethyl <i>N</i> -({[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]amino}carbonyl)glycinate	454
788	1-(3-methylphenyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	458
789	1-(4-methylphenyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	458
790	ethyl <i>N</i> -({[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]amino}carbonyl)-beta-alaninate	468
791	1-(4-cyanophenyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	469

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
792	<i>N</i> -({[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]amino}carbonyl)benzamide	472
793	1-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]-3-(2-phenylethyl)urea	473
794	1-(4-methylbenzyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	472
795	1-(2-methylbenzyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	472
796	1-(4-ethylphenyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	472
797	1-(3-methoxyphenyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	474
798	1-(2-fluoro-5-methylphenyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	476
799	1-(3-fluoro-4-methylphenyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	476
800	1-(4-chlorophenyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	479
801	2-[({[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]amino}carbonyl)amino]ethyl 2-methylacrylate	480
802	1-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]-3-(1,1,3,3-tetramethylbutyl)urea	480
803	ethyl 4-[({[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]amino}carbonyl)amino]butanoate	482
804	1-[4-(cyanomethyl)phenyl]-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	483
805	1-(2,3-dihydro-1 <i>H</i> -inden-5-yl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	483
806	1-(3-acetylphenyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	484

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
807	1-(4-acetylphenyl)-3-[2-(2'-oxospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	486
808	1-(4-isopropylphenyl)-3-[2-(2'-oxospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	486
809	1-(2-methoxybenzyl)-3-[2-(2'-oxospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	486
810	1-(4-methoxybenzyl)-3-[2-(2'-oxospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	488
811	1-(4-methoxy-2-methylphenyl)-3-[2-(2'- oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'-indol]- 1'(2' <i>H</i>)-yl)ethyl]urea	4882
812	1-(4-chloro-2-methylphenyl)-3-[2-(2'-oxospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	488
813	1-(3-chloro-4-methylphenyl)-3-[2-(2'-oxospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	493
814	1-(3-chloro-2-methylphenyl)-3-[2-(2'-oxospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	493
815	1-(5-chloro-2-methylphenyl)-3-[2-(2'-oxospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	493
816	1-(2-chlorobenzyl)-3-[2-(2'-oxospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	493
817	1-(1-naphthyl)-3-[2-(2'-oxospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	493
818	1-(2-naphthyl)-3-[2-(2'-oxospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	494
819	1-(3-chloro-2-fluorophenyl)-3-[2-(2'-oxospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	494
820	1-[2-(2'-oxospiro[furo[2,3-f][1,3]benzodioxole-7,3'- indol]-1'(2' <i>H</i>)-yl)ethyl]-3-(5,6,7,8- tetrahydronaphthalen-1-yl)urea	497
821	1-(4-tert-butylphenyl)-3-[2-(2'-oxospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	498
822	1-(4-butylphenyl)-3-[2-(2'-oxospiro[furo[2,3- f][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	500

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
823	1-[2-(4-ethylphenyl)ethyl]-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	500
824	1-(2,3-dihydro-1,4-benzodioxin-6-yl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	500
825	methyl 4-[(2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl)amino]carbonyl)amino]benzoate	502
826	1-(2-ethoxybenzyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	502
827	1-(3,4-dimethoxyphenyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	502
828	1-(3,5-dimethoxyphenyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	504
829	1-(3-chloro-4-methoxyphenyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	504
830	1-[4-(difluoromethoxy)phenyl]-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	509
831	1-[2-(difluoromethoxy)phenyl]-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	510
832	1-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]-3-[3-(trifluoromethyl)phenyl]urea	510
833	1-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]-3-[2-(trifluoromethyl)phenyl]urea	512
834	1-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]-3-[4-(trifluoromethyl)phenyl]urea	512
835	1-(3,4-dichlorophenyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	512
836	1-(2,3-dichlorophenyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	513

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
837	1-(3,5-dichlorophenyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	513
838	ethyl 4-[[[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]amino]carbonyl]amino]benzoate	513
839	ethyl 2-[[[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]amino]carbonyl]amino]benzoate	516
840	1-[2-(1,3-benzodioxol-5-yl)ethyl]-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	516
841	methyl 2-methyl-3-[[[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]amino]carbonyl]amino]benzoate	516
842	1-(4-butoxyphenyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	516
843	1-(2-methoxy-4-nitrophenyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	516
844	1-biphenyl-2-yl-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	519
845	1-[4-methyl-3-(trifluoromethyl)phenyl]-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	520
846	1-(2,4-dichlorobenzyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	526
847	1-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]-3-[2-(trifluoromethoxy)phenyl]urea	527
848	1-[4-fluoro-2-(trifluoromethyl)phenyl]-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	528
849	1-(5- <i>tert</i> -butyl-2-methoxyphenyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	530

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
850	1-[2-(3,5-dimethoxyphenyl)ethyl]-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	530
851	1-(9 <i>H</i> -fluoren-2-yl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	532
852	1-(9 <i>H</i> -fluoren-9-yl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	532
853	1-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]-3-(3,4,5-trimethoxyphenyl)urea	532
854	1-(diphenylmethyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	534
855	1-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]-3-(2-phenoxyphenyl)urea	534
856	1-(2-biphenyl-4-ylethyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	536
857	1-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]-3-(3,4,5-trimethoxybenzyl)urea	548
858	1-(2-nitrophenyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	548
859	1-(1,3-benzodioxol-5-yl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	489
860	1-[4-(dimethylamino)phenyl]-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	488
861	1-(2-fluorobenzyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	487
862	1-(4-fluoro-3-methylphenyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	476
863	1-(3-fluorobenzyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	476
864	1-(cyclohexylmethyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	476
865	1-(2-methylphenyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	464

Compound Number	Name	MS (<i>m/z</i> , <i>M</i> + 1)
866	1-[4-(6-methyl-1,3-benzothiazol-2-yl)phenyl]-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	458

EXAMPLE 20

Synthesis of 1'-pentyl-7*H*-spiro[furo[3,4-*f*][1,3]benzodioxole-5,3'-indol]-2'(1'*H*)-one

- 5 Following the procedure as described in EXAMPLE 1, and making non-critical variations using 3-hydroxy-3-[6-(hydroxymethyl)-1,3-benzodioxol-5-yl]-1-pentyl-1,3-dihydro-2*H*-indol-2-one to replace 1-(2-cyclopropylethyl)-3-(6-hydroxy-1,3-benzodioxol-5-yl)-3-(hydroxymethyl)-1,3-dihydro-2*H*-indol-2-one, the title compound was obtained (45%) as a colorless solid: mp 113-115 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.24-7.33 (m, 1H), 7.12 (dd, 1H), 7.01 (t, 1H), 6.87 (d, 1H), 6.74 (s, 1H), 6.15 (s, 1H), 5.92 (dd, 2H), 5.48 (d, 1H), 5.27 (d, 1H), 3.76-3.56 (m, 2H), 1.71-1.64- (m, 2H), 1.37-1.27- (m, 4H), 0.89-0.84 (m, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 175.9, 148.7, 148.1, 143.6, 133.7, 132.1, 130.3, 129.8, 125.3, 125.0, 123.1, 113.5, 109.1, 108.7, 101.9, 101.7, 88.7, 74.4, 40.0, 29.7, 29.0, 25.3, 13.3; MS (ES+) *m/z* 352.1 (*M* + 1).

EXAMPLE 21

Synthesis of 1'-pentylspiro[indeno[5,6-*d*][1,3]dioxole-5,3'-indole]-2',7(1'*H*,6*H*)-dione

- To a solution of [3-(1,3-benzodioxol-5-yl)-2-oxo-1-pentyl-2,3-dihydro-1*H*-indol-3-yl]acetic acid (0.28 g, 0.73 mmol) was added one drop of DMF and oxalyl chloride (0.32 mL, 3.7 mmol) in toluene (10 mL). The mixture was stirred at ambient temperature overnight and concentrated under vacuum to dryness to afford a brown oil. This substance was dissolved in dichloromethane (15.0 mL) followed by the addition of tin (IV) chloride (0.07 mL, 0.57 mmol) at 0 °C. The mixture was stirred at ambient temperature overnight and quenched with ice water. The mixture was poured into water (100 mL), and the mixture was extracted with dichloromethane (150 mL). The organic layer was washed with water, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to flash column chromatography to afford the title compound (0.09 g, 67%) as a white solid: ¹H NMR (300 MHz, CDCl₃) δ 7.31 (td, 1H), 7.14 (s, 1H), 7.02 (td, 1H), 6.97-6.92 (m, 2H),

6.22 (s, 1H), 6.03-5.98 (m, 2H), 3.87-3.63 (m, 2H), 3.17 (d, 1H), 2.85 (d, 1H), 1.79-1.66 (m, 2H), 1.41-1.30 (m, 4H), 0.88 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 201.4, 177.5, 154.8, 151.8, 149.6, 143.1, 132.5, 131.6, 128.9, 123.4, 123.2, 108.9, 103.5, 102.6, 102.5, 53.8, 47.7, 40.5, 29.0, 27.1, 22.3, 14.0; MS (ES⁺), *m/z* 386.1 (M + 23), 364.1 (M + 1).

EXAMPLE 22

Synthesis of 1-pentyl-6'*H*-spiro[indole-3,5'-naphtho[2,3-*d*][1,3]dioxole]-2,8'(1*H*,7'*H*)-dione

Following the procedure as described in EXAMPLE 21, and making non-critical variations using 3-[3-(1,3-benzodioxol-5-yl)-2-oxo-1-pentyl-2,3-dihydro-1*H*-indol-3-yl]propanoic acid to replace [3-(1,3-benzodioxol-5-yl)-2-oxo-1-pentyl-2,3-dihydro-1*H*-indol-3-yl]acetic acid, the title compound was obtained (32%) as a white solid: ¹H NMR (300 MHz, CDCl₃) δ 7.57 (s, 1H), 7.37-7.28 (m, 1H), 7.08-7.03 (m, 2H), 6.95 (d, 1H), 6.02 (s, 1H), 5.95-5.91 (m, 2H), 3.73 (t, 2H), 3.37-3.24 (m, 1H), 2.79-2.67 (m, 1H), 2.41-2.32 (m, 2H), 1.76-1.64 (m, 2H), 1.38-1.28 (m, 4H), 0.87 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 195.4, 177.4, 152.3, 148.0, 142.7, 138.9, 133.6, 128.8, 128.4, 124.1, 122.9, 108.9, 106.9, 106.6, 101.9, 51.7, 40.2, 33.1, 32.8, 29.0, 27.1, 22.3, 14.0; MS (ES⁺) *m/z* 400.1 (M + 23), 378.1 (M + 1).

EXAMPLE 23

Synthesis of 1'-pentyl-6,7-dihydrospiro[indeno[5,6-*d*][1,3]dioxole-5,3'-indol]-2'(1'*H*)-one

A mixture of 1'-pentylspiro[indeno[5,6-*d*][1,3]dioxole-5,3'-indole]-2',7'(1'*H*,6*H*)-dione (0.04 g, 0.11 mmol), triethylsilane (1.50 mL) and trifluoroacetic acid (2.00 mL, excess) was stirred at ambient temperature overnight. The mixture was concentrated *in vacuo* to dryness. The residue was subjected to flash column chromatography to afford the title compound (0.02 g, 47%) as an oil: ¹H NMR (300 MHz, CDCl₃) δ 7.25 (td, 1H), 7.06-6.95 (m, 2H), 6.88 (d, 1H), 6.77 (s, 1H), 6.05 (s, 1H), 5.88-5.82 (m, 2H), 3.81-3.60 (m, 2H), 3.37-3.24 (m, 1H), 3.13-3.01 (m, 1H), 2.70-2.59 (m, 1H), 2.44-2.32 (m, 1H), 1.76-1.64 (m, 2H), 1.39-1.28 (m, 4H), 0.88 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 179.5, 147.9, 147.0, 142.9, 138.2, 136.7, 134.7, 128.1, 123.5, 122.6, 108.3, 105.3, 103.6, 101.2, 59.9, 40.0, 38.3, 31.6, 29.0, 27.1, 22.6, 14.0; MS (ES⁺) *m/z* 372.1 (M +

23), 350.1 (M + 1).

EXAMPLE 24

Synthesis of 1-pentyl-7',8'-dihydro-6'*H*-spiro[indole-3,5'-naphtho[2,3-*d*][1,3]dioxol]-2(1*H*)-one

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Following the procedure as described in EXAMPLE 23, and making non-critical variations using 1-pentyl-6'*H*-spiro[indole-3,5'-naphtho[2,3-*d*][1,3]dioxole]-2,8'(1*H*,7'*H*)-dione to replace 1'-pentylspiro[indeno[5,6-*d*][1,3]dioxole-5,3'-indole]-2',7'(1'*H*,6*H*)-dione, the title compound was obtained (69%) as an oil: ¹H NMR (300 MHz, CDCl₃) δ 7.25 (td, 1H), 7.08-6.94 (m, 2H), 6.90 (d, 1H), 6.60 (s, 1H), 5.89 (s, 1H), 5.81-5.76 (m, 2H), 3.81-3.66 (m, 2H), 2.96-2.77 (m, 2H), 2.38-2.24 (m, 1H), 2.17-2.06 (m, 1H), 2.02-1.83 (m, 2H), 1.78-1.65 (m, 2H), 1.42-1.29 (m, 4H), 0.89 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 180.3, 146.7, 146.1, 142.4, 137.3, 131.6, 127.8, 127.8, 124.1, 122.5, 109.0, 108.3, 107.3, 100.7, 52.0, 40.0, 34.0, 29.4, 29.1, 27.1, 22.4, 18.8, 14.0; MS (ES+) *m/z* 364.1 (M + 1).

15

EXAMPLE 25

Synthesis of 8',8'-difluoro-1-pentyl-7',8'-dihydro-6'*H*-spiro[indole-3,5'-naphtho[2,3-*d*][1,3]dioxol]-2(1*H*)-one

20

A mixture of 1-pentyl-6'*H*-spiro[indole-3,5'-naphtho[2,3-*d*][1,3]dioxole]-2,8'(1*H*,7'*H*)-dione (0.02 g, 0.05 mmol), bis(2-methoxyethyl)aminosulfur trifluoride (0.50 mL) and one drop of ethanol was stirred at 85 °C for 72 hours in a Teflon bottle and quenched by slowly addition of water. The mixture was poured into water (100 mL) and extracted with ethyl acetate (100 mL). The organic layer was washed with water, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to flash column chromatography to afford the title compound (0.01 g, 47%) as an oil: ¹H NMR (300 MHz, CDCl₃) δ 7.57 (s, 1H), 7.38-7.28 (m, 1H), 7.09-7.01 (m, 2H), 6.95 (d, 1H), 6.03 (s, 1H), 5.96-5.90 (m, 2H), 3.73 (t, 2H), 3.38-3.24 (m, 1H), 2.79-2.67 (m, 1H), 2.41-2.32 (m, 2H), 1.77-1.63 (m, 2H), 1.39-1.28 (m, 4H), 0.90 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 195.4, 177.4, 152.3, 148.0, 142.7, 138.9, 133.6, 128.8, 128.4, 124.1, 122.9, 108.9, 106.9, 106.6, 101.9, 51.7, 40.2, 33.1, 32.8, 29.0, 27.1, 22.3, 14.0; MS (ES+) *m/z* 422.2 (M + 23), 380.2 (M + 1).

30

EXAMPLE 26

Synthesis of 7-hydroxy-1'-pentyl-6,7-dihydrospiro[indeno[5,6-*d*][1,3]dioxole-5,3'-indol]-2'(1'*H*)-one

5 To a solution of 1-pentyl-6'*H*-spiro[indole-3,5'-naphtho[2,3-*d*][1,3]dioxole]-2,8'(1*H*,7'*H*)-dione (0.20 g, 0.55 mmol) in methanol (10.0 mL) was added sodium borohydride (0.03 g, 0.83 mmol). The reaction mixture was stirred at ambient temperature for 2 h and poured into of water (100 mL) and extracted with ethyl acetate (100 mL). The organic layer was washed with water, dried over sodium sulfate and
10 filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to flash column chromatography to afford the title compound (0.18 g, 90%) as an oil: ¹H NMR (300 MHz, CDCl₃) δ 7.36-7.29 (m, 1H), 7.11-6.99 (m, 3H), 6.93 (d, 1H), 5.98 (s, 1H), 5.94-5.87 (m, 2H), 5.16 (d, 1H), 3.80-3.61 (m, 2H), 2.69 (br, 1H), 2.39 (d, 1H), 1.75-1.62 (m, 2H), 1.38-1.22 (m, 4H), 0.87 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 180.5,
15 148.9, 148.5, 143.7, 140.5, 136.9, 132.1, 128.7, 123.7, 123.3, 108.8, 105.7, 103.2, 101.5, 74.8, 59.6, 40.4, 28.9, 27.0, 22.3, 14.0; MS (ES+) *m/z* 388.4 (M + 23).

EXAMPLE 27

Synthesis of 7-methoxy-1'-pentyl-6,7-dihydrospiro[indeno[5,6-*d*][1,3]dioxole-5,3'-indol]-2'(1'*H*)-one

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To a solution of 7-hydroxy-1'-pentyl-6,7-dihydrospiro[indeno[5,6-*d*][1,3]dioxole-5,3'-indol]-2'(1'*H*)-one (0.05 g, 0.14 mmol) in THF (10.0 mL) was added sodium hydride (0.01 mg, 0.21 mmol) at 0 °C. The reaction mixture was stirred for half an hour followed by the addition of iodomethane (0.50 mL). The mixture was stirred at ambient
25 temperature for two hours, then poured into water (100 mL), and extracted with ethyl acetate (100 mL). The organic layer was washed with water, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to flash column chromatography to afford the title compound (0.03 g, 57%) as an oil: ¹H NMR (300 MHz, CDCl₃) δ 7.26-7.18 (m, 1H), 6.98-6.82 (m, 4H), 6.10 (s, 1H), 5.88 (s, 2H), 5.26 t, 1H), 3.88-3.63 (m, 2H), 3.45 (s, 3H), 2.71-2.54 (m, 2H), 1.80-1.65 (m, 2H), 1.45-1.29 (m, 4H), 0.90 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 178.3,
30 148.9, 148.4, 142.4, 136.8, 136.6, 135.1, 128.1, 123.1, 122.6, 108.5, 105.0, 103.2,

101.5, 82.7, 57.9, 55.6, 43.4, 40.3, 29.1, 27.2, 22.4, 14.0: MS (ES+) m/z 402.4 ($M + 23$).

