



(51) International Patent Classification:

C07C 311/29 (2006.01) C07D 205/12 (2006.01)
 A61K 31/18 (2006.01) C07D 207/404 (2006.01)
 A61K 31/185 (2006.01) C07D 211/54 (2006.01)
 A61K 31/335 (2006.01) C07D 213/61 (2006.01)
 A61K 31/395 (2006.01) C07D 213/71 (2006.01)
 A61K 31/41 (2006.01) C07D 233/84 (2006.01)
 A61K 31/4196 (2006.01) C07D 235/04 (2006.01)
 A61K 31/421 (2006.01) C07D 239/38 (2006.01)
 A61K 31/426 (2006.01) C07D 249/08 (2006.01)
 A61K 31/44 (2006.01) C07D 263/32 (2006.01)
 A61K 31/445 (2006.01) C07D 277/30 (2006.01)
 A61K 31/495 (2006.01) C07D 295/15 (2006.01)
 A61K 31/505 (2006.01) C07D 295/26 (2006.01)
 A61K 31/5375 (2006.01) C07D 305/06 (2006.01)
 C07C 309/42 (2006.01) C07D 305/08 (2006.01)
 C07C 317/22 (2006.01) C07D 307/64 (2006.01)
 C07C 317/24 (2006.01) C07D 487/04 (2006.01)
 C07D 205/06 (2006.01)

(21) International Application Number:

PCT/CA2020/050969

(22) International Filing Date:

10 July 2020 (10.07.2020)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

62/873,666 12 July 2019 (12.07.2019) US
 62/934,762 13 November 2019 (13.11.2019) US
 62/966,407 27 January 2020 (27.01.2020) US

(71) Applicant: CANOPY GROWTH CORPORATION

[CA/CA]; 1 Hershey Drive, Smiths Falls, Ontario K7A 0A8 (CA).

(72) Inventors: AHMAR, Siawash; 206 Lawrence Ave E,

Toronto, Ontario M4N 1T2 (CA). GNANASEKARAN, Krishna Kumar; 4591 Gattineau Avenue, Mississauga, Ontario L4Z 2R9 (CA). OMEARA, Jeffrey Alan; 16 Mill Pond Drive, Halton Hills, Ontario L7G 4S6 (CA). PARK,

Ji Sung; 931 Sydenham Lane, Milton, Ontario L9T 8J4 (CA).

(74) Agent: GOWLING WLG (CANADA) LLP et al.; Suite 1600, 421 - 7 Avenue SW, Calgary, Alberta T2P 4K9 (CA).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, IT, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

- with international search report (Art. 21(3))
- in black and white; the international application as filed contained color or greyscale and is available for download from PATENTSCOPE

(54) Title: CANNABINOID DERIVATIVES

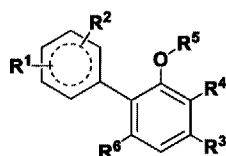


Figure (I).

(57) Abstract: This disclosure relates to cannabinoid derivatives of formula (I), pharmaceutical compositions comprising them, and methods of using the cannabinoid derivatives in treating or preventing a diseases associated with a cannabinoid receptor in a subject in need thereof, wherein the cannabinoid receptor is one or more of CB1, CB2, 5HT1A, 5HT2A, GPR18, GPR55, GPR119, TRPV1, TPRV2, PPAR γ or a μ -opioid receptor.

CANNABINOID DERIVATIVES

BACKGROUND OF THE DISCLOSURE

Cross-Reference to Related Applications

[0001] This application claims priority to and benefit of United States Provisional Patent Application Serial Number 62/873,666 filed on July 12, 2019; United States Provisional Patent Application Serial Number 62/934,762 filed on November 13, 2019; and United States Provisional Patent Application Serial Number 62/966,407 filed on January 27, 2020, each of which is hereby incorporated by reference in its entirety.

Field of the Disclosure

[0002] This disclosure relates generally to cannabinoid derivatives, pharmaceutical compositions comprising them, and methods of using the cannabinoid derivatives.

Technical Background

[0003] Every individual has an endocannabinoid system comprised of chemical receptors in the brain, immune system, and central nervous system, for example including the cannabinoid 1 (CB1) receptor and cannabinoid 2 (CB2) receptor. The endocannabinoid system regulates many important physiological processes and several components of the endocannabinoid system, such as receptors, transporters, endocannabinoids and enzymes involved in the synthesis and degradation of endocannabinoids, are under active investigation as targets to treat a diverse array of indications.

[0004] CB1 and CB2 receptors are a class of cell membrane receptors belonging to the G protein-coupled receptor (GPCR) superfamily. The CB1 and CB2 receptors are distinguished from each other by their amino acid sequence, tissue distribution, signaling mechanisms, and ability to bind sub-type specific ligands. The CB1 receptor is mainly expressed in the central nervous system (CNS), lungs, liver, adipose tissue, and kidneys, and the CB2 receptor is mainly localized in immune cells (e.g. macrophages and T-cells), on cells that are involved in bone formation and bone loss, and in the gastrointestinal system. These receptors have been associated with many human diseases including obesity, diabetes, fibrosis, liver diseases, cardiovascular disease, cancer, pain, inflammation, MS spasticity, and glaucoma, among others.

[0005] Cannabinoids are compounds active on cannabinoid receptors in humans and have been implicated in many of the pharmacological benefits on the diseases noted above.

Cannabinoids of plant origin, also known as phytocannabinoids, are abundant in *Cannabis*. Medical use of cannabis and associated phytocannabinoids is becoming widely accepted in many countries, including the United States, as an alternative form of medicine. Many states have legalized its use for qualified medical conditions such as chronic pain, epilepsy, sleep disorders, anxiety, cancer, glaucoma, nausea, amyotrophic lateral sclerosis (ALS), Alzheimer's disease, Crohn's disease, Post-traumatic Stress Disorder (PTSD), arthritis, fibromyalgia, and others.

[0006] In addition to the CB1 and CB2 receptors, other receptors have also been implicated in modulating the activity of cannabinoids in the human and/or animal body. For example, the serotonin receptors, such as 5HT1A and 5HT2A, are likewise GPCRs that have been identified as cannabinoid targets. The serotonin receptors modulate the release of many neurotransmitters, including glutamate, GABA, dopamine, epinephrine/norepinephrine and acetylcholine, as well as many hormones. Like the CB1 and CB2 receptors, the serotonin receptors influence various biological and neurological processes, such as anxiety, appetite, cognition, and mood, among others. Other receptors identified as being influenced by cannabinoid or cannabinoid-like compounds include GPR18, GPR55, GPR119, TRPV1, TRPV2, PPARs (e.g. PPAR γ), and the μ -opioid receptors. Indeed, binding of these receptors may be responsible for off-target effects of cannabinoids.

[0007] One of the most common ways that cannabinoids are used for medicinal use in many countries is through smoking of cannabis. Although proven to be beneficial in certain indications, smoking medical cannabis has disadvantages. For example, the smoke from the plant matter comprises carcinogens and other toxins in addition to the desired cannabinoids. Heavy cannabis use through smoking has also been associated with accelerated pulmonary decline, lung damage, and emphysema. Another disadvantage of smoking medical cannabis is difficulty in maintaining control over the proper dosing of medicinal cannabis due to active ingredients fluctuations (e.g., the amounts of active ingredients may differ depending on the differences present in plant varieties as well as changing growing conditions which result in intravarietal variations). Finally, consumption through smoking has a relatively low bioavailability of target compounds compared to other delivery methods.

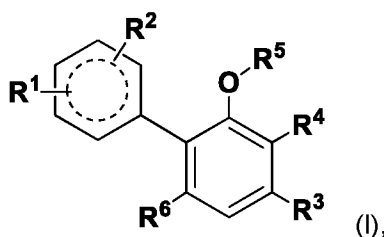
[0008] A less common way to utilize cannabis for medical use is to extract beneficial cannabinoids from cannabis. Many extraction processes have been developed for isolating and purifying natural cannabinoids. But there has been difficulty in isolating individual cannabinoids

at high levels of purity, both for active ingredients for use in medicine and product manufacturing and/or as standards for use in research and development.

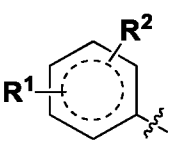
[0009] Therefore, there exists a need for novel ligands of cannabinoid receptors that have the potential for therapeutic benefit.

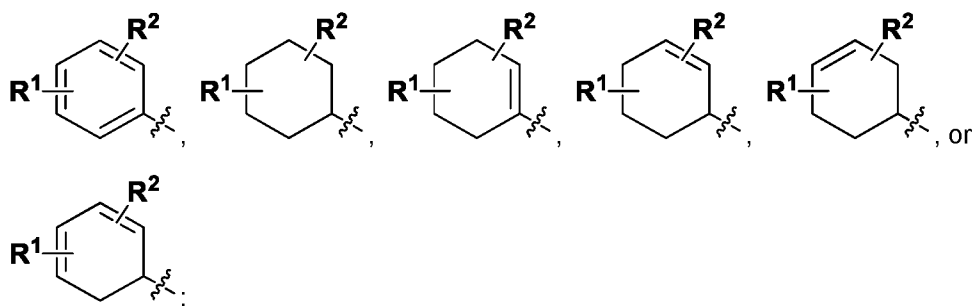
SUMMARY OF THE DISCLOSURE

[0010] One aspect of the present disclosure relates to compounds of formula (I):