EXAMPLE 28

Synthesis of 1'-pentyl-6,7-dihydro-5*H*-spiro[1,3-dioxolo[4,5-*g*]isoquinoline-8,3'-indole]-2',5(1'*H*)-dione

A mixture of 1'-pentylspiro[indeno[5,6-*d*][1,3]dioxole-5,3'-indole]-2',7(1'*H*,6*H*)-dione (0.10 g, 0.28 mmol), sodium azide (0.09 g, 1.40 mmol) and trifluoroacetic acid (2.00 mL) was stirred at 50 °C overnight. The mixture was poured into water (100 mL) and extracted with ethyl acetate (100 mL). The organic layer was washed with water, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to flash column chromatography to afford the title compound (0.08 g, 74%) as a white solid: ¹H NMR (300 MHz, CDCl₃) δ 7.60 (s, 1H), 7.30 (td, 1H), 7.20 (dd, 1H), 6.98 (td, 1H), 6.93 (d, 1H), 6.32 (br, 1H), 6.21 (s, 1H), 5.97-5.92 (m, 2H), 4.02 (dd, 1H), 3.87-3.70 (m, 2H), 3.47 (dd, 1H), 1.80-1.66 (m, 2H), 1.42-4.30 (m, 4H), 0.90 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 175.8, 165.2, 151.6, 147.9, 141.7, 134.3, 130.9, 129.0, 124.5, 123.2, 122.9, 109.0, 108.5, 105.4, 101.9, 51.9, 48.2, 40.4, 29.1, 27.1, 22.3, 14.0; MS (ES+) m/z 379.3 ($M + 1$).

EXAMPLE 29

Synthesis of 2'-oxo-1'-pentyl-*N*-pyridin-2-yl-1',2'-dihydrospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indole]-4'-carboxamide

A mixture of 4'-bromo-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one (0.28 g, 0.65 mmol), tetrakis(triphenylphosphine)palladium(0) (0.08 g, 10 mole%), triethylamine (0.33 g, 0.50 mL, 3.25 mmol) and 2-aminopyridine (0.12 g, 1.30 mmol) in *N,N*-dimethylformamide (5.00 mL) was subjected to carbon monoxide (40 Psi). The reaction mixture was heated at 80 °C for 16 h. After cooling down to ambient temperature, the reaction mixture was diluted with ethyl acetate (20.0 mL), washed with water (3 x 20.0 mL), brine (2 x 20.0 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography to give the title compound (0.04 g, 14%) as a solid: ¹H NMR (300 MHz, CDCl₃) δ 8.52 (d, 1H), 7.87 (br, 1H), 7.69-7.62 (m, 3H), 7.53-7.51 (m, 1H), 7.47-7.38 (m, 3H), 7.04-6.98 (m, 1H), 5.79 (d, 2H), 4.97 (ABq, 2H),

3.84-3.66 (m, 2H), 1.77-1.67 (m, 2H), 1.38-1.33 (m, 4H), 0.90 (t, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 177.5, 158.2, 156.7, 149.2, 143.5, 142.1, 132.2, 132.0, 131.9, 131.8, 129.6, 128.6, 128.4, 121.8, 118.2, 110.7, 102.0, 101.4, 93.9, 79.5, 77.2, 58.5, 40.6, 29.0, 27.0, 22.3, 14.0; MS (ES+) m/z 473.2 ($M + 2$).

5

EXAMPLE 29.1

Synthesis of *N*-(3-methoxyphenyl)-2'-oxo-1'-pentyl-1',2'-dihydrospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indole]-4'-carboxamide

Following the procedure described in EXAMPLE 29, and making non-critical variations using 3-methoxyaniline to replace 2-aminopyridine, the title compound was
10 obtained (20%) as a colorless solid: mp 173-175 °C; ^1H NMR (300 MHz, CDCl_3) δ 7.42 (t, 1H), 7.30-7.27 (m, 1H), 7.14 (t, 1H), 7.04-6.97 (m, 2H), 7.23 (s, 1H), 6.74-6.62 (m, 2H), 6.31 (s, 1H), 6.16 (s, 1H), 5.83 (dd, 2H), 4.87-5.01 (m, 2H), 3.91-3.63 (m, 5H), 1.73-1.78 (m, 2H), 1.37-1.32 (m, 4H), 0.93-0.86 (m, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 177.8, 165.1, 159.9, 149.3, 143.6, 143.5, 142.1, 138.1, 134.5, 129.7, 129.5, 127.9,
15 122.4, 118.3, 112.2, 110.7, 110.5, 105.6, 101.9, 101.6, 94.3, 79.2, 58.3, 55.3, 40.5, 28.9, 26.9, 22.3, 13.9; MS (ES+) m/z 501.5 ($M + 1$).

EXAMPLE 30

Synthesis of 2'-oxo-1'-pentyl-1',2'-dihydrospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indole]-4'-carbonitrile

20 A mixture of 4'-bromo-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one (0.10 g, 0.23 mmol), tris(dibenzylideneacetone)dipalladium(0) (0.21 g, 0.23 mmol) and 2-(di-*tert*-butylphosphino)biphenyl (0.07, 0.23 mmol), tributyltin cyanide (0.07 g, 0.23 mmol) and potassium cyanide (0.02 g, 0.23 mmol) was purged with nitrogen and anhydrous acetonitrile (10.0 mL) was added. The reaction mixture was
25 refluxed for 16 h. After cooling down to ambient temperature, the reaction mixture was diluted with ethyl acetate (20.0 mL), washed with water (20.0 mL), brine (20.0 mL), dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The brown residue was subjected to column chromatography eluting with ethyl acetate/hexane (65%) to give the title compound (0.03 g, 33%) which
30 was recrystallized from ether to get a colorless solid: mp 128-129 °C; ^1H NMR (300 MHz, CDCl_3) δ 9.10 (s, 1H), 7.42-7.37 (m, 1H), 7.29-7.27 (m, 1H), 7.09 (d, 1H), 6.53 (s, 1H), 6.03 (s, 1H), 5.87 (dd, 2H), 4.91 (q, 2H), 3.86-3.63 (m, 2H), 1.74-1.62 (m, 2H), 1.43-1.26 (m, 4H), 0.89 (t, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 176.5, 157.1, 149.5,

143.5, 142.4, 135.4, 129.7, 128.3, 126.4, 116.3, 114.8, 112.3, 108.8, 102.2, 93.7, 78.7, 58.3, 40.6, 28.9, 26.7, 22.2, 13.9; MS (ES+) m/z 377.5 ($M + 1$).

EXAMPLE 31

Synthesis of 1'-hexylspiro[1,3-dioxolo[4,5-g]chromene-8,3'-indole]-2',6'(1'*H*,7'*H*)-dione

5 To a solution of 2-(1-hexyl-3-(6-hydroxybenzo[d][1,3]dioxol-5-yl)-2-oxoindolin-3-yl)acetate (0.19 g, 0.43 mmol) in THF:H₂O (2:1) was added lithium hydroxide (0.04 g, 0.86 mmol). The mixture was stirred at ambient temperature for 4 hrs. The organic solvent was removed *in vacuo* and the pH of the aqueous residue was adjusted to 2 followed by extraction with ethyl acetate. The organic layer was dried over anhydrous
10 sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness and the residue was subjected to column chromatography eluting with 25% ethyl acetate/hexane to yield the title compound (0.09 g, 53%) as a white solid: ¹H NMR (300 MHz, CDCl₃) δ 7.33 (dt, 1H), 7.14-7.03 (m, 2H), 6.93 (d, 1H), 6.66 (s, 1H), 6.06 (s, 1H), 5.88 (dd, 2H), 3.76-3.63 (m, 2H), 2.94 (q, 2H), 1.69-1.62 (m, 2H) 1.34-1.22 (m,
15 6H), 0.83 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 175.9, 165.8, 148.3, 147.2, 144.6, 142.6, 129.9, 129.6, 123.8, 123.4, 114.7, 109.2, 105.1, 101.9, 99.8, 49.6, 40.3, 37.2, 31.2, 27.2, 26.4, 22.4, 13.9; MS (ES+) m/z 394.5 ($M + 1$).

EXAMPLE 32

Synthesis of 1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one

20 A mixture of 6-bromo-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one (0.10 g, 0.27 mmol) and palladium/carbon (0.09 g, 0.01 mmol) in methanol/ethyl acetate (1/1, 4.00 mL) was stirred under hydrogen at atmospheric pressure for 16 h. The solvent was evaporated and the black residue was subjected to column chromatography (ethyl acetate/hexane, 1/6) to give the title compound (0.08 g, 97%) as a white solid: ¹H NMR
25 (300 MHz, CDCl₃) δ 7.30 (dd, 1H), 7.18 (dd, 1H), 7.20 (d, 1H), 7.02 (dd, 1H), 6.96-6.90 (m, 2H), 6.79 (dd, 1H), 6.69 (d, 1H), 4.93 (d, 1H), 4.67 (d, 1H), 3.89-3.64 (m, 2H), 1.81-1.66 (m, 2H), 1.44-1.31 (m, 4H), 0.92 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 177.2, 160.7, 142.5, 132.8, 129.7, 129.0, 128.8, 123.9, 123.3, 123.1, 121.3, 110.4, 108.6, 58.1, 40.4, 29.0, 27.2, 22.3, 14.0; MS (ES+) m/z 308.5 ($M + 1$).

30

EXAMPLE 33

Synthesis of 6-anilino-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one

To a solution of 6-bromo-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one (0.08 g, 0.19 mmol) in anhydrous toluene (4.00 mL) was added aniline (0.03 g, 0.29

mmol), xanthphos (0.02 g, 0.03 mmol) and tris(dibenzylideneacetone)dipalladium(0) (0.02 g, 0.02 mmol). The reaction mixture was refluxed for 16 h, cooled down to ambient temperature and concentrated *in vacuo* to dryness. The black residue was subjected to column chromatography (ethyl acetate/hexane, 1/7) to give the title
 5 compound (0.05 g, 62%) as a yellow oil: ¹H NMR (300 MHz, CDCl₃) δ 7.40-7.25 (m, 6H), 7.18 (d, 1H), 7.12-7.05 (m, 3H), 6.98-6.90 (m, 2H), 6.71 (d, 1H), 6.57 (d, 1H), 6.48 (dd, 1H), 4.93 (d, 1H), 4.67 (d, 1H), 3.88-3.64 (m, 2H), 1.80-1.65 (m, 2H), 1.45-1.30 (m, 4H), 0.92 (t, 3H); MS (ES+) *m/z* 399.5 (M + 1).

EXAMPLE 34

10 Synthesis of 6-morpholin-4-yl-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'-(1'*H*)-one (1:1)
 Following the procedure as described in EXAMPLE 33, and making non-critical variations using morphine to replace aniline, the title compound was obtained (42%) as a brown oil: ¹H NMR (300 MHz, CDCl₃) δ 7.32 (d, 1H), 7.15 (d, 1H), 7.05 (dd, 1H), 6.91 (d, 1H), 6.59 (d, 1H), 6.50 (d, 1H), 6.35 (dd, 1H), 4.95 (d, 1H), 4.65 (d, 1H), 3.89-3.60
 15 (m, 6H), 3.15-3.05 (m, 4H), 1.80-1.68 (m, 2H), 1.43-1.34 (m, 4H), 0.92 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 177.5, 162.2, 153.4, 142.6, 132.9, 128.7, 123.9, 123.4, 123.0, 120.1, 108.9, 108.5, 97.9, 80.3, 66.9, 57.7, 49.4, 40.3, 29.0, 27.1, 22.4, 14.0; MS (ES+) *m/z* 393.5 (M + 1).

EXAMPLE 35

20 Synthesis of 6-amino-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'-(1'*H*)-one
A. Synthesis of 6-[(diphenylmethylene)amino]-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'-(1'*H*)-one
 To a solution of 6-bromo-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'-(1'*H*)-one (0.10 g, 0.26 mmol) in anhydrous toluene (5.00 mL) was added benzophenone imine
 25 (0.09 g, 0.52 mmol), sodium *t*-butoxide (0.03 g, 0.36 mmol), tris(dibenzylideneacetone) dipalladium(0) (0.01 g, 0.07 mmol) and (±)-2,2'-bis(diphenylphosphino)-1,1'-binaphthalene (0.12 g, 0.19 mmol). The reaction mixture was refluxed for 16 h, cooled down to ambient temperature, diluted with dichloromethane (50.0 mL) and filtered through a celite bed. The filtrate was concentrated *in vacuo* to dryness to give the title
 30 compound which was used in next step without purification.
B. Synthesis of 6-amino-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'-(1'*H*)-one
 To a solution of 6-[(diphenylmethylene)amino]-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'-(1'*H*)-one in anhydrous tetrahydrofuran (4.00 mL) was added aqueous 10%

hydrochloric acid (2.00 mL). The reaction mixture was stirred for 15 min, diluted with aqueous sodium bicarbonate (5.00 mL) and extracted with ethyl acetate (3 x 25.0 mL). The combined organic solution was dried over sodium sulfate and filtered. The filtrate was concentrated in *vacuo* to dryness. The residue was subjected to column chromatography (ethyl acetate/hexane, 1/1) to give the title compound (0.02 g, 24% yield) as a yellow oil: ¹H NMR (300 MHz, CDCl₃) δ 7.26 (td, 1H), 7.12 (d, 1H), 6.99 (dd, 1H), 6.89 (d, 1H), 6.43 (d, 1H), 6.23 (d, 1H), 6.08 (dd, 1H), 4.86 (d, 1H), 4.60 (d, 1H), 3.86-3.60 (m, 2H), 1.77-1.65 (m, 2H), 1.41-1.30 (m, 4H), 0.89 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 177.8, 171.2, 162.1, 148.7, 142.5, 133.1, 128.6, 127.8, 123.9, 123.7, 123.0, 118.5, 108.5, 108.4, 97.2, 80.2, 77.6, 77.4, 77.2, 76.8, 64.0, 60.4, 57.6, 40.3, 29.7, 29.0, 27.1, 22.6, 22.4, 22.1, 19.1, 14.2, 14.0, 13.7; MS (ES+) *m/z* 323.5 (M + 1).

EXAMPLE 36

Synthesis of 1'-pentyl-6-phenoxySpiro[1-benzofuran-3,3'-indol]-2'(1'H)-one

To a solution of 6-bromo-1'-pentylSpiro[1-benzofuran-3,3'-indol]-2'(1'H)-one (0.08 g, 0.19 mmol) in anhydrous dioxane (4.00 mL) was added copper iodide (0.01 g, 0.01 mmol), *N,N*-dimethyl glycine hydrochloride (0.01 g, 0.01 mmol), cesium carbonate (0.17 g, 0.52 mmol) and phenol (0.03 g, 0.32 mmol). The resulted mixture was refluxed for 16 h under nitrogen, diluted with dichloromethane (50.0 mL) and filtered through a celite bed. The filtrate was concentrated in *vacuo* to dryness. The residue was subjected to column chromatography (ethyl acetate/hexane, 1/6) to give the title compound (0.07 g, 87%) as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 7.36-7.28 (m, 3H), 7.20-7.00 (m, 4H), 6.92 (d, 1H), 6.62 (dd, 1H), 6.58 (br, 1H), 6.44 (dd, 1H), 4.95 (d, 1H), 4.71 (d, 1H), 3.92-3.64 (m, 2H), 1.70-1.68 (m, 2H), 1.43-1.34 (m, 4H), 0.92 (t, 3H); MS (ES+) *m/z* 400.5 (M + 1).

EXAMPLE 37

Synthesis of 1'-pentyl-6-pyridin-3-ylSpiro[1-benzofuran-3,3'-indol]-2'(1'H)-one

A mixture of 6-bromo-1'-pentylSpiro[1-benzofuran-3,3'-indol]-2'(1'H)-one (0.08 g, 0.19 mmol), pyridine-3-boronic acid (0.05 g, 0.41 mmol), palladium acetate (0.002 g, 0.07 mmol), tri-*O*-tolylphosphine (0.0015 g, 0.005 mmol), 2 M sodium carbonate (1.00 mL) and 1,2-dimethoxyethane (9.00 mL) was heated at reflux for 16 hours under N₂. The solvent was evaporated and the black residue was extracted with ethyl acetate (4 x 15.0 mL). The combined organics was dried over sodium sulfate and filtered. The filtrate was concentrated in *vacuo* to dryness. The residue was subjected to column

chromatography (ethyl acetate/hexane, 4/1) to give the title compound (0.07 g, 67% yield) as a white solid: ^1H NMR (300 MHz, CDCl_3) δ 8.60 (br, 1H), 7.85 (d, 1H), 7.45-7.24 (m, 3H), 7.20-7.10 (m, 2H), 7.12-6.98 (m, 2H), 6.95 (d, 1H), 6.81 (d, 1H), 5.05 (d, 1H), 4.78 (d, 1H), 3.89-3.64 (m, 2H), 1.80-1.68 (m, 2H), 1.43-1.34 (m, 4H), 0.92 (t, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 176.9, 161.6, 149.5, 147.3, 142.6, 139.9, 136.4, 135.6, 133.4, 130.1, 129.2, 124.9, 121.7, 119.5, 110.3, 109.7, 107.7, 80.1, 57.8, 42.3, 28.8, 27.1, 22.3, 14.85; MS (ES+) m/z 385.5 ($M + 1$).

EXAMPLE 38

Synthesis of 1'-pentyl-6-pyridin-4-ylspiro[1-benzofuran-3,3'-indol]-2'-(1'H)-one

Following the procedure as described in EXAMPLE 37, and making non-critical variations using 4-pyridine boronic acid to replace 3-pyridine boronic acid, the title compound was obtained (38%) as white solid: mp 107-110 °C; ^1H NMR (300 MHz, CDCl_3) δ 8.64-8.58 (m, 2H), 7.45-7.40 (m, 2H), 7.31 (dt, 1H), 7.19-7.13 (m, 2H), 6.93 (d, 1H), 6.79 (d, 1H), 4.95 (d, 1H), 4.75 (d, 1H), 3.88-3.64 (m, 2H), 1.80-1.68 (m, 2H), 1.43-1.34 (m, 4H), 0.90 (t, 3H); MS (ES+) m/z 385.5 ($M + 1$).

EXAMPLE 39

Synthesis of 6-(methylsulfonyl)-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'-(1'H)-one

A mixture of 6-bromo-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'-(1'H)-one (0.60 g, 1.55 mmol), sodium methanesulfonate (0.19 g, 1.86 mmol), copper iodide (0.03 g, 0.16 mmol), and L-proline (0.04 g, 0.31 mmol) in dimethyl sulfoxide (3.00 mL) was heated at 100 °C for 2 days under N_2 . The reaction mixture was diluted with water (50.0 mL) and extracted with ethyl acetate (4 x 15.0 mL). The combined organics was dried over sodium sulfate and filtered. The filtrate was concentrated in *vacuo* to dryness. The residue was subjected to column chromatography (ethyl acetate/hexane, 2/3) to give the title compound (0.03 g, 46%) as a light yellow oil: ^1H NMR (300 MHz, CDCl_3) δ 7.46-7.48 (m, 1H), 7.38 (dt, 1H), 7.34 (dt, 1H), 7.13-7.02 (m, 2H), 6.94 (d, 1H), 6.86 (d, 1H), 5.03 (d, 1H), 4.78 (d, 1H), 3.87-3.64 (m, 2H), 3.02 (s, 3H), 1.79-1.68 (m, 2H), 1.41-1.32 (m, 4H), 0.90 (t, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 176.1, 161.2, 142.6, 142.1, 135.4, 131.5, 129.5, 124.3, 124.0, 123.5, 120.7, 109.5, 109.0, 80.5, 57.7, 44.5, 40.6, 29.0, 27.1, 22.3, 14.0; MS (ES+) m/z 386.5 ($M + 1$).

EXAMPLE 40

Synthesis of 1'-pentyl-6-(phenylsulfonyl)spiro[1-benzofuran-3,3'-indol]-2'(1'H)-one

Following the procedure as described in EXAMPLE 39, and making non-critical variations using sodium phenyl sulfinate to replace sodium methanesulfinate, the title compound was obtained (50%) as a yellowish oil: ¹H NMR (300 MHz, CDCl₃) δ 7.94-7.88 (m, 2H), 7.60-7.44 (m, 4H), 7.40 (dd, 1H), 7.31 (dt, 1H), 7.10-6.99 (m, 2H), 6.92 (d, 1H), 6.78 (d, 1H), 4.98 (d, 1H), 4.72 (d, 1H), 3.84-3.61 (m, 2H), 1.75-1.65 (m, 2H), 1.39-1.30 (m, 4H), 0.88 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 176.1, 161.2, 143.2, 142.5, 141.2, 134.9, 133.3, 129.4, 129.3, 127.8, 124.1, 124.0, 123.5, 121.1, 109.8, 108.9, 80.5, 57.7, 40.5, 29.0, 27.1, 22.3, 14.0; MS (ES+) *m/z* 448.5 (M + 1).

EXAMPLE 41

Synthesis of 1'-pentyl-5-phenoxy spiro[1-benzofuran-3,3'-indol]-2'(1'H)-one

Following the procedure as described in EXAMPLE 36, and making non-critical variations using 5-bromo-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(1'H)-one to replace 6-bromo-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(1'H)-one, the title compound was obtained (10% yield) as a colorless oil: ¹H NMR (300 MHz, CDCl₃) δ 7.32-7.10 (m, 5H), 7.06-6.82 (m, 6H), 6.42 (d, 1H), 4.95 (d, 1H), 4.71 (d, 1H), 3.82-3.62 (m, 2H), 1.75-1.63 (m, 2H), 1.43-1.34 (m, 4H), 0.85 (t, 3H); MS (ES+) *m/z* 400.4 (M + 1).

EXAMPLE 42

20 Synthesis of 1'-(diphenylmethyl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)spiro[1-benzofuran-3,3'-indol]-2'(1'H)-one

A mixture of 5-bromo-1'-(diphenylmethyl)spiro[1-benzofuran-3,3'-indol]-2'(1'H)-one (3.00 g, 6.22 mmol), bis(pinacolato)diboron (1.80 g, 7.09 mmol), (1,1'-bis(diphenylphosphino)ferrocene)dichloropalladium(II) (0.45 g, 9 mole%), and potassium acetate (5.49 g, 56.0 mmol) in anhydrous dimethyl sulfoxide (40.0 mL) was stirred at 100 °C under N₂ for 16 h. The reaction mixture was diluted with water (600 mL). The aqueous mixture was extracted with ethyl acetate (3 x 200 mL). The combined organic layers were dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo*. The residue was subjected to column chromatography (ethyl acetate/hexane, 1/6) to give the title compound (1.00 g, 30%) as a white solid: ¹H NMR (300 MHz, CDCl₃) δ 7.68 (dd, 1H), 7.40-7.25 (m, 10H), 7.18 (br, 1H), 7.11 (dd, 1H), 7.06-6.91 (m, 4H), 6.50 (d, 1H), 4.99 (d, 1H), 4.74 (d, 1H), 1.27 (d, 12H); MS (ES+) *m/z* 530.32 (M + 1).

EXAMPLE 43

Synthesis of 1'-(diphenylmethyl)-5-hydroxyspiro[1-benzofuran-3,3'-indol]-2'(1'H)-one

A mixture of 1'-(diphenylmethyl)-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)spiro[1-benzofuran-3,3'-indol]-2'(1'H)-one (4.50 g, 8.50 mmol), hydrogen peroxide
5 (4.86 mL, 30% solution, 42.5 mmol), sodium hydroxide (16.38 mL, 10% solution, 40.82 mmol) in methanol was stirred at 0 °C for 30 min and ambient temperature for 16 h. The reaction mixture was quenched with sodium bisulfite. The pH of the reaction mixture was adjusted to 4 using 14% hydrochloric acid. The mixture was extracted with ethyl acetate (3 x 250 mL). The combined organic layers was dried over
10 anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo*. The residue was triturated with hexane (20.0 mL), followed by ether (15.0 mL) to give the title compound (3.20 g, 90%) as a white solid: ¹H NMR (300 MHz, CDCl₃) δ 7.45-7.38 (m, 10H), 7.13 (dd, 1H), 7.07-6.91 (m, 3H), 6.79 (d, 1H), 6.63 (dd, 1H), 6.50 (d, 1H), 6.12 (d, 1H), 4.96 (d, 1H), 4.69 (d, 1H); MS (ES+) *m/z* 420.23 (M + 1).

15

EXAMPLE 44

Synthesis of 5-hydroxyspiro[1-benzofuran-3,3'-indol]-2'(1'H)-one

Following the procedure as described in EXAMPLE 1.28, and making non-critical variations using 1'-(diphenylmethyl)-5-hydroxyspiro[1-benzofuran-3,3'-indol]-2'(1'H)-one to replace 1'-(diphenylmethyl)-5'-methylspiro[furo[2,3-*f*][1,3]benzodioxole-
20 7,3'-indol]-2'(1'H)-one, the title compound was obtained (48%) as a white solid: ¹H NMR (300 MHz, DMSO-*d*₆) δ 10.58 (s, 1H), 8.85 (s, 1H), 7.21 (dt, 1H), 7.06 (d, 1H), 6.94 (dd, 1H), 6.89 (d, 1H), 6.72 (d, 1H), 6.54 (dd, 1H), 6.02 (d, 1H), 4.70 (d, 1H), 4.57 (d, 1H); MS (ES+) *m/z* 254.2 (M + 1).

25

EXAMPLE 45

Synthesis of 2'-oxo-1',2'-dihydrospiro[1-benzofuran-3,3'-indol]-5-yl trifluoromethanesulfonate:

To a mixture of 5-hydroxyspiro[1-benzofuran-3,3'-indol]-2'(1'H)-one (0.18 g, 0.70 mmol) and trifluoromethane sulfonic anhydride (0.26 g, 0.91 mmol) in dichloromethane (5.00 mL) was added triethylamine (0.14 g, 1.93 mmol) at 0 °C. The
30 reaction mixture was stirred at ambient temperature for 16 h and diluted with dichloromethane (100 mL). After washing with aqueous saturated sodium chloride (2 x 20.0 mL), the organic layer was dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo*. The residue was subjected to column

chromatography (ethyl acetate/hexane, 1/2) to give the title compound (0.07 g, 25%) as a light yellow solid: ^1H NMR (300 MHz, CDCl_3) δ 7.92 (br, 1H), 7.29 (dt, 1H), 7.15-7.03 (m, 3H), 7.99-6.94 (m, 2H), 6.69 (d, 1H), 5.03 (d, 1H), 4.76 (d, 1H); MS (ES+) m/z 386.5 ($M + 1$).

5

EXAMPLE 46

Synthesis of 2'-oxo-1'-[[5-(trifluoromethyl)-2-furyl]methyl]-1',2'-dihydrospiro[1-benzofuran-3,3'-indol]-5-yl trifluoromethanesulfonate

To a mixture of 2'-oxo-1',2'-dihydrospiro[1-benzofuran-3,3'-indol]-5-yl trifluoromethanesulfonate (0.42 g, 1.10 mmol) and sodium hydroxide (0.07 g, 1.65 mmol) in *N,N*-dimethylformamide (5.00 mL) was added 2-(bromomethyl)-5-(trifluoromethyl)furan (0.50 g, 2.20 mmol) at 0 °C. The reaction mixture was stirred at ambient temperature for 16 h and diluted with ethyl acetate (200 mL). After washing with aqueous saturated sodium chloride (2 x 20.0 mL), the organic layer was dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo*. The residue was subjected to column chromatography (ethyl acetate/hexane, 1/3) to give the title compound (0.47 g, 80%) as a clear oil: ^1H NMR (300 MHz, CDCl_3) δ 7.34 (t, 1H), 7.18-6.94 (m, 5H), 6.74 (dd, 1H), 6.55 (dd, 1H), 6.40 (d, 1H), 5.09-4.72 (m, 4H); MS (ES+) m/z 534.4 ($M + 1$).

15

EXAMPLE 47

20 Synthesis of 5-pyridin-3-yl-1'-[[5-(trifluoromethyl)-2-furyl]methyl]spiro[1-benzofuran-3,3'-indol]-2'($1'H$)-one hydrochloride

Following the procedure as described in EXAMPLE 4.2, and making non-critical variations using 2'-oxo-1'-[[5-(trifluoromethyl)-2-furyl]methyl]-1',2'-dihydrospiro[1-benzofuran-3,3'-indol]-5-yl trifluoromethanesulfonate to replace 2-(4'-bromo-5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2' *H*)-yl)-*N*-(2-fluorophenyl)acetamide, and pyridin-3-ylboronic acid to replace pyrimidine-5-boronic acid, 5-pyridin-3-yl-1'-[[5-(trifluoromethyl)-2-furyl]methyl]spiro[1-benzofuran-3,3'-indol]-2'($1'H$)-one was obtained (74%) as a white solid, which was treated with HCl in ether to give the title compound: mp 98-100 °C; ^1H NMR (300 MHz, CD_3OD) δ 8.96 (br, 1H), 8.74-8.65 (m, 2H), 8.04 (dd, 1H), 7.73 (dd, 1H), 7.37 (dt, 1H), 7.25-7.09 (m, 5H), 6.95 (dd, 1H), 6.67 (d, 1H), 5.20-4.83 (m, 4H); ^{13}C NMR (75 MHz, CD_3OD) δ 175.7, 161.3, 151.1, 142.1, 140.2, 138.6, 137.5, 137.4, 130.0, 129.4, 128.1, 127.5, 125.6, 125.5, 122.3, 122.1, 120.8, 111.4, 111.3, 109.7, 108.1, 107.7, 78.7, 58.3, 34.9; MS (ES+) m/z 463.1 ($M + 1$).

30

EXAMPLE 48

Synthesis of 1'-pentyl-5-pyridin-3-ylspiro[1-benzofuran-3,3'-indol]-2'-(1'H)-one

Following the procedure as described in EXAMPLE 4.2, and making non-critical variations using 5-bromo-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'-(1'H)-one to replace
5 2-(4'-bromo-5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2' H)-yl)-N-(2-fluorophenyl)acetamide, and pyridin-3-ylboronic acid to replace pyrimidine-5-boronic acid, the title compound was obtained (70%) was obtained as a white solid: ¹H NMR (300 MHz, CDCl₃) δ 8.55 (br, 1H), 7.65 (d, 1H), 7.45-6.98 (m, 7H), 6.92 (d, 1H), 6.85 (d, 1H), 4.98 (d, 1H), 4.72 (d, 1H), 3.89-3.64 (m, 2H), 1.80-1.68 (m, 2H), 1.43-1.34 (m,
10 4H), 0.86 (t, 3H); MS (ES+) *m/z* 385.5 (M + 1).

EXAMPLE 49

Synthesis of 1'-pentyl-5-pyrimidin-5-ylspiro[1-benzofuran-3,3'-indol]-2'-(1'H)-one

Following the procedure as described in EXAMPLE 4.2, and making non-critical variations using 5-bromo-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'-(1'H)-one to replace
15 2-(4'-bromo-5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2' H)-yl)-N-(2-fluorophenyl)acetamide, the title compound was obtained (40%) was obtained as a white solid: mp 115-117 °C; ¹H NMR (300 MHz, CDCl₃) δ 9.08 (s, 1H), 8.74 (s, 1H), 7.41 (dd, 1H), 7.33 (dt, 1H), 7.16 (dd, 1H), 7.11-7.01 (m, 2H), 6.95 (d, 1H), 6.86 (d, 1H), 5.01 (d, 1H), 4.75 (d, 1H), 3.89-3.64 (m, 2H), 1.80-1.68 (m, 2H), 1.43-1.34 (m,
20 4H), 0.88 (t, 3H); MS (ES+) *m/z* 386.4 (M + 1).

EXAMPLE 50

Synthesis of 1'-pentyl-5-pyridin-4-ylspiro[1-benzofuran-3,3'-indol]-2'-(1'H)-one

Following the procedure as described in EXAMPLE 4.2, and making non-critical variations using 5-bromo-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'-(1'H)-one to replace
25 2-(4'-bromo-5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2' H)-yl)-N-(2-fluorophenyl)acetamide, and pyridin-4-ylboronic acid to replace pyrimidine-5-boronic acid, the title compound was obtained (95%) as a white solid: ¹H NMR (300 MHz, CDCl₃) δ 8.55-8.47 (m, 2H), 7.52-7.46 (dd, 1H), 7.35-7.26 (m, 3H), 7.15 (dd, 1H), 7.07-7.00 (m, 2H), 6.97-6.92 (m, 2H), 4.99 (d, 1H), 4.73 (d, 1H), 3.89-3.67 (m, 2H), 1.80-
30 1.68 (m, 2H), 1.43-1.34 (m, 4H), 0.92 (t, 3H); MS (ES+) *m/z* 385.5 (M + 1).

EXAMPLE 51

Synthesis of 2'-oxo-1'-pentyl-1',2'-dihydrospiro[1-benzofuran-3,3'-indole]-5-carbonitrile

Following the procedure as described in EXAMPLE 30, and making non-critical

variations using 5-bromo-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one to replace 4'-bromo-1'-pentylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one, the title compound was obtained (78%) as a white solid: ¹H NMR (300 MHz, CDCl₃) δ 7.51 (dt, 1H), 7.34 (dt, 1H), 7.12-6.91 (m, 5H), 5.01 (d, 1H), 4.76 (d, 1H), 3.86-3.63 (m, 2H), 1.80-1.68 (m, 2H), 1.43-1.32 (m, 4H), 0.92 (t, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 176.2, 164.1, 142.6, 134.8, 131.4, 130.8, 129.6, 127.8, 123.9, 123.5, 118.8, 111.5, 109.1, 104.7, 80.6, 57.3, 40.6, 29.0, 27.1, 22.3, 14.0; MS (ES+) *m/z* 333.5 (*M* + 1).

EXAMPLE 52

Synthesis of *N*-(2-fluorophenyl)-2-(2'-oxo-5-pyridin-3-ylspiro[1-benzofuran-3,3'-indol]-1'(2'*H*)-yl)acetamide

Following the procedure as described in EXAMPLE 37, and making non-critical variations using 2-(5-bromo-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2'*H*)-yl)-*N*-(2-fluorophenyl)acetamide to replace 6-bromo-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one, the title compound was obtained (55% yield) as a white solid: mp 98-100 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.60-8.53 (m, 2H), 8.14 (dd, 1H), 7.65 (dd, 1H), 7.41 (dd, 1H), 7.32-6.90 (m, 11H), 5.02 (d, 1H), 4.76 (d, 1H), 4.72 (d, 1H), 4.56 (d, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 177.9, 164.8, 160.9, 154.2, 151.0, 147.1, 141.7, 134.2, 131.7, 131.5, 129.9, 129.4, 129.1, 125.1, 124.6, 124.5, 124.2, 124.0, 122.5, 122.2, 115.1, 114.8, 111.0, 109.1, 80.0, 58.1, 44.6; MS (ES+) *m/z* 466.4 (*M* + 1).