or an enantiomer, diastereomer, racemate, tautomer, or metabolite thereof, or a pharmaceutically acceptable salt, solvate or hydrate of the compound, enantiomer, diastereomer, racemate, tautomer, or metabolite, wherein

the  moiety is



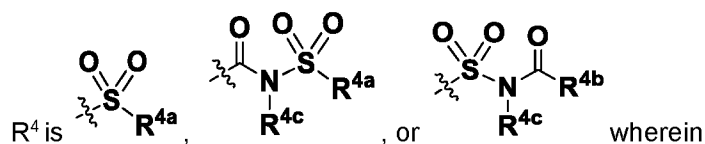
R¹ is hydrogen, halo, C₁-C₈ alkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, -CO₂H, -(C₀-C₄ alkyl)-C(O)O(C₁-C₆ alkyl), -(C₀-C₄ alkyl)-OC(O)O-(C₁-C₆ alkyl), -OR^{1a}, -(C₁-C₄ alkyl)OR^{1a}, -SR^{1a}, -(C₁-C₄ alkyl)SR^{1a}, -NR^{1b}R^{1c}, -(C₁-C₄ alkyl)NR^{1b}R^{1c}, -(C₁-C₄ alkyl)C(O)NR^{1b}R^{1c}, -(C₀-C₄ alkyl)-aryl, -(C₀-C₄ alkyl)-heteroaryl, -(C₀-C₄ alkyl)-cycloalkyl, -(C₀-C₄ alkyl)-heterocycloalkyl, or oxo when attached to a ring of appropriate saturation, wherein

R^{1a}, R^{1b}, and R^{1c} are independently hydrogen, C₁-C₄ alkyl, or -C(O)(C₁-C₄) alkyl;

R^2 is hydrogen, halo, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, C_2 - C_8 alkynyl, $-CO_2H$, $-(C_0-C_4 \text{ alkyl})-C(O)O(C_1-C_6 \text{ alkyl})$, $-(C_0-C_4 \text{ alkyl})-OC(O)O-(C_1-C_6 \text{ alkyl})$, $-OR^{2a}$, $-(C_1-C_4 \text{ alkyl})OR^{2a}$, $-SR^{2a}$, $-(C_1-C_4 \text{ alkyl})SR^{2a}$, $-NR^{2b}R^{2c}$, $-(C_1-C_4 \text{ alkyl})NR^{2b}R^{2c}$, $-(C_1-C_4 \text{ alkyl})C(O)NR^{2b}R^{2c}$, $-(C_0-C_4 \text{ alkyl})$ -aryl, $-(C_0-C_4 \text{ alkyl})$ -heteroaryl, $-(C_0-C_4 \text{ alkyl})$ -cycloalkyl, $-(C_0-C_4 \text{ alkyl})$ -heterocycloalkyl, or oxo when attached to a ring of appropriate saturation, wherein

R^{2a} , R^{2b} , and R^{2c} are independently hydrogen, C_1 - C_4 alkyl, or $-C(O)(C_1-C_4 \text{ alkyl})$ alkyl;

R^3 is hydrogen, C_1 - C_{12} alkyl, C_2 - C_{12} alkenyl, C_2 - C_{12} alkynyl, $-(OCH_2CH_2)_{0-6}O(C_1-C_8 \text{ alkyl})$, $-(C_0-C_4 \text{ alkyl})-NR^{3a}R^{3b}$, $-(C_0-C_4 \text{ alkyl})$ -aryl, $-(C_0-C_4 \text{ alkyl})$ -heteroaryl, $-(C_0-C_4 \text{ alkyl})$ -cycloalkyl or $-(C_0-C_4 \text{ alkyl})$ -heterocycloalkyl, wherein R^{3a} and R^{3b} are each independently hydrogen or C_1 - C_6 alkyl;



R^{4a} is C_1 - C_8 alkyl, C_2 - C_8 alkenyl, C_2 - C_8 alkynyl, $-OR^{4e}$, $-(C_1-C_4 \text{ alkyl})OR^{4e}$, $-(C_1-C_4 \text{ alkyl})-C(O)(C_1-C_4 \text{ alkyl})$, $-(C_0-C_4 \text{ alkyl})$ -aryl, $-(C_0-C_4 \text{ alkyl})$ -heteroaryl, $-(C_0-C_4 \text{ alkyl})$ -cycloalkyl, $-(C_0-C_4 \text{ alkyl})$ -heterocycloalkyl, $-NR^{4d}R^{4e}$, or $-(C_1-C_4 \text{ alkyl})NR^{4d}R^{4e}$, and