EXAMPLE 53

Synthesis of 1'-[(5-fluoro-1*H*-benzimidazol-2-yl)methyl]spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one

A mixture of (2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'(2'*H*)-yl)acetic acid (0.50 g, 1.47 mmol) and 4-fluorobenzene-1,2-diamine (0.15 g, 1.18 mmol) in anhydrous toluene (20.0 mL) was refluxed overnight under N₂. The reaction mixture was diluted with water (250 mL) and extracted with ethyl acetate (2 x 200 mL). The combined organic extracts was dried over anhydrous sodium sulfate and filtered. The filtrate was concentrated *in vacuo* to dryness. The residue was subjected to column chromatography (ethyl acetate/hexane, 2/1) to give the title compound (0.13 g, 22%): mp 138 -142 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.47-7.39 (m, 1H), 7.32-7.22 (m, 2H), 7.16-6.93 (m, 3H), 6.18 (s, 1H), 6.07 (s, 1H), 5.84-5.78 (m, 2H), 5.20-5.14 (m, 2H), 4.98 (d, 1H), 4.60 (d, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 179.2, 161.3, 158.1, 156.2,

149.2, 149.1, 142.5, 141.2, 131.5, 129.5, 124.4, 124.0, 118.0, 111.6, 111.2, 109.9, 103.1, 101.7, 93.5, 80.5, 58.5, 38.9; MS (ES+) m/z 430.2 (M + 1).

EXAMPLE 54

Synthesis of 1'-(diphenylmethyl)-5-pyridin-3-ylspiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one

5 Following the procedure as described in EXAMPLE 4.2, and making non-critical variations using 5-bromo-1'-(diphenylmethyl)spiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one to replace 2-(4'-bromo-5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'(2' *H*)-yl)-*N*-(2-fluorophenyl)acetamide, and pyridin-3-ylboronic acid to replace pyrimidine-5-boronic acid, the title compound was obtained (74%) as a white solid: mp 204-207 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.62-8.46 (m, 2H), 7.62 (d, 1H), 7.43-7.26 (m, 11H), 7.16 (dd, 1H), 7.03-6.94 (m, 4H), 6.76 ((d, 1H), 6.54 (d, 1H), 5.09 (d, 1H), 4.82 (d, 1H); MS (ES+) *m/z* 481.5 (M + 1).

EXAMPLE 55

Synthesis of *tert*-butyl 3-(2'-oxo-1',2'-dihydrospiro[1-benzofuran-3,3'-indol]-5-

15 yl)piperidine-1-carboxylate

A. Synthesis of 5-piperidin-3-ylspiro[1-benzofuran-3,3'-indol]-2'(1*H*)-one:

Following the procedure as described in EXAMPLE 1.28, and making non-critical variations using 1'-(diphenylmethyl)-5-pyridin-3-ylspiro[1-benzofuran-3,3'-indol]-2'(1'*H*)-one to replace 1'-(diphenylmethyl)-5'-methylspiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'(1'*H*)-one, the title compound was obtained that was used in the next step.

B. Synthesis of *tert*-butyl 3-(2'-oxo-1',2'-dihydrospiro[1-benzofuran-3,3'-indol]-5-yl)piperidine-1-carboxylate

To a mixture of 5-piperidin-3-ylspiro[1-benzofuran-3,3'-indol]-2'(1*H*)-one, triethylamine (0.95 g, 9.36 mmol) in anhydrous dichloromethane (15.0 mL) was added di-*tert*-butyl dicarbonate (1.02 g, 4.68 mmol) at 0 °C. The reaction mixture was stirred at ambient temperature and stirred over night under N₂, diluted with dichloromethane (100 mL) and filtered through celite. The filtrate was concentrated *in vacuo* to dryness. The brown residue was subjected to column chromatography (ethyl acetate/hexane, 1/1) to give the title compound (0.50 g, 40%) as a white solid: mp 120-123 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.82 (br, 1H), 7.23-7.21 (m, 2H), 7.14-6.86 (m, 5H), 6.63 (br, 1H), 4.95 (d, 1H), 4.69 (d, 1H), 4.10-4.00 (m, 2H), 2.70-2.45 (m, 2H), 1.95-1.80 (m, 2H), 1.48-1.38 (m, 11H); MS (ES+) *m/z* 443.4 (M + 1).

EXAMPLE 56

Synthesis of *tert*-butyl 3-(2'-oxo-1'-[[5-(trifluoromethyl)-2-furyl]methyl]-1',2'-dihydrospiro[1-benzofuran-3,3'-indol]-5-yl)piperidine-1-carboxylate

Following the procedure as described in PREPARATION 1A, and making non-critical variations using *tert*-butyl 3-(2'-oxo-1',2'-dihydrospiro[1-benzofuran-3,3'-indol]-5-yl)piperidine-1-carboxylate to replace 4-bromoindole, and 2-(bromomethyl)-5-(trifluoromethyl)furan to replace 1-bromopentane, the title compound was obtained (10%) as a white solid: mp 59-61 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.34-7.23 (m, 2H), 7.12 (d, 1H), 7.04-6.96 (m, 2H), 6.89 (d, 1H), 6.75 (s, 1H), 6.50 (s, 1H), 6.41 (s, 1H), 5.10-4.86 (m, 3H), 4.66 (d, 1H), 4.16-3.94 (m, 2H), 2.68-2.38 (m, 2H), 1.90-1.60 (m, 3H), 1.40 (s, 10H), 1.27-1.21 (m, 1H); MS (ES+) *m/z* 591.2 (M + 23).

EXAMPLE 57

Synthesis of 5-pyridin-4-yl-1'-[[5-(trifluoromethyl)-2-furyl]methyl]spiro[1-benzofuran-3,3'-indol]-2'-(1'*H*)-one hydrochloride

Following the procedure as described in EXAMPLE 4.2, and making non-critical variations using 2'-oxo-1'-[[5-(trifluoromethyl)-2-furyl]methyl]-1',2'-dihydrospiro[1-benzofuran-3,3'-indol]-5-yl trifluoromethanesulfonate to replace 2-(4'-bromo-5,6-difluoro-2'-oxospiro[1-benzofuran-3,3'-indol]-1'-(2' *H*)-yl)-*N*-(2-fluorophenyl)acetamide, and pyridin-4-ylboronic acid to replace pyrimidine-5-boronic acid, 5-pyridin-4-yl-1'-[[5-(trifluoromethyl)-2-furyl]methyl]spiro[1-benzofuran-3,3'-indol]-2'-(1'*H*)-one was obtained as a white solid, which was treated with HCl in ether to give the title compound (54%): mp 108-110 °C; ¹H NMR (300 MHz, CDCl₃) δ 8.57-8.47 (m, 2H), 7.52 (dd, 1H), 7.37-7.29 (m, 3H), 7.18 (dd, 1H), 7.12-7.00 (m, 3H), 6.92 (d, 1H), 6.75 (dd, 1H), 6.43 (d, 1H), 5.11-4.83 (m, 3H), 4.75 (d, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 176.2, 164.3, 156.7, 151.5, 141.5, 140.8, 131.5, 131.1, 130.7, 129.8, 127.7, 124.3, 124.1, 123.4, 123.1, 112.9, 112.2, 110.0, 109.4, 80.9, 57.5, 37.3; MS (ES+) *m/z* 466.4 (M + 1).

EXAMPLE 58

Synthesis of 5-methoxy-1'-methylspiro [1-benzofuran-3,3'-indol]-2'-(1'*H*)-one

To a mixture of 5-hydroxyspiro[1-benzofuran-3,3'-indol]-2'-(1'*H*)-one (0.10 g, 0.39 mmol), triphenylphosphine (0.20 g, 0.76 mmol) and methanol (0.05 g, 1.6 mmol) in anhydrous tetrahydrofuran was added diethyl azodicarboxylate (0.14 g, 0.80 mmol) at 0 °C. The reaction mixture was stirred at ambient temperature under N₂ for 16 h and concentrated *in vacuo* to dryness. The brown residue was subjected to column

chromatography (ethyl acetate/hexane, 1/1) to give the title compound (0.02 g, 14% yield) as a yellowish solid: mp 159-161 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.32 (dt, 1H), 7.14 (d, 1H), 7.05 (t, 1H), 6.93-6.83 (m, 2H), 6.74 (dd, 1H), 6.25 (d, 1H), 4.89 (d, 1H), 4.63 (d, 1H), 3.63 (s, 3H), 3.28 (s, 3H); MS (ES+) 282.3 (M + 1).

5

EXAMPLE 59

Synthesis of *N*-[2-(2'-oxospiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-1'-(2'*H*)-yl)ethyl]-2-(trifluoromethoxy)benzamide

Following the procedure as described in EXAMPLE 17, and making non-critical variations using 1'-(2-aminoethyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one to replace 1'-(3-aminopropyl)spiro[furo[2,3-*f*][1,3]benzodioxole-7,3'-indol]-2'-(1'*H*)-one, and 2-(trifluoromethoxy)benzoyl chloride to replace 3-chlorothiophene-2-carbonyl chloride, the title compound was obtained (91%) as a colorless solid: mp 183-184 °C; ¹H NMR (300 MHz, CDCl₃) δ 7.86-7.83 (m, 1H), 7.50-7.45 (m, 1H), 7.37-7.27 (m, 3H), 7.16-7.11 (m, 2H), 7.07-7.02 (m, 1H), 6.84 (t, 1H), 6.47 (s, 1H), 6.10 (s, 1H), 5.82 (dd, 15 2H), 4.87 (d, 1H), 4.64 (d, 1H), 4.10-3.94 (m, 2H), 3.90-3.68 (m, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 178.2, 165.0, 155.9, 148.8, 145.9, 142.3, 141.9, 132.4, 132.1, 131.3, 129.2, 127.6, 127.3, 124.0, 123.6, 121.2, 121.1, 119.2, 108.7, 103.0, 101.4, 93.6, 80.4, 58.2, 39.5, 38.2; MS (ES+) *m/z* 513.4 (M + 1).

BIOLOGICAL ASSAYS

20 Various techniques are known in the art for testing the activity of compounds of the invention. In order that the invention described herein may be more fully understood, the following biological assays are set forth. It should be understood that these examples are for illustrative purposes only and are not to be construed as limiting this invention in any manner.

25

BIOLOGICAL EXAMPLE 1

Guanidine Influx Assay (*in vitro* assay)

This example describes an *in vitro* assay for testing and profiling test agents against human or rat sodium channels stably expressed in cells of either an endogenous or recombinant origin. The assay is also useful for determining the IC₅₀ of a sodium channel blocking compound. The assay is based on the guanidine flux 30 assay described by Reddy, N.L., et al., *J Med Chem* (1998), 41(17):3298-302.

The guanidine influx assay is a radiotracer flux assay used to determine ion flux activity of sodium channels in a high-throughput microplate-based format. The assay

uses ^{14}C -guanidine hydrochloride in combination with various known sodium channel modulators, to assay the potency of test agents. Potency is determined by an IC_{50} calculation. Selectivity is determined by comparing potency of the compound for the channel of interest to its potency against other sodium channels (also called 'selectivity
5 profiling').

Each of the test agents is assayed against cells that express the sodium channel of interest. Voltage gated sodium channels are either TTX sensitive or insensitive. This property is useful when evaluating the activities of a channel of interest when it resides in a mixed population with other sodium channels. The
10 following Table 1 lists certain cell lines which are useful in screening for a certain sodium channel activity in the presence or absence of TTX.

Table 1

CELL LINE	mRNA Expression	Functional Characterization
CHO-K1 (Chinese Hamster Ovary; recommended host cell line) ATTC accession number CCL-61	• Na_v1.4 expression has been shown by RT-PCR • No other Na_v expression has been detected	• The 18-20-fold increase in [¹⁴C] Guanidine influx was completely blocked using TTX. (Na_v1.4 is a TTX sensitive channel)
L6 (rat myoblast cell) ATTC Number CRL-1458	• Expression of Na_v1.4 and 1.5	• The 10-15 fold increase in [¹⁴C] Guanidine influx was only partially blocked by TTX (Na_v1.5 is TTX resistant)
SH-SY5Y (Human neuroblastoma) ATTC Number CRL-2266	• Published Expression of Na_v1.9 and Na_v1.7 (Blum et al)	• The 10-16-fold increase in [¹⁴C] Guanidine influx above background. • was partially blocked by TTX (Na_v1.9 is TTX resistant)
SK-N-BE2C (a human neuroblastoma cell line ATCC Number CRL-2268)	• Expression of Na_v1.8	• Stimulation of BE2C cells with pyrethroids results in a 6 fold increase in [¹⁴C] Guanidine influx above background. • TTX partially blocked influx (Na_v1.8 is TTX resistant)
PC12 (rat pheochromocytoma) ATTC Number CRL-1721	• Expression of Na_v1.2 expression	• The 8-12-fold increase in [¹⁴C] Guanidine influx was completely blocked using TTX. (Na_v1.2 is a TTX sensitive channel)

It is also possible to employ recombinant cells expressing these sodium channels. Cloning and propagation of recombinant cells are known to those skilled in the art (see, for example, Klugbauer, N, et al., *EMBO J.* (1995), 14(6):1084-90; and Lossin, C., et al., *Neuron* (2002), 34, pp. 877-884)

Cells expressing the channel of interest are grown according to the supplier or in the case of a recombinant cell in the presence of selective growth media such as G418 (Gibco/Invitrogen). The cells are disassociated from the culture dishes with an enzymatic solution (1X) Trypsin/EDTA (Gibco/Invitrogen) and analyzed for density and

viability using haemocytometer (Neubauer). Disassociated cells are washed and resuspended in their culture media then plated into Scintiplates (Beckman Coulter Inc.) (approximately 100,000 cells/ well) and incubated at 37 °C/5 % CO₂ for 20-24 hours. After an extensive wash with Low sodium HEPES-buffered saline solution (LNBSS) (150 mM Choline Chloride, 20 nM HEPES (Sigma), 1mM Calcium Chloride, 5mM Potassium Chloride, 1 mM Magnesium Chloride, 10 mM Glucose) agents diluted with LNBSS are added to each well. (Varying concentrations of test agent may be used). The activation/radiolabel mixture contains aconitine (Sigma), and ¹⁴C-guanidine hydrochloride (ARC).

After loading the cells with test agent and activation/radiolabel mixture, the Scintiplates are incubated at ambient temperature. Following the incubation, the Scintiplates are extensively washed with LNBSS supplemented with guanidine (Sigma). The Scintiplates are dried and then counted using a Wallac MicroBeta TriLux (Perkin-Elmer Life Sciences). The ability of the test agent to block sodium channel activity is determined by comparing the amount of ¹⁴C-guanidine present inside the cells expressing the different sodium channels. Based on this data, a variety of calculations, as set out elsewhere in this specification, may be used to determine whether a test agent is selective for a particular sodium channel.

IC₅₀ value of a test agent for a specific sodium channel may be determined using the above general method. IC₅₀ may be determined using a 3, 8, 10, 12 or 16 point curve in duplicate or triplicate with a starting concentration of 1, 5 or 10µM diluted serially with a final concentration reaching the sub-nanomolar, nanomolar and low micromolar ranges. Typically the mid-point concentration of test agent is set at 1 µM, and sequential concentrations of half dilutions greater or smaller are applied (e.g. 0.5 µM; 5 µM and 0.25 µM; 10 µM and 0.125 µM; 20 µM etc.). The IC₅₀ curve is calculated using the 4 Parameter Logistic Model or Sigmoidal Dose-Response Model formula (fit = $A + ((B-A)/(1 + ((C/x)^D)))$).

The fold selectivity, factor of selectivity or multiple of selectivity, is calculated by dividing the IC₅₀ value of the test sodium channel by the reference sodium channel, for example, Na_v1.5.

Representative compounds of the invention, when tested in the above assay using a known cell line that expresses a sodium channel, demonstrated an IC₅₀ (nM) activity level as set forth below in Table 2 wherein "A" refers to an IC₅₀ activity level of from 1 nM to 10 nM, "B" refers to an IC₅₀ activity level from 10 nM to 100 nM, "C" refers to an IC₅₀ activity level from 100 nM to 1000 nM, and "D" refers to an IC₅₀ activity level

equal to or greater than 1000 nM. The Example numbers provided in Table 2 correspond to the Example numbers herein:

Table 2

Example Number	Compound Name	IC ₅₀ Activity Data (nM)
Example 1	1'-(2-cyclopropylethyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	A
Example 2	(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetic acid	D
Example 3	<i>N</i> -(4-chlorobenzyl)-2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	C
Example 4	4'-[6-(dimethylamino)pyridin-3-yl]-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	C
Example 5	4'-[(6-methoxypyridin-3-yl)amino]-1'-pentylspiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	C
Example 6	2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzoic acid	D
Example 7	<i>N</i> -[2-(4-chlorophenyl)ethyl]-2-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	C
Example 8	3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzoic acid	C
Example 9	<i>N</i> -[2-(3-chlorophenyl)ethyl]-3-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	C
Example 10	1'-(4-fluorobenzyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	B
Example 11	4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzoic acid	D
Example 12	<i>N</i> -(3-fluorophenyl)-4-[(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)methyl]benzamide	C

Example Number	Compound Name	IC ₅₀ Activity Data (nM)
Example 13	1'-(3-hydroxypropyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	B
Example 15	1'-{3-[(cyclopropylmethyl)amino]propyl}spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	D
Example 16	1'-(3-aminopropyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	D
Example 17	3-chloro- <i>N</i> -[3-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)propyl]thiophene-2-carboxamide	B
Example 18	1'-(2-aminoethyl)spiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-2'(1' <i>H</i>)-one	D
Example 19	1-(4-fluorophenyl)-3-[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]urea	D
Example 20	1'-pentyl-7 <i>H</i> -spiro[furo[3,4- <i>f</i>][1,3]benzodioxole-5,3'-indol]-2'(1' <i>H</i>)-one	A
Example 21	1'-pentylspiro[indeno[5,6- <i>d</i>][1,3]dioxole-5,3'-indole]-2',7(1' <i>H</i> ,6 <i>H</i>)-dione	A
Example 22	1-pentyl-6' <i>H</i> -spiro[indole-3,5'-naphtho[2,3- <i>d</i>][1,3]dioxole]-2,8'(1 <i>H</i> ,7' <i>H</i>)-dione	A
Example 23	1'-pentyl-6,7-dihydrospiro[indeno[5,6- <i>d</i>][1,3]dioxole-5,3'-indol]-2'(1' <i>H</i>)-one	C
Example 24	1-pentyl-7',8'-dihydro-6' <i>H</i> -spiro[indole-3,5'-naphtho[2,3- <i>d</i>][1,3]dioxol]-2(1 <i>H</i>)-one	A
Example 26	7-hydroxy-1'-pentyl-6,7-dihydrospiro[indeno[5,6- <i>d</i>][1,3]dioxole-5,3'-indol]-2'(1' <i>H</i>)-one	D
Example 27	7-methoxy-1'-pentyl-6,7-dihydrospiro[indeno[5,6- <i>d</i>][1,3]dioxole-5,3'-indol]-2'(1' <i>H</i>)-one	D
Example 28	1'-pentyl-6,7-dihydro-5 <i>H</i> -spiro[1,3-dioxolo[4,5- <i>g</i>]isoquinoline-8,3'-indole]-2',5(1' <i>H</i>)-dione	D

Example Number	Compound Name	IC ₅₀ Activity Data (nM)
Example 29	2'-oxo-1'-pentyl- <i>N</i> -pyridin-2-yl-1',2'-dihydrospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indole]-4'-carboxamide	D
Example 30	2'-oxo-1'-pentyl-1',2'-dihydrospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indole]-4'-carbonitrile	B
Example 31	1'-hexylspiro[1,3-dioxolo[4,5- <i>g</i>]chromene-8,3'-indole]-2',6'(1' <i>H</i> ,7 <i>H</i>)-dione	D
Example 32	1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(1' <i>H</i>)-one	B
Example 33	6-anilino-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(1' <i>H</i>)-one	D
Example 34	6-morpholin-4-yl-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(1' <i>H</i>)-one	D
Example 36	1'-pentyl-6-phenoxy spiro[1-benzofuran-3,3'-indol]-2'(1' <i>H</i>)-one	D
example 37	1'-pentyl-6-pyridin-3-ylspiro[1-benzofuran-3,3'-indol]-2'(1' <i>H</i>)-one	D
Example 38	1'-pentyl-6-pyridin-4-ylspiro[1-benzofuran-3,3'-indol]-2'(1' <i>H</i>)-one	C
Example 39	6-(methylsulfonyl)-1'-pentylspiro[1-benzofuran-3,3'-indol]-2'(1' <i>H</i>)-one	D
Example 40	1'-pentyl-6-(phenylsulfonyl)spiro[1-benzofuran-3,3'-indol]-2'(1' <i>H</i>)-one	C
Example 41	1'-pentyl-5-phenoxy spiro[1-benzofuran-3,3'-indol]-2'(1' <i>H</i>)-one	D
Example 48	1'-pentyl-5-pyridin-3-ylspiro[1-benzofuran-3,3'-indol]-2'(1' <i>H</i>)-one	C
Example 49	1'-pentyl-5-pyrimidin-5-ylspiro[1-benzofuran-3,3'-indol]-2'(1' <i>H</i>)-one	C
Example 50	1'-pentyl-5-pyridin-4-ylspiro[1-benzofuran-3,3'-indol]-2'(1' <i>H</i>)-one	C

Example Number	Compound Name	IC ₅₀ Activity Data (nM)
Example 51	2'-oxo-1'-pentyl-1',2'-dihydrospiro[1-benzofuran-3,3'-indole]-5-carbonitrile	C
Example 52	<i>N</i> -(2-fluorophenyl)-2-(2'-oxo-5-pyridin-3-ylspiro[1-benzofuran-3,3'-indol]-1'(2' <i>H</i>)-yl)acetamide	C
Example 54	1'-(diphenylmethyl)-5-pyridin-3-ylspiro[1-benzofuran-3,3'-indol]-2'(1' <i>H</i>)-one	D
Example 55	<i>tert</i> -butyl 3-(2'-oxo-1',2'-dihydrospiro[1-benzofuran-3,3'-indol]-5-yl)piperidine-1-carboxylate	D
Example 59	<i>N</i> -[2-(2'-oxospiro[furo[2,3- <i>f</i>][1,3]benzodioxole-7,3'-indol]-1'(2' <i>H</i>)-yl)ethyl]-2-(trifluoromethoxy)benzamide	C

BIOLOGICAL EXAMPLE 2

Electrophysiological Assay (*In vitro* assay)

Cells expressing the channel of interest are cultured in DMEM growth media (Gibco) with 0.5mg/mL G418, +/-1% PSG, and 10% heat-inactivated fetal bovine serum at 37C° and 5% CO₂. For electrophysiological recordings, cells are plated on 10mm dishes.

Whole cell recordings are examined by established methods of whole cell voltage clamp (Bean et al., *op. cit.*) using an Axopatch 200B amplifier and Clampex software (Axon Instruments, Union City, CA). All experiments are performed at ambient temperature. Electrodes are fire-polished to resistances of 2-4 Mohms. Voltage errors and capacitance artifacts are minimized by series resistance compensation and capacitance compensation, respectively. Data are acquired at 40 kHz and filtered at 5 kHz. The external (bath) solution consists of: NaCl (140 mM), KCl (5 mM), CaCl₂ (2 mM), MgCl₂ (1 mM), HEPES (10 mM) at pH 7.4. The internal (pipette) solution consists of (in mM): NaCl (5), CaCl₂ (0.1) MgCl₂ (2), CsCl (10), CsF (120), HEPES (10), EGTA (10), at pH 7.2.

To estimate the steady-state affinity of compounds for the resting and inactivated state of the channel (*K_r* and *K_i*, respectively), 12.5 ms test pulses to depolarizing voltages from -60 to +90 mV from a holding potential of -110 mV is used to construct current-voltage relationships (I-V curves). A voltage near the peak of the

IV-curve (−30 to 0 mV) is used as the test pulse throughout the remainder of the experiment. Steady-state inactivation (availability) curves is then constructed by measuring the current activated during a 8.75 ms test pulse following 1 second conditioning pulses to potentials ranging from −110 to −10 mV. To monitor channels at steady-state, a single "diary" protocol with a holding potential of −110mV is created to record the resting state current (10ms test pulse), the current after fast inactivation (5 ms pre-pulse of −80 to −50 mV followed by a 10 ms test pulse), and the current during various holding potentials (35 ms ramp to test pulse levels). Compounds are applied during the "diary" protocol and the block is monitored at 15 s intervals.

After the compounds equilibrate, the voltage-dependence of the steady-state inactivation in the presence of the compound is determined. Compounds that block the resting state of the channel decrease the current elicited during test pulses from all holding potentials, whereas compounds that primarily block the inactivated state decrease the current elicited during test pulses at more depolarized potentials. The currents at the resting state (I_{rest}) and the currents during the inactivated state ($I_{inactivated}$) are used to calculate steady-state affinity of compounds. Based on the Michaelis-Menton model of inhibition, the K_r and K_i is calculated as the concentration of compound needed to cause 50% inhibition of the I_{rest} or the $I_{inactivated}$, respectively.

$$\% \text{ inhibition} = \frac{V_{max} * [Drug]^h}{[Drug]^h + K_m^h}$$

V_{max} is the rate of inhibition, h is the Hill coefficient (for interacting sites), K_m is Michaelis-Menten constant, and $[Drug]$ is the concentration of the test compound. At 50% inhibition ($\frac{1}{2}V_{max}$) of the I_{rest} or $I_{inactivated}$, the drug concentration is numerically equal to K_m and approximates the K_r and K_i , respectively.

BIOLOGICAL EXAMPLE 3

In Vivo Assay for Benign Prostate Hyperplasia (BPH)

The effectiveness of the compounds of the present invention for treating BPH can be demonstrated by the following *in vivo* assay.

Dogs are dosed orally with test compounds at oral doses of between 0 mg/kg and 100 mg/kg for a period of 4 weeks. A control group receives placebo. The animals are sacrificed and the prostate glands dissected out, dabbed dry and then weighed. Test compounds are efficacious in a dose dependent manner within a range

of 5 mg/kg and 100 mg/kg if they significantly reduce the weight of the prostate in dogs when compared to the vehicle treated (0 mg/kg) controls.

BIOLOGICAL EXAMPLE 4

In Vivo Assay for Antihypercholesterolemia Efficacy and Antiatherosclerotic Efficacy

5 The effectiveness of the compounds of the present invention for treating hypercholesterolemia can be demonstrated by the following *in vivo* assay.

Dogs have cardiovascular systems similar to that of humans, making them ideal for studying the effects of medicinal compounds designed to treat cardiovascular disorders.

10 Dogs are dosed orally at a range of 0 mg/kg to 100 mg/kg daily with test compounds for a period of 2- 4 weeks. After 2 and 4 weeks the animals are bled and their serum collected for total cholesterol analysis and compared to the animals dosed with vehicle alone (0 mg/kg).

15 The measurement of cholesterol is one of the most common tests performed in the clinical laboratory setting. Simple fluorometric methods for the sensitive quantitation of total cholesterol in plasma or serum are commonly used. In one assay, cholesteryl esters in the sample are first hydrolyzed by cholesterol esterase. All cholesterol, whether previously esterified or existing free in the circulation, is then oxidized by cholesterol oxidase to the corresponding ketone and hydrogen peroxide.

20 ADHP (10-acetyl-3,7-dihydroxyphenoxazine) is utilized as a highly sensitive and stable probe for hydrogen peroxide. Horseradish peroxidase catalyzes the reaction of ADHP with hydrogen peroxide to yield the highly fluorescent product resorufin, which can be monitored using excitation wavelengths of 565-580 nm and emission wavelengths of 585-595 nm.

BIOLOGICAL EXAMPLE 5

In Vivo Assay for Treatment of Pruritis

25 The compounds of the invention can be evaluated for their activity as antipruritic agents by *in vivo* test using rodent models. One established model for peripherally elicited pruritus is through the injection of serotonin into the rostral back area (neck) in hairless rats. Prior to serotonin injections (e.g., 2 mg/ml, 50 μ L), a dose

30 of a compound of the present invention can be applied systemically through oral, intravenous or intraperitoneal routes or topically to a circular area fixed diameter (e.g. 18 mm). Following dosing, the serotonin injections are given in the area of the topical

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dosing. After serotonin injection the animal behaviour is monitored by video recording for 20 min-1.5 h, and the number of scratches in this time compared to vehicle treated animals. Thus, application of a compound of the current invention could suppress serotonin-induced scratching in rats.

* * * * *

All of the U.S. patents, U.S. patent application publications, U.S. patent applications, foreign patents, foreign patent applications and non-patent publications referred to in this specification and/or listed in the Application Data Sheet are incorporated herein by reference, in their entirety.

Although the foregoing invention has been described in some detail to facilitate understanding, it will be apparent that certain changes and modifications may be practiced within the scope of the appended claims. Accordingly, the described embodiments are to be considered as illustrative and not restrictive, and the invention is not to be limited to the details given herein, but may be modified within the scope and equivalents of the appended claims.

Throughout this specification and the claims which follow, unless the context requires otherwise, the word "comprise", and variations such as "comprises" and "comprising", will be understood to imply the inclusion of a stated integer or step or group of integers or steps but not the exclusion of any other integer or step or group of integers or steps.

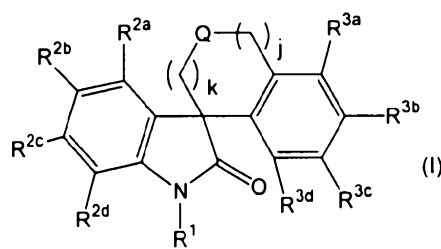
The reference in this specification to any prior publication (or information derived from it), or to any matter which is known, is not, and should not be taken as an acknowledgment or admission or any form of suggestion that that prior publication (or information derived from it) or known matter forms part of the common general knowledge in the field of endeavour to which this specification relates.

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THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A method of treating hypercholesterolemia in a mammal, wherein the method comprises administering to the mammal in need thereof a therapeutically effective amount of a compound of formula (I):



wherein:

j and k are each independently 0, 1, 2 or 3;

Q is $-C(R^{1a})H-$, $-O-$, $-S(O)_m-$ (where m is 1 or 2), $-CF_2-$, $-C(O)O-$, $-C(O)N(R^5)-$ or $-N(R^5)C(O)-$;

R^{1a} is $-OR^5$;

R^1 is hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$, $-R^9-S(O)_m-R^5$ (where m is 0, 1 or 2), $-R^8-OR^5$, $-R^8-CN$, $-R^9-P(O)(OR^5)_2$, or $-R^9-O-R^9-OR^5$;

or R^1 is aralkyl substituted by $-C(O)N(R^6)R^7$ where:

R^6 is hydrogen, alkyl, aryl or aralkyl; and

R^7 is hydrogen, alkyl, haloalkyl, $-R^9-CN$, $-R^9-OR^5$, $-R^9-N(R^4)R^5$, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

or R^6 and R^7 , together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^6 and R^7 may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, $-R^8-CN$, $-R^8-OR^5$, heterocyclyl and heteroaryl;

or R^1 is aralkyl optionally substituted by one or more substituents selected from the group consisting of $-R^8-OR^5$, $-C(O)OR^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl,

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heterocyclyl and heteroaryl;

or R^1 is $-R^9-N(R^{10})R^{11}$, $-R^9-N(R^{12})C(O)R^{11}$ or $-R^9-N(R^{10})C(O)N(R^{10})R^{11}$ where:

each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl,

heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$,

$-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or

$-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl,

heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may

be optionally substituted by one or more substituents selected from the

group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro,

$-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

or R^1 is heterocyclylalkyl or heteroarylalkyl where the heterocyclylalkyl or the

heteroarylalkyl group is optionally substituted by one or more substituents selected

from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl,

aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$,

$-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$

(where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of

hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy,

cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl,

heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$,

$-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$,

$-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$,

$-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$,

$-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$,

and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each

n is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl,

heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for

R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more

substituents selected from the group consisting of alkyl, alkenyl, alkynyl,

alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl,

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aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$, $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not $-C(O)OCH_3$, $-C(O)NH_2$, iodo or cyano;

or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2d} are as defined above;

or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;

R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;

or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3d} are as defined above;

or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3b} are as defined above;

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each R^4 and R^5 is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl, and heteroarylalkyl;

or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl;

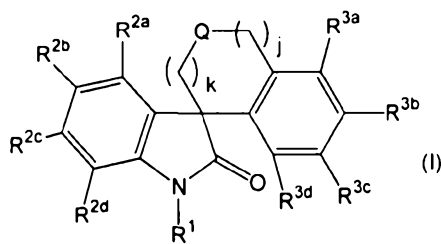
each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and

each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain;

or a stereoisomer, enantiomer or tautomer thereof;

or a pharmaceutically acceptable salt or solvate thereof.

2. A method of treating benign prostatic hyperplasia in a mammal, wherein the method comprises administering to the mammal in need thereof a therapeutically effective amount of a compound of formula (I):



wherein:

j and k are each independently 0, 1, 2 or 3;

Q is $-C(R^{1a})H-$, $-O-$, $-S(O)_m-$ (where m is 1 or 2), $-CF_2-$, $-C(O)O-$, $-C(O)N(R^5)-$ or $-N(R^5)C(O)-$;

R^{1a} is $-OR^5$;

R^1 is hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$, $-R^9-S(O)_m-R^5$ (where m is 0, 1 or 2), $-R^8-OR^5$, $-R^8-CN$, $-R^9-P(O)(OR^5)_2$, or $-R^9-O-R^9-OR^5$;

or R^1 is aralkyl substituted by $-C(O)N(R^6)R^7$ where:

R^6 is hydrogen, alkyl, aryl or aralkyl; and

R^7 is hydrogen, alkyl, haloalkyl, $-R^9-CN$, $-R^9-OR^5$, $-R^9-N(R^4)R^5$, aryl, aralkyl,

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cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

or R^6 and R^7 , together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^6 and R^7 may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, $-R^8-CN$, $-R^8-OR^5$, heterocyclyl and heteroaryl;

or R^1 is aralkyl optionally substituted by one or more substituents selected from the group consisting of $-R^8-OR^5$, $-C(O)OR^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

or R^1 is $-R^9-N(R^{10})R^{11}$, $-R^9-N(R^{12})C(O)R^{11}$ or $-R^9-N(R^{10})C(O)N(R^{10})R^{11}$ where:

each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, $-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

or R^1 is heterocyclylalkyl or heteroarylalkyl where the heterocyclylalkyl or the heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$ (where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$,

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-S(O)_mR⁴, -OS(O)₂CF₃, -R⁸-C(O)R⁴, -C(S)R⁴, -C(R⁴)₂C(O)R⁵, -R⁸-C(O)OR⁴,
 -C(S)OR⁴, -R⁸-C(O)N(R⁴)R⁵, -C(S)N(R⁴)R⁵, -N(R⁵)C(O)R⁴, -N(R⁵)C(S)R⁴,
 -N(R⁵)C(O)OR⁴, -N(R⁵)C(S)OR⁴, -N(R⁵)C(O)N(R⁴)R⁵, -N(R⁵)C(S)N(R⁴)R⁵,
 -N(R⁵)S(O)_nR⁴, -N(R⁵)S(O)_nN(R⁴)R⁵, -R⁸-S(O)_nN(R⁴)R⁵, -N(R⁵)C(=NR⁵)N(R⁴)R⁵,
 and -N(R⁵)C(=N-CN)N(R⁴)R⁵, wherein each m is independently 0, 1, or 2 and each
 n is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl,

heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for

R^{2a}, R^{2b}, R^{2c} and R^{2d} may be optionally substituted by one or more

substituents selected from the group consisting of alkyl, alkenyl, alkynyl,

alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl,

aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl,

heteroarylalkyl, -R⁸-CN, -R⁸-NO₂, -R⁸-OR⁵, -R⁸-N(R⁴)R⁵, -S(O)_mR⁴,

-R⁸-S(O)_nN(R⁴)R⁵, -R⁸-C(O)R⁴, -R⁸-C(O)OR⁴, -R⁸-C(O)N(R⁴)R⁵,

-N(R⁵)C(O)R⁴, and -N(R⁵)S(O)_nR⁴, wherein each m is independently 0, 1,

or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not -C(O)OCH₃, -C(O)NH₂, iodo or cyano;

or R^{2a} and R^{2b}, together with the carbon ring atoms to which they are directly attached,

may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl,

and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c}, together with the carbon ring atoms to which they are directly attached,

may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl,

and R^{2a} and R^{2d} are as defined above;

or R^{2c} and R^{2d}, together with the carbon ring atoms to which they are directly attached,

may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl,

and R^{2a} and R^{2b} are as defined above;

R^{3a}, R^{3b}, R^{3c} and R^{3d} are each independently selected from the group consisting of

hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy,

cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl,

heteroaryl, heteroarylalkyl, -R⁸-CN, -R⁸-NO₂, -R⁸-OR⁵, -R⁸-N(R⁴)R⁵, -N=C(R⁴)R⁵,

-S(O)_mR⁴, -OS(O)₂CF₃, -R⁸-C(O)R⁴, -C(S)R⁴, -C(R⁴)₂C(O)R⁵, -R⁸-C(O)OR⁴,

-C(S)OR⁴, -R⁸-C(O)N(R⁴)R⁵, -C(S)N(R⁴)R⁵, -N(R⁵)C(O)R⁴, -N(R⁵)C(S)R⁴,

-N(R⁵)C(O)OR⁴, -N(R⁵)C(S)OR⁴, -N(R⁵)C(O)N(R⁴)R⁵, -N(R⁵)C(S)N(R⁴)R⁵,

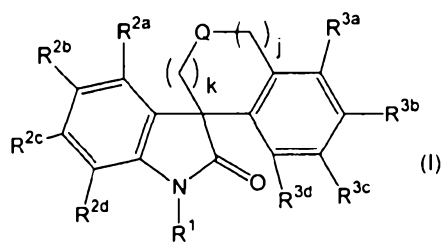
-N(R⁵)S(O)_nR⁴, -N(R⁵)S(O)_nN(R⁴)R⁵, -R⁸-S(O)_nN(R⁴)R⁵, -N(R⁵)C(=NR⁵)N(R⁴)R⁵,

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- and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;
- or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;
- or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3d} are as defined above;
- or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3b} are as defined above;
- each R^4 and R^5 is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;
- or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl;
- each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and
- each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain;
- or a stereoisomer, enantiomer or tautomer thereof;
- or a pharmaceutically acceptable salt or solvate thereof.

3. A method of treating pruritis in a mammal, wherein the method comprises administering to the mammal in need thereof a therapeutically effective amount of a compound of formula (I):



wherein:

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j and k are each independently 0, 1, 2 or 3;

Q is $-C(R^{1a})H-$, $-O-$, $-S(O)_m-$ (where m is 1 or 2), $-CF_2-$, $-C(O)O-$, $-C(O)N(R^5)-$ or $-N(R^5)C(O)-$;

R^{1a} is $-OR^5$;

R^1 is hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$, $-R^9-S(O)_m-R^5$ (where m is 0, 1 or 2), $-R^8-OR^5$, $-R^8-CN$, $-R^9-P(O)(OR^5)_2$, or $-R^9-O-R^9-OR^5$;

or R^1 is aralkyl substituted by $-C(O)N(R^6)R^7$ where:

R^6 is hydrogen, alkyl, aryl or aralkyl; and

R^7 is hydrogen, alkyl, haloalkyl, $-R^9-CN$, $-R^9-OR^5$, $-R^9-N(R^4)R^5$, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

or R^6 and R^7 , together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^6 and R^7 may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, $-R^8-CN$, $-R^8-OR^5$, heterocyclyl and heteroaryl;

or R^1 is aralkyl optionally substituted by one or more substituents selected from the group consisting of $-R^8-OR^5$, $-C(O)OR^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

or R^1 is $-R^9-N(R^{10})R^{11}$, $-R^9-N(R^{12})C(O)R^{11}$ or $-R^9-N(R^{10})C(O)N(R^{10})R^{11}$ where:

each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro,

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$-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

or R^1 is heterocyclalkyl or heteroarylalkyl where the heterocyclalkyl or the

heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$ (where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of

hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl,

heterocyclyl, heterocyclalkyl, heteroaryl and heteroarylalkyl groups for R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$, $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not $-C(O)OCH_3$, $-C(O)NH_2$, iodo or cyano;

or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2d} are as defined above;

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or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;

R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;

or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3d} are as defined above;

or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3b} are as defined above;

each R^4 and R^5 is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;

or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl;

each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and

each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain;

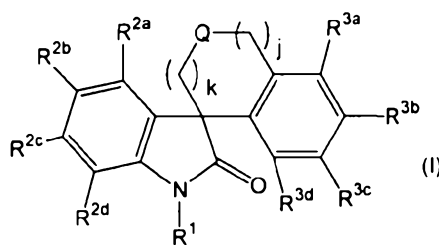
or a stereoisomer, enantiomer or tautomer thereof;

or a pharmaceutically acceptable salt or solvate thereof.

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4. A method of treating hormone sensitive cancer in a mammal, wherein the method comprises administering to the mammal in need thereof a therapeutically effective amount of a compound of formula (I):



wherein:

j and k are each independently 0, 1, 2 or 3;

Q is $-C(R^{1a})H-$, $-O-$, $-S(O)_m-$ (where m is 1 or 2), $-CF_2-$, $-C(O)O-$, $-C(O)N(R^5)-$ or $-N(R^5)C(O)-$;

R^{1a} is $-OR^5$;

R^1 is hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$, $-R^9-S(O)_m-R^5$ (where m is 0, 1 or 2), $-R^8-OR^5$, $-R^8-CN$, $-R^9-P(O)(OR^5)_2$, or $-R^9-O-R^9-OR^5$;

or R^1 is aralkyl substituted by $-C(O)N(R^6)R^7$ where:

R^6 is hydrogen, alkyl, aryl or aralkyl; and

R^7 is hydrogen, alkyl, haloalkyl, $-R^9-CN$, $-R^9-OR^5$, $-R^9-N(R^4)R^5$, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

or R^6 and R^7 , together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^6 and R^7 may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, $-R^8-CN$, $-R^8-OR^5$, heterocyclyl and heteroaryl;

or R^1 is aralkyl optionally substituted by one or more substituents selected from the group consisting of $-R^8-OR^5$, $-C(O)OR^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

or R^1 is $-R^9-N(R^{10})R^{11}$, $-R^9-N(R^{12})C(O)R^{11}$ or $-R^9-N(R^{10})C(O)N(R^{10})R^{11}$ where:

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each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, $-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

or R^1 is heterocyclylalkyl or heteroarylalkyl where the heterocyclylalkyl or the heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$ (where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$,

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$-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$,
 $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1,
 or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not $-C(O)OCH_3$, $-C(O)NH_2$, iodo or cyano;

or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl,
 and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl,
 and R^{2a} and R^{2d} are as defined above;

or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl,
 and R^{2a} and R^{2b} are as defined above;

R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of
 hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy,
 cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl,
 heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$,
 $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$,
 $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$,
 $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$,
 $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$,
 and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and
 each n is independently 1 or 2;

or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and
 R^{3c} and R^{3d} are as defined above;

or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and
 R^{3a} and R^{3d} are as defined above;

or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and
 R^{3a} and R^{3b} are as defined above;

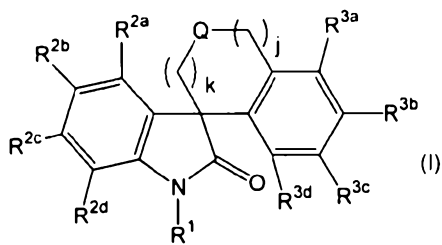
each R^4 and R^5 is independently selected from the group consisting of hydrogen, alkyl,
 alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl,

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heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;
 or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl;
 each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and
 each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain;
 or a stereoisomer, enantiomer or tautomer thereof;
 or a pharmaceutically acceptable salt or solvate thereof.

5. A method of treating hypercholesterolemia in a mammal, wherein the method comprises administering to the mammal in need thereof a therapeutically effective amount of a compound of formula (I):



wherein:

j is 0 and k is 1 or 2;

Q is $-C(R^{1a})H-$, $-C(O)-$, $-CF_2-$, $-C(O)O-$ or $-N(R^5)C(O)-$;

R^{1a} is hydrogen or $-OR^5$;

R^1 is ethyl, *n*-propyl, 1-methylethyl, *n*-butyl, *n*-pentyl, 1,1-dimethylethyl, 3-methylhexyl, 2-methylhexyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$, $-R^9-S(O)_m-R^5$ (where m is 0, 1 or 2), $-R^8-OR^5$, $-R^8-CN$, $-R^9-P(O)(OR^5)_2$, or $-R^9-O-R^9-OR^5$;

or R^1 is aralkyl substituted by $-C(O)N(R^6)R^7$ where:

R^6 is hydrogen, alkyl, aryl or aralkyl; and

R^7 is hydrogen, alkyl, haloalkyl, $-R^9-CN$, $-R^9-OR^5$, $-R^9-N(R^4)R^5$, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

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or R^6 and R^7 , together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^6 and R^7 may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, $-R^8-CN$, $-R^8-OR^5$, heterocyclyl and heteroaryl;

or R^1 is aralkyl optionally substituted by one or more substituents selected from the group consisting of $-R^8-OR^5$, $-C(O)OR^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

or R^1 is $-R^9-N(R^{10})R^{11}$, $-R^9-N(R^{12})C(O)R^{11}$ or $-R^9-N(R^{10})C(O)N(R^{10})R^{11}$ where:

each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, $-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

or R^1 is heterocyclylalkyl or heteroarylalkyl where the heterocyclylalkyl or the heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$ (where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$,

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-N(R⁵)C(O)OR⁴, -N(R⁵)C(S)OR⁴, -N(R⁵)C(O)N(R⁴)R⁵, -N(R⁵)C(S)N(R⁴)R⁵,
 -N(R⁵)S(O)_nR⁴, -N(R⁵)S(O)_nN(R⁴)R⁵, -R⁸-S(O)_nN(R⁴)R⁵, -N(R⁵)C(=NR⁵)N(R⁴)R⁵,
 and -N(R⁵)C(=N-CN)N(R⁴)R⁵, wherein each m is independently 0, 1, or 2 and each
 n is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl,

heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for
 R^{2a}, R^{2b}, R^{2c} and R^{2d} may be optionally substituted by one or more
 substituents selected from the group consisting of alkyl, alkenyl, alkynyl,
 alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl,
 aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl,
 heteroarylalkyl, -R⁸-CN, -R⁸-NO₂, -R⁸-OR⁵, -R⁸-N(R⁴)R⁵, -S(O)_mR⁴,
 -R⁸-S(O)_nN(R⁴)R⁵, -R⁸-C(O)R⁴, -R⁸-C(O)OR⁴, -R⁸-C(O)N(R⁴)R⁵,
 -N(R⁵)C(O)R⁴, and -N(R⁵)S(O)_nR⁴, wherein each m is independently 0, 1,
 or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not -C(O)OCH₃, -C(O)NH₂, iodo or cyano;

or R^{2a} and R^{2b}, together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl,
 and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c}, together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl,
 and R^{2a} and R^{2d} are as defined above;

or R^{2c} and R^{2d}, together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl,
 and R^{2a} and R^{2b} are as defined above;

R^{3a}, R^{3b}, R^{3c} and R^{3d} are each independently selected from the group consisting of
 hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy,
 cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl,
 heteroaryl, heteroarylalkyl, -R⁸-CN, -R⁸-NO₂, -R⁸-OR⁵, -R⁸-N(R⁴)R⁵, -N=C(R⁴)R⁵,
 -S(O)_mR⁴, -OS(O)₂CF₃, -R⁸-C(O)R⁴, -C(S)R⁴, -C(R⁴)₂C(O)R⁵, -R⁸-C(O)OR⁴,
 -C(S)OR⁴, -R⁸-C(O)N(R⁴)R⁵, -C(S)N(R⁴)R⁵, -N(R⁵)C(O)R⁴, -N(R⁵)C(S)R⁴,
 -N(R⁵)C(O)OR⁴, -N(R⁵)C(S)OR⁴, -N(R⁵)C(O)N(R⁴)R⁵, -N(R⁵)C(S)N(R⁴)R⁵,
 -N(R⁵)S(O)_nR⁴, -N(R⁵)S(O)_nN(R⁴)R⁵, -R⁸-S(O)_nN(R⁴)R⁵, -N(R⁵)C(=NR⁵)N(R⁴)R⁵,
 and -N(R⁵)C(N=C(R⁴)R⁵)N(R⁴)R⁵, wherein each m is independently 0, 1, or 2 and
 each n is independently 1 or 2;

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or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;

or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^d are as defined above;

or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3b} are as defined above;

each R^4 and R^5 is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;

or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl;

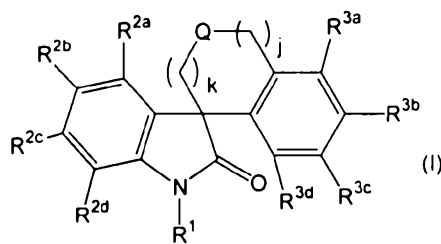
each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and

each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain;

or a stereoisomer, enantiomer or tautomer thereof;

or a pharmaceutically acceptable salt or solvate thereof.

6. A method of treating benign prostatic hyperplasia in a mammal, wherein the method comprises administering to the mammal in need thereof a therapeutically effective amount of a compound of formula (I):



wherein:

j is 0 and k is 1 or 2;

Q is $-C(R^{1a})H-$, $-C(O)-$, $-CF_2-$, $-C(O)O-$ or $-N(R^5)C(O)-$;

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R^{1a} is hydrogen or $-OR^5$;

R^1 is ethyl, *n*-propyl, 1-methylethyl, *n*-butyl, *n*-pentyl, 1,1-dimethylethyl, 3-methylhexyl, 2-methylhexyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$, $-R^9-S(O)_m-R^5$ (where *m* is 0, 1 or 2), $-R^8-OR^5$, $-R^8-CN$, $-R^9-P(O)(OR^5)_2$, or $-R^9-O-R^9-OR^5$;

or R^1 is aralkyl substituted by $-C(O)N(R^6)R^7$ where:

R^6 is hydrogen, alkyl, aryl or aralkyl; and

R^7 is hydrogen, alkyl, haloalkyl, $-R^9-CN$, $-R^9-OR^5$, $-R^9-N(R^4)R^5$, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

or R^6 and R^7 , together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^6 and R^7 may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, $-R^8-CN$, $-R^8-OR^5$, heterocyclyl and heteroaryl;

or R^1 is aralkyl optionally substituted by one or more substituents selected from the group consisting of $-R^8-OR^5$, $-C(O)OR^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

or R^1 is $-R^9-N(R^{10})R^{11}$, $-R^9-N(R^{12})C(O)R^{11}$ or $-R^9-N(R^{10})C(O)N(R^{10})R^{11}$ where:

each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, $-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

or R^1 is heterocyclylalkyl or heteroarylalkyl where the heterocyclylalkyl or the

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heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$ (where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$, $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not $-C(O)OCH_3$, $-C(O)NH_2$, iodo or cyano;

or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2d} are as defined above;

or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl,

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and R^{2a} and R^{2b} are as defined above;

R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;

or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^d are as defined above;

or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3b} are as defined above;

each R^4 and R^5 is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;

or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl;

each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and

each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain;

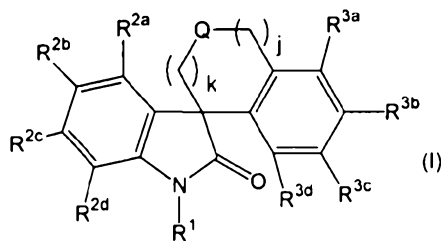
or a stereoisomer, enantiomer or tautomer thereof;

or a pharmaceutically acceptable salt or solvate thereof.

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7. A method of treating pruritis in a mammal, wherein the method comprises administering to the mammal in need thereof a therapeutically effective amount of a compound of formula (I):



wherein:

j is 0 and k is 1 or 2;

Q is $-\text{C}(\text{R}^{1a})\text{H}-$, $-\text{C}(\text{O})-$, $-\text{CF}_2-$, $-\text{C}(\text{O})\text{O}-$ or $-\text{N}(\text{R}^5)\text{C}(\text{O})-$;

R^{1a} is hydrogen or $-\text{OR}^5$;

R^1 is ethyl, *n*-propyl, 1-methylethyl, *n*-butyl, *n*-pentyl, 1,1-dimethylethyl, 3-methylhexyl, 2-methylhexyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, $-\text{R}^8-\text{C}(\text{O})\text{R}^5$, $-\text{R}^8-\text{C}(\text{O})\text{OR}^5$, $-\text{R}^8-\text{C}(\text{O})\text{N}(\text{R}^4)\text{R}^5$, $-\text{S}(\text{O})_2-\text{R}^5$, $-\text{R}^9-\text{S}(\text{O})_m-\text{R}^5$ (where m is 0, 1 or 2), $-\text{R}^8-\text{OR}^5$, $-\text{R}^8-\text{CN}$, $-\text{R}^9-\text{P}(\text{O})(\text{OR}^5)_2$, or $-\text{R}^9-\text{O}-\text{R}^9-\text{OR}^5$;

or R^1 is aralkyl substituted by $-\text{C}(\text{O})\text{N}(\text{R}^6)\text{R}^7$ where:

R^6 is hydrogen, alkyl, aryl or aralkyl; and

R^7 is hydrogen, alkyl, haloalkyl, $-\text{R}^9-\text{CN}$, $-\text{R}^9-\text{OR}^5$, $-\text{R}^9-\text{N}(\text{R}^4)\text{R}^5$, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

or R^6 and R^7 , together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^6 and R^7 may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, $-\text{R}^8-\text{CN}$, $-\text{R}^8-\text{OR}^5$, heterocyclyl and heteroaryl;

or R^1 is aralkyl optionally substituted by one or more substituents selected from the group consisting of $-\text{R}^8-\text{OR}^5$, $-\text{C}(\text{O})\text{OR}^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

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or R^1 is $-R^9-N(R^{10})R^{11}$, $-R^9-N(R^{12})C(O)R^{11}$ or $-R^9-N(R^{10})C(O)N(R^{10})R^{11}$ where:

each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, $-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

or R^1 is heterocyclylalkyl or heteroarylalkyl where the heterocyclylalkyl or the heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$ (where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl,

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heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$,
 $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$,
 $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1,
 or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not $-C(O)OCH_3$, $-C(O)NH_2$, iodo or cyano;

or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl,
 and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl,
 and R^{2a} and R^{2d} are as defined above;

or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl,
 and R^{2a} and R^{2b} are as defined above;

R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of
 hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy,
 cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl,
 heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$,
 $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$,
 $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$,
 $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$,
 $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$,
 and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and
 each n is independently 1 or 2;

or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached,
 form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c}
 and R^{3d} are as defined above;

or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and
 R^{3a} and R^{3d} are as defined above;

or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and
 R^{3a} and R^{3b} are as defined above;

each R^4 and R^5 is independently selected from the group consisting of hydrogen, alkyl,

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alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl, and heteroarylalkyl;

or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a heterocycl or heteroaryl;

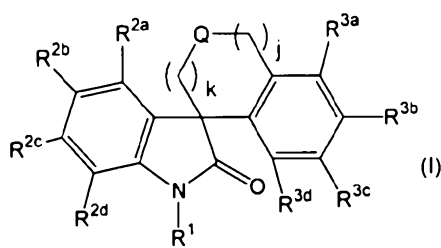
each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and

each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain;

or a stereoisomer, enantiomer or tautomer thereof;

or a pharmaceutically acceptable salt or solvate thereof.

8. A method of treating hormone sensitive cancer in a mammal, wherein the method comprises administering to the mammal in need thereof a therapeutically effective amount of a compound of formula (I):



wherein:

j is 0 and k is 1 or 2;

Q is $-C(R^{1a})H-$, $-C(O)-$, $-CF_2-$, $-C(O)O-$ or $-N(R^5)C(O)-$;

R^{1a} is hydrogen or $-OR^5$;

R^1 is ethyl, *n*-propyl, 1-methylethyl, *n*-butyl, *n*-pentyl, 1,1-dimethylethyl, 3-methylhexyl,

2-methylhexyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl,

heteroaryl, heterocyclyl, $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$,

$-R^9-S(O)_m-R^5$ (where m is 0, 1 or 2), $-R^8-OR^5$, $-R^8-CN$, $-R^9-P(O)(OR^5)_2$, or

$-R^9-O-R^9-OR^5$;

or R^1 is aralkyl substituted by $-C(O)N(R^6)R^7$ where:

R^6 is hydrogen, alkyl, aryl or aralkyl; and

R^7 is hydrogen, alkyl, haloalkyl, $-R^9-CN$, $-R^9-OR^5$, $-R^9-N(R^4)R^5$, aryl, aralkyl,

cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclalkyl, heteroaryl, or

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heteroarylalkyl;

or R^6 and R^7 , together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^6 and R^7 may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, $-R^8-CN$, $-R^8-OR^5$, heterocyclyl and heteroaryl;

or R^1 is aralkyl optionally substituted by one or more substituents selected from the group consisting of $-R^8-OR^5$, $-C(O)OR^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

or R^1 is $-R^9-N(R^{10})R^{11}$, $-R^9-N(R^{12})C(O)R^{11}$ or $-R^9-N(R^{10})C(O)N(R^{10})R^{11}$ where:

each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, $-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

or R^1 is heterocyclylalkyl or heteroarylalkyl where the heterocyclylalkyl or the heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$ (where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$,

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-C(S)OR⁴, -R⁸-C(O)N(R⁴)R⁵, -C(S)N(R⁴)R⁵, -N(R⁵)C(O)R⁴, -N(R⁵)C(S)R⁴,
 -N(R⁵)C(O)OR⁴, -N(R⁵)C(S)OR⁴, -N(R⁵)C(O)N(R⁴)R⁵, -N(R⁵)C(S)N(R⁴)R⁵,
 -N(R⁵)S(O)_nR⁴, -N(R⁵)S(O)_nN(R⁴)R⁵, -R⁸-S(O)_nN(R⁴)R⁵, -N(R⁵)C(=NR⁵)N(R⁴)R⁵,
 and -N(R⁵)C(=N-CN)N(R⁴)R⁵, wherein each m is independently 0, 1, or 2 and each
 n is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl,

heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for
 R^{2a}, R^{2b}, R^{2c} and R^{2d} may be optionally substituted by one or more
 substituents selected from the group consisting of alkyl, alkenyl, alkynyl,
 alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl,
 aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl,
 heteroarylalkyl, -R⁸-CN, -R⁸-NO₂, -R⁸-OR⁵, -R⁸-N(R⁴)R⁵, -S(O)_mR⁴,
 -R⁸-S(O)_nN(R⁴)R⁵, -R⁸-C(O)R⁴, -R⁸-C(O)OR⁴, -R⁸-C(O)N(R⁴)R⁵,
 -N(R⁵)C(O)R⁴, and -N(R⁵)S(O)_nR⁴, wherein each m is independently 0, 1,
 or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not -C(O)OCH₃, -C(O)NH₂, iodo or cyano;

or R^{2a} and R^{2b}, together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl,
 and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c}, together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl,
 and R^{2a} and R^{2d} are as defined above;

or R^{2c} and R^{2d}, together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl,
 and R^{2a} and R^{2b} are as defined above;

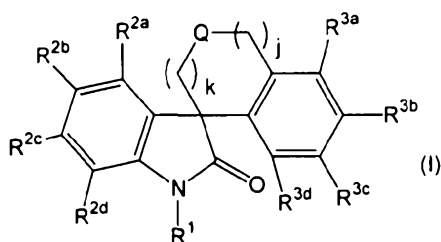
R^{3a}, R^{3b}, R^{3c} and R^{3d} are each independently selected from the group consisting of
 hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy,
 cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl,
 heteroaryl, heteroarylalkyl, -R⁸-CN, -R⁸-NO₂, -R⁸-OR⁵, -R⁸-N(R⁴)R⁵, -N=C(R⁴)R⁵,
 -S(O)_mR⁴, -OS(O)₂CF₃, -R⁸-C(O)R⁴, -C(S)R⁴, -C(R⁴)₂C(O)R⁵, -R⁸-C(O)OR⁴,
 -C(S)OR⁴, -R⁸-C(O)N(R⁴)R⁵, -C(S)N(R⁴)R⁵, -N(R⁵)C(O)R⁴, -N(R⁵)C(S)R⁴,
 -N(R⁵)C(O)OR⁴, -N(R⁵)C(S)OR⁴, -N(R⁵)C(O)N(R⁴)R⁵, -N(R⁵)C(S)N(R⁴)R⁵,
 -N(R⁵)S(O)_nR⁴, -N(R⁵)S(O)_nN(R⁴)R⁵, -R⁸-S(O)_nN(R⁴)R⁵, -N(R⁵)C(=NR⁵)N(R⁴)R⁵,
 and -N(R⁵)C(N=C(R⁴)R⁵)N(R⁴)R⁵, wherein each m is independently 0, 1, or 2 and

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- each n is independently 1 or 2;
- or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;
- or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3d} are as defined above;
- or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3b} are as defined above;
- each R^4 and R^5 is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl, and heteroarylalkyl;
- or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl;
- each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and
- each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain;
- or a stereoisomer, enantiomer or tautomer thereof;
- or a pharmaceutically acceptable salt or solvate thereof.

9. Use of a compound of formula (I):



wherein:

j and k are each independently 0, 1, 2 or 3;

Q is $-C(R^{1a})H-$, $-O-$, $-S(O)_m-$ (where m is 1 or 2), $-CF_2-$, $-C(O)O-$, $-C(O)N(R^5)-$ or $-N(R^5)C(O)-$;

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R^{1a} is $-OR^5$;

R^1 is hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$, $-R^9-S(O)_m-R^5$ (where m is 0, 1 or 2), $-R^8-OR^5$, $-R^8-CN$, $-R^9-P(O)(OR^5)_2$, or $-R^9-O-R^9-OR^5$;

or R^1 is aralkyl substituted by $-C(O)N(R^6)R^7$ where:

R^6 is hydrogen, alkyl, aryl or aralkyl; and

R^7 is hydrogen, alkyl, haloalkyl, $-R^9-CN$, $-R^9-OR^5$, $-R^9-N(R^4)R^5$, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

or R^6 and R^7 , together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^6 and R^7 may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, $-R^8-CN$, $-R^8-OR^5$, heterocyclyl and heteroaryl;

or R^1 is aralkyl optionally substituted by one or more substituents selected from the group consisting of $-R^8-OR^5$, $-C(O)OR^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

or R^1 is $-R^9-N(R^{10})R^{11}$, $-R^9-N(R^{12})C(O)R^{11}$ or $-R^9-N(R^{10})C(O)N(R^{10})R^{11}$ where:

each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, $-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

or R^1 is heterocyclylalkyl or heteroarylalkyl where the heterocyclylalkyl or the heteroarylalkyl group is optionally substituted by one or more substituents selected

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from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$ (where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$, $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not $-C(O)OCH_3$, $-C(O)NH_2$, iodo or cyano;

or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2d} are as defined above;

or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;

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R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;

or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3d} are as defined above;

or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3b} are as defined above;

each R^4 and R^5 is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;

or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl;

each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and

each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain;

or a stereoisomer, enantiomer or tautomer thereof;

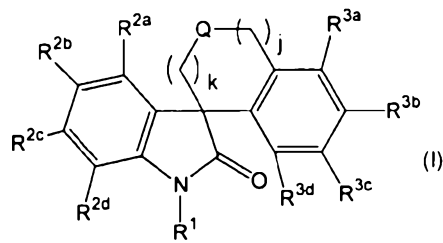
or a pharmaceutically acceptable salt or solvate thereof,

in the manufacture of a medicament for the treatment of hypercholesterolemia.

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10. Use of a compound of formula (I):



wherein:

j and k are each independently 0, 1, 2 or 3;

Q is $-C(R^{1a})H-$, $-O-$, $-S(O)_m-$ (where m is 1 or 2), $-CF_2-$, $-C(O)O-$, $-C(O)N(R^5)-$ or $-N(R^5)C(O)-$;

R^{1a} is $-OR^5$;

R^1 is hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$, $-R^9-S(O)_m-R^5$ (where m is 0, 1 or 2), $-R^8-OR^5$, $-R^8-CN$, $-R^9-P(O)(OR^5)_2$, or $-R^9-O-R^9-OR^5$;

or R^1 is aralkyl substituted by $-C(O)N(R^6)R^7$ where:

R^6 is hydrogen, alkyl, aryl or aralkyl; and

R^7 is hydrogen, alkyl, haloalkyl, $-R^9-CN$, $-R^9-OR^5$, $-R^9-N(R^4)R^5$, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclalkyl, heteroaryl, or heteroarylalkyl;

or R^6 and R^7 , together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclalkyl, heteroaryl and heteroarylalkyl groups for R^6 and R^7 may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, $-R^8-CN$, $-R^8-OR^5$, heterocyclyl and heteroaryl;

or R^1 is aralkyl optionally substituted by one or more substituents selected from the group consisting of $-R^8-OR^5$, $-C(O)OR^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

or R^1 is $-R^9-N(R^{10})R^{11}$, $-R^9-N(R^{12})C(O)R^{11}$ or $-R^9-N(R^{10})C(O)N(R^{10})R^{11}$ where:
each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

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each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, $-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

or R^1 is heterocyclylalkyl or heteroarylalkyl where the heterocyclylalkyl or the heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$ (where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$, $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$,

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$-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not $-C(O)OCH_3$, $-C(O)NH_2$, iodo or cyano;

or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2d} are as defined above;

or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;

R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;

or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3d} are as defined above;

or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3b} are as defined above;

each R^4 and R^5 is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;

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or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl;

each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and

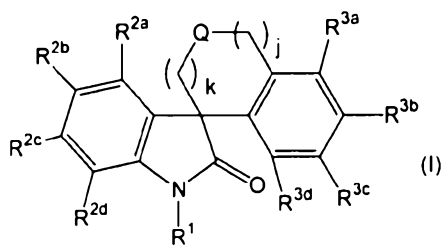
each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain;

or a stereoisomer, enantiomer or tautomer thereof;

or a pharmaceutically acceptable salt or solvate thereof,

in the manufacture of a medicament for the treatment of benign prostatic hyperplasia.

11. Use of a compound of formula (I):



wherein:

j and k are each independently 0, 1, 2 or 3;

Q is $-C(R^{1a})H-$, $-O-$, $-S(O)_m-$ (where m is 1 or 2), $-CF_2-$, $-C(O)O-$, $-C(O)N(R^5)-$ or $-N(R^5)C(O)-$;

R^{1a} is $-OR^5$;

R^1 is hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$, $-R^9-S(O)_m-R^5$ (where m is 0, 1 or 2), $-R^8-OR^5$, $-R^8-CN$, $-R^9-P(O)(OR^5)_2$, or $-R^9-O-R^9-OR^5$;

or R^1 is aralkyl substituted by $-C(O)N(R^6)R^7$ where:

R^6 is hydrogen, alkyl, aryl or aralkyl; and

R^7 is hydrogen, alkyl, haloalkyl, $-R^9-CN$, $-R^9-OR^5$, $-R^9-N(R^4)R^5$, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

or R^6 and R^7 , together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

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and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^6 and R^7 may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, $-R^8-CN$, $-R^8-OR^5$, heterocyclyl and heteroaryl;

or R^1 is aralkyl optionally substituted by one or more substituents selected from the group consisting of $-R^8-OR^5$, $-C(O)OR^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

or R^1 is $-R^9-N(R^{10})R^{11}$, $-R^9-N(R^{12})C(O)R^{11}$ or $-R^9-N(R^{10})C(O)N(R^{10})R^{11}$ where:

each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, $-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

or R^1 is heterocyclylalkyl or heteroarylalkyl where the heterocyclylalkyl or the heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$ (where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$,

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and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl,

heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$, $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not $-C(O)OCH_3$, $-C(O)NH_2$, iodo or cyano;

or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2d} are as defined above;

or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;

R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

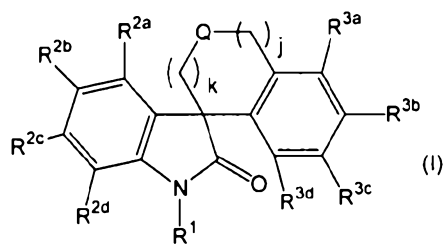
or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and

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R^{3c} and R^{3d} are as defined above;
 or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and
 R^{3a} and R^{3d} are as defined above;
 or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached,
 may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and
 R^{3a} and R^{3b} are as defined above;
 each R^4 and R^5 is independently selected from the group consisting of hydrogen, alkyl,
 alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl,
 heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;
 or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together
 with the nitrogen atom to which they are attached, may form a heterocyclyl or
 heteroaryl;
 each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched
 alkenylene chain or a straight or branched alkynylene chain; and
 each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain
 or a straight or branched alkynylene chain;
 or a stereoisomer, enantiomer or tautomer thereof;
 or a pharmaceutically acceptable salt or solvate thereof,
 in the manufacture of a medicament for the treatment of pruritis.

12. Use of a compound of formula (I):



wherein:

j and k are each independently 0, 1, 2 or 3;

Q is $-C(R^{1a})H-$, $-O-$, $-S(O)_m-$ (where m is 1 or 2), $-CF_2-$, $-C(O)O-$, $-C(O)N(R^5)-$ or
 $-N(R^5)C(O)-$;

R^{1a} is $-OR^5$;

R^1 is hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl,

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heteroaryl, heterocyclyl, $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$, $-R^9-S(O)_m-R^5$ (where m is 0, 1 or 2), $-R^8-OR^5$, $-R^8-CN$, $-R^9-P(O)(OR^5)_2$, or $-R^9-O-R^9-OR^5$;

or R^1 is aralkyl substituted by $-C(O)N(R^6)R^7$ where:

R^6 is hydrogen, alkyl, aryl or aralkyl; and

R^7 is hydrogen, alkyl, haloalkyl, $-R^9-CN$, $-R^9-OR^5$, $-R^9-N(R^4)R^5$, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

or R^6 and R^7 , together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^6 and R^7 may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, $-R^8-CN$, $-R^8-OR^5$, heterocyclyl and heteroaryl;

or R^1 is aralkyl optionally substituted by one or more substituents selected from the group consisting of $-R^8-OR^5$, $-C(O)OR^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

or R^1 is $-R^9-N(R^{10})R^{11}$, $-R^9-N(R^{12})C(O)R^{11}$ or $-R^9-N(R^{10})C(O)N(R^{10})R^{11}$ where:

each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, $-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

or R^1 is heterocyclylalkyl or heteroarylalkyl where the heterocyclylalkyl or the heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$,

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$-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$
(where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of
hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy,
cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl,
heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$,
 $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$,
 $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$,
 $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$,
 $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$,
and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each
n is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl,

heterocyclyl, heterocyclalkyl, heteroaryl and heteroarylalkyl groups for
 R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more
substituents selected from the group consisting of alkyl, alkenyl, alkynyl,
alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl,
aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl,
heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$,
 $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$,
 $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1,
or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not $-C(O)OCH_3$, $-C(O)NH_2$, iodo or cyano;

or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached,
may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl,
and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached,
may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl,
and R^{2a} and R^{2d} are as defined above;

or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached,
may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl,
and R^{2a} and R^{2b} are as defined above;

R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of
hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy,

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cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;

or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3d} are as defined above;

or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3b} are as defined above;

each R^4 and R^5 is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;

or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl;

each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and

each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain;

or a stereoisomer, enantiomer or tautomer thereof;

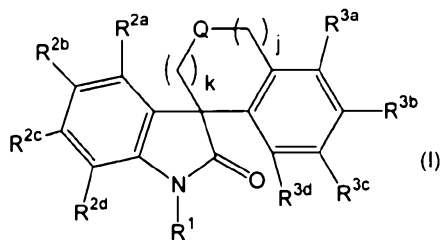
or a pharmaceutically acceptable salt or solvate thereof,

in the manufacture of a medicament for the treatment of hormone sensitive cancer.

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13. Use of a compound of formula (I):



wherein:

j is 0 and k is 1 or 2;

Q is $-C(R^{1a})H-$, $-C(O)-$, $-CF_2-$, $-C(O)O-$ or $-N(R^5)C(O)-$;

R^{1a} is hydrogen or $-OR^5$;

R^1 is ethyl, *n*-propyl, 1-methylethyl, *n*-butyl, *n*-pentyl, 1,1-dimethylethyl, 3-methylhexyl,

2-methylhexyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl,

heteroaryl, heterocyclyl, $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$,

$-R^9-S(O)_m-R^5$ (where m is 0, 1 or 2), $-R^8-OR^5$, $-R^8-CN$, $-R^9-P(O)(OR^5)_2$, or

$-R^9-O-R^9-OR^5$;

or R^1 is aralkyl substituted by $-C(O)N(R^6)R^7$ where:

R^6 is hydrogen, alkyl, aryl or aralkyl; and

R^7 is hydrogen, alkyl, haloalkyl, $-R^9-CN$, $-R^9-OR^5$, $-R^9-N(R^4)R^5$, aryl, aralkyl,

cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

or R^6 and R^7 , together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl,

heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^6 and R^7 may

be optionally substituted by one or more substituents selected from the

group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, $-R^8-CN$,

$-R^8-OR^5$, heterocyclyl and heteroaryl;

or R^1 is aralkyl optionally substituted by one or more substituents selected from the group

consisting of $-R^8-OR^5$, $-C(O)OR^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl,

heterocyclyl and heteroaryl;

or R^1 is $-R^9-N(R^{10})R^{11}$, $-R^9-N(R^{12})C(O)R^{11}$ or $-R^9-N(R^{10})C(O)N(R^{10})R^{11}$ where:

each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

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each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl,

heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, $-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

or R^1 is heterocyclylalkyl or heteroarylalkyl where the heterocyclylalkyl or the

heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$ (where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl,

heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$, $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$,

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$-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not $-C(O)OCH_3$, $-C(O)NH_2$, iodo or cyano;

or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2d} are as defined above;

or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;

R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;

or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3d} are as defined above;

or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3b} are as defined above;

each R^4 and R^5 is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;

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or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl;

each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and

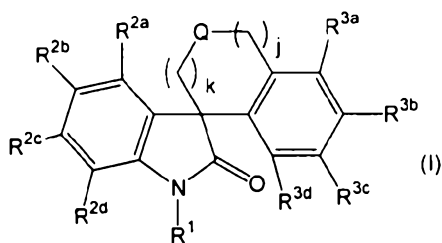
each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain;

or a stereoisomer, enantiomer or tautomer thereof;

or a pharmaceutically acceptable salt or solvate thereof,

in the manufacture of a medicament for the treatment of hypercholesterolemia.

14. Use of a compound of formula (I):



wherein:

j is 0 and k is 1 or 2;

Q is $-C(R^{1a})H-$, $-C(O)-$, $-CF_2-$, $-C(O)O-$ or $-N(R^5)C(O)-$;

R^{1a} is hydrogen or $-OR^5$;

R^1 is ethyl, *n*-propyl, 1-methylethyl, *n*-butyl, *n*-pentyl, 1,1-dimethylethyl, 3-methylhexyl, 2-methylhexyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$, $-R^9-S(O)_m-R^5$ (where m is 0, 1 or 2), $-R^8-OR^5$, $-R^8-CN$, $-R^9-P(O)(OR^5)_2$, or $-R^9-O-R^9-OR^5$;

or R^1 is aralkyl substituted by $-C(O)N(R^6)R^7$ where:

R^6 is hydrogen, alkyl, aryl or aralkyl; and

R^7 is hydrogen, alkyl, haloalkyl, $-R^9-CN$, $-R^9-OR^5$, $-R^9-N(R^4)R^5$, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

or R^6 and R^7 , together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

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and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^6 and R^7 may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, $-R^8-CN$, $-R^8-OR^5$, heterocyclyl and heteroaryl;

or R^1 is aralkyl optionally substituted by one or more substituents selected from the group consisting of $-R^8-OR^5$, $-C(O)OR^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

or R^1 is $-R^9-N(R^{10})R^{11}$, $-R^9-N(R^{12})C(O)R^{11}$ or $-R^9-N(R^{10})C(O)N(R^{10})R^{11}$ where:

each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, $-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

or R^1 is heterocyclylalkyl or heteroarylalkyl where the heterocyclylalkyl or the heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$ (where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$,

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and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl,

heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for

R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more

substituents selected from the group consisting of alkyl, alkenyl, alkynyl,

alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl,

aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl,

heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$,

$-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$,

$-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1,

or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not $-C(O)OCH_3$, $-C(O)NH_2$, iodo or cyano;

or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached,

may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl,

and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached,

may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl,

and R^{2a} and R^{2d} are as defined above;

or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached,

may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl,

and R^{2a} and R^{2b} are as defined above;

R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of

hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy,

cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl,

heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$,

$-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$,

$-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$,

$-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$,

$-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$,

and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and

each n is independently 1 or 2;

or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached,

form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c}

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and R^{3d} are as defined above;

or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^d are as defined above;

or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3b} are as defined above;

each R^4 and R^5 is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl, and heteroarylalkyl;

or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl;

each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and

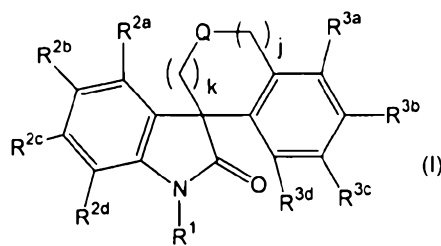
each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain;

or a stereoisomer, enantiomer or tautomer thereof;

or a pharmaceutically acceptable salt or solvate thereof,

in the manufacture of a medicament for the treatment of benign prostatic hyperplasia.

15. Use of a compound of formula (I):



wherein:

j is 0 and k is 1 or 2;

Q is $-C(R^{1a})H-$, $-C(O)-$, $-CF_2-$, $-C(O)O-$ or $-N(R^5)C(O)-$;

R^{1a} is hydrogen or $-OR^5$;

R^1 is ethyl, *n*-propyl, 1-methylethyl, *n*-butyl, *n*-pentyl, 1,1-dimethylethyl, 3-methylhexyl, 2-methylhexyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl,

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heteroaryl, heterocyclyl, $-R^8-C(O)R^5$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^4)R^5$, $-S(O)_2-R^5$, $-R^9-S(O)_m-R^5$ (where m is 0, 1 or 2), $-R^8-OR^5$, $-R^8-CN$, $-R^9-P(O)(OR^5)_2$, or $-R^9-O-R^9-OR^5$;

or R^1 is aralkyl substituted by $-C(O)N(R^6)R^7$ where:

R^6 is hydrogen, alkyl, aryl or aralkyl; and

R^7 is hydrogen, alkyl, haloalkyl, $-R^9-CN$, $-R^9-OR^5$, $-R^9-N(R^4)R^5$, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

or R^6 and R^7 , together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^6 and R^7 may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, $-R^8-CN$, $-R^8-OR^5$, heterocyclyl and heteroaryl;

or R^1 is aralkyl optionally substituted by one or more substituents selected from the group consisting of $-R^8-OR^5$, $-C(O)OR^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

or R^1 is $-R^9-N(R^{10})R^{11}$, $-R^9-N(R^{12})C(O)R^{11}$ or $-R^9-N(R^{10})C(O)N(R^{10})R^{11}$ where:

each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, $-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

or R^1 is heterocyclylalkyl or heteroarylalkyl where the heterocyclylalkyl or the heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$,

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$-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$
(where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of
hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy,
cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl,
heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$,
 $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$,
 $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$,
 $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$,
 $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$,
and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each
n is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl,

heterocyclyl, heterocyclalkyl, heteroaryl and heteroarylalkyl groups for
 R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more
substituents selected from the group consisting of alkyl, alkenyl, alkynyl,
alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl,
aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl,
heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$,
 $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$,
 $-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1,
or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not $-C(O)OCH_3$, $-C(O)NH_2$, iodo or cyano;

or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached,
may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl,
and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached,
may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl,
and R^{2a} and R^{2d} are as defined above;

or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached,
may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl,
and R^{2a} and R^{2b} are as defined above;

R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of
hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy,

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cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;

or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^d are as defined above;

or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3b} are as defined above;

each R^4 and R^5 is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;

or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl;

each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and

each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain;

or a stereoisomer, enantiomer or tautomer thereof;

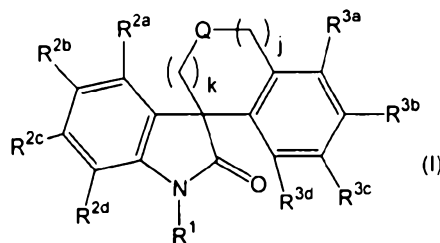
or a pharmaceutically acceptable salt or solvate thereof,

in the manufacture of a medicament for the treatment of pruritis.

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16. Use of a compound of formula (I):



wherein:

j is 0 and k is 1 or 2;

Q is $-\text{C}(\text{R}^{1a})\text{H}-$, $-\text{C}(\text{O})-$, $-\text{CF}_2-$, $-\text{C}(\text{O})\text{O}-$ or $-\text{N}(\text{R}^5)\text{C}(\text{O})-$;

R^{1a} is hydrogen or $-\text{OR}^5$;

R^1 is ethyl, *n*-propyl, 1-methylethyl, *n*-butyl, *n*-pentyl, 1,1-dimethylethyl, 3-methylhexyl, 2-methylhexyl, alkenyl, alkynyl, haloalkyl, aryl, cycloalkyl, cycloalkylalkyl, heteroaryl, heterocyclyl, $-\text{R}^8-\text{C}(\text{O})\text{R}^5$, $-\text{R}^8-\text{C}(\text{O})\text{OR}^5$, $-\text{R}^8-\text{C}(\text{O})\text{N}(\text{R}^4)\text{R}^5$, $-\text{S}(\text{O})_2-\text{R}^5$, $-\text{R}^9-\text{S}(\text{O})_m-\text{R}^5$ (where *m* is 0, 1 or 2), $-\text{R}^8-\text{OR}^5$, $-\text{R}^8-\text{CN}$, $-\text{R}^9-\text{P}(\text{O})(\text{OR}^5)_2$, or $-\text{R}^9-\text{O}-\text{R}^9-\text{OR}^5$;

or R^1 is aralkyl substituted by $-\text{C}(\text{O})\text{N}(\text{R}^6)\text{R}^7$ where:

R^6 is hydrogen, alkyl, aryl or aralkyl; and

R^7 is hydrogen, alkyl, haloalkyl, $-\text{R}^9-\text{CN}$, $-\text{R}^9-\text{OR}^5$, $-\text{R}^9-\text{N}(\text{R}^4)\text{R}^5$, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, or heteroarylalkyl;

or R^6 and R^7 , together with the nitrogen to which they are attached, may form a heterocyclyl or heteroaryl;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl groups for R^6 and R^7 may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, $-\text{R}^8-\text{CN}$, $-\text{R}^8-\text{OR}^5$, heterocyclyl and heteroaryl;

or R^1 is aralkyl optionally substituted by one or more substituents selected from the group consisting of $-\text{R}^8-\text{OR}^5$, $-\text{C}(\text{O})\text{OR}^5$, halo, haloalkyl, alkyl, nitro, cyano, aryl, aralkyl, heterocyclyl and heteroaryl;

or R^1 is $-\text{R}^9-\text{N}(\text{R}^{10})\text{R}^{11}$, $-\text{R}^9-\text{N}(\text{R}^{12})\text{C}(\text{O})\text{R}^{11}$ or $-\text{R}^9-\text{N}(\text{R}^{10})\text{C}(\text{O})\text{N}(\text{R}^{10})\text{R}^{11}$ where:

each R^{10} is hydrogen, alkyl, aryl, aralkyl or heteroaryl;

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each R^{11} is hydrogen, alkyl, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^9-OC(O)R^5$, $-R^9-C(O)OR^5$, $-R^9-C(O)N(R^4)R^5$, $-R^9-C(O)R^5$, $-R^9-N(R^4)R^5$, $-R^9-OR^5$, or $-R^9-CN$; and

R^{12} is hydrogen, alkyl, aryl, aralkyl or $-C(O)R^5$;

and wherein each aryl, aralkyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclalkyl, heteroaryl and heteroarylalkyl groups for R^{10} and R^{11} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, cycloalkyl, aryl, aralkyl, halo, haloalkyl, nitro, $-R^8-CN$, $-R^8-OR^5$, $-R^8-C(O)R^5$, heterocyclyl and heteroaryl;

or R^1 is heterocyclalkyl or heteroarylalkyl where the heterocyclalkyl or the heteroarylalkyl group is optionally substituted by one or more substituents selected from the group consisting of oxo, alkyl, halo, haloalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, $-R^8-N(R^4)R^5$, $-R^8-C(O)N(R^4)R^5$, $-R^8-N(R^5)C(O)R^4$, $-R^8-S(O)_mR^4$ (where m is 0, 1 or 2), $-R^8-CN$, or $-R^8-NO_2$;

R^{2a} , R^{2b} , R^{2c} and R^{2d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(=N-CN)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and wherein each of the cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl and heteroarylalkyl groups for R^{2a} , R^{2b} , R^{2c} and R^{2d} may be optionally substituted by one or more substituents selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-S(O)_mR^4$, $-R^8-S(O)_nN(R^4)R^5$, $-R^8-C(O)R^4$, $-R^8-C(O)OR^4$, $-R^8-C(O)N(R^4)R^5$,

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$-N(R^5)C(O)R^4$, and $-N(R^5)S(O)_nR^4$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

and provided that R^{2c} is not $-C(O)OCH_3$, $-C(O)NH_2$, iodo or cyano;

or R^{2a} and R^{2b} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2c} and R^{2d} are as defined above;

or R^{2b} and R^{2c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2d} are as defined above;

or R^{2c} and R^{2d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, aryl, heterocyclyl and heteroaryl, and R^{2a} and R^{2b} are as defined above;

R^{3a} , R^{3b} , R^{3c} and R^{3d} are each independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, alkoxy, halo, haloalkyl, haloalkenyl, haloalkoxy, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, aralkenyl, heterocyclyl, heterocyclylalkyl, heteroaryl, heteroarylalkyl, $-R^8-CN$, $-R^8-NO_2$, $-R^8-OR^5$, $-R^8-N(R^4)R^5$, $-N=C(R^4)R^5$, $-S(O)_mR^4$, $-OS(O)_2CF_3$, $-R^8-C(O)R^4$, $-C(S)R^4$, $-C(R^4)_2C(O)R^5$, $-R^8-C(O)OR^4$, $-C(S)OR^4$, $-R^8-C(O)N(R^4)R^5$, $-C(S)N(R^4)R^5$, $-N(R^5)C(O)R^4$, $-N(R^5)C(S)R^4$, $-N(R^5)C(O)OR^4$, $-N(R^5)C(S)OR^4$, $-N(R^5)C(O)N(R^4)R^5$, $-N(R^5)C(S)N(R^4)R^5$, $-N(R^5)S(O)_nR^4$, $-N(R^5)S(O)_nN(R^4)R^5$, $-R^8-S(O)_nN(R^4)R^5$, $-N(R^5)C(=NR^5)N(R^4)R^5$, and $-N(R^5)C(N=C(R^4)R^5)N(R^4)R^5$, wherein each m is independently 0, 1, or 2 and each n is independently 1 or 2;

or R^{3a} and R^{3b} , together with the carbon ring atoms to which they are directly attached, form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3c} and R^{3d} are as defined above;

or R^{3b} and R^{3c} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3d} are as defined above;

or R^{3c} and R^{3d} , together with the carbon ring atoms to which they are directly attached, may form a fused ring selected from cycloalkyl, heterocyclyl, aryl or heteroaryl, and R^{3a} and R^{3b} are as defined above;

each R^4 and R^5 is independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, alkoxyalkyl, cycloalkyl, cycloalkylalkyl, aryl, aralkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl;

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or when R^4 and R^5 are each attached to the same nitrogen atom, then R^4 and R^5 , together with the nitrogen atom to which they are attached, may form a heterocyclyl or heteroaryl;

each R^8 is a direct bond or a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain; and

each R^9 is a straight or branched alkylene chain, a straight or branched alkenylene chain or a straight or branched alkynylene chain;

or a stereoisomer, enantiomer or tautomer thereof;

or a pharmaceutically acceptable salt or solvate thereof,

in the manufacture of a medicament for the treatment of hormone sensitive cancer.

17. Method according to any one of claims 1 to 8 substantially as hereinbefore described with reference to any one of the examples.

18. Use according to any one of claims 9 to 16 substantially as hereinbefore described with reference to any one of the examples.