R^{4b} is C_1 - C_8 alkyl, C_2 - C_8 alkenyl, C_2 - C_8 alkynyl, $-CH_2-(OCH_2CH_2)_{0-6}O(C_1-C_8 \text{ alkyl})$, $-(C_1-C_4 \text{ alkyl})OR^{4e}$, $-(C_1-C_4 \text{ alkyl})-C(O)(C_1-C_4 \text{ alkyl})$, $-(C_1-C_4 \text{ alkyl})-C(O)O(R^{4e})$, $-(C_0-C_4 \text{ alkyl})$ -aryl, $-(C_0-C_4 \text{ alkyl})$ -heteroaryl, $-(C_0-C_4 \text{ alkyl})$ -cycloalkyl, $-(C_0-C_4 \text{ alkyl})$ -heterocycloalkyl, or $-(C_1-C_4 \text{ alkyl})NR^{4d}R^{4e}$, wherein

R^{4d} is hydrogen, C_1 - C_6 alkyl, $-(C_1-C_4 \text{ alkyl})-C(O)(C_1-C_4 \text{ alkyl})$, $-(C_1-C_4 \text{ alkyl})-C(O)O(R^{4e})$, $-(C_1-C_4 \text{ alkyl})-OC(O)(R^{4e})$, $-(C_0-C_4 \text{ alkyl})$ -aryl, $-(C_0-C_4 \text{ alkyl})$ -heteroaryl, $-(C_0-C_4 \text{ alkyl})$ -cycloalkyl, or $-(C_0-C_4 \text{ alkyl})$ -heterocycloalkyl,

R^{4e} is hydrogen or C_1 - C_4 alkyl, and

R^{4c} is hydrogen or C_1 - C_4 alkyl;

R^5 is hydrogen, C_1 - C_8 alkyl, $-(C_1-C_4 \text{ alkyl})-O-(C_0-C_4 \text{ alkyl})$, $-C(O)(C_1-C_4 \text{ alkyl})$, $-C(O)O(C_1-C_4 \text{ alkyl})$, $-C(O)NH_2$, $-C(O)NH(C_1-C_4 \text{ alkyl})$, $-C(O)N(C_1-C_4 \text{ alkyl})_2$, $-(C_1-C_4 \text{ alkyl})C(O)O(C_1-C_4 \text{ alkyl})$, or $-(C_1-C_4 \text{ alkyl})OC(O)(C_1-C_4 \text{ alkyl})$; and

A8142866WO

R⁶ is hydrogen or -OR^{6a}, wherein R^{6a} is hydrogen, C₁-C₈ alkyl, -(C₁-C₄ alkyl)-O-(C₀-C₄ alkyl), -C(O)(C₁-C₄ alkyl), -C(O)O(C₁-C₄ alkyl), -C(O)NH₂, -C(O)NH(C₁-C₄ alkyl), -C(O)N(C₁-C₄ alkyl)₂, -(C₁-C₄ alkyl)C(O)O(C₁-C₄ alkyl), or -(C₁-C₄ alkyl)OC(O)(C₁-C₄ alkyl);

wherein

each alkyl, alkenyl and alkynyl is unsubstituted, halogenated (e.g., fluorinated, chlorinated), substituted with one or two hydroxyl or C₁-C₆ alkoxy groups, or substituted with one or two oxo groups;

each cycloalkyl has 3-10 ring carbons and is saturated or partially unsaturated, and optionally includes one or two fused cycloalkyl rings, each fused ring having 3-8 ring members, and is substituted with 0-6 R⁷;

each heterocycloalkyl has 3-10 ring members and 1-3 heteroatoms where each is independently nitrogen, oxygen or sulfur and is saturated or partially unsaturated, and optionally includes one or two fused cycloalkyl rings, each having 3-8 ring members, and is substituted with 0-6 R⁷;

each aryl is a phenyl or a naphthyl, and optionally includes one or two fused cycloalkyl or heterocycloalkyl rings, each fused cycloalkyl or heterocycloalkyl ring having 4-8 ring members, and is substituted with 0-5 R⁸;

each heteroaryl is a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms, where each is independently nitrogen, oxygen or sulfur or a 8-10 membered bicyclic heteroaryl having 1-5 heteroatoms where each is independently nitrogen, oxygen or sulfur, and optionally includes one or two fused cycloalkyl or heterocycloalkyl rings, each fused cycloalkyl or heterocycloalkyl ring having 4-8 ring members, and is substituted with 0-5 R⁸,

in which

each R⁷ is independently oxo, C₁-C₄ alkyl, -Cl, -F, -Br, -CN, -SF₅, -N₃, nitro, -SR^A, -S(O)₁₋₂R^A, -OR^A, -(C₀-C₃ alkyl)-OR^B, -NR^BR^A, -C(O)R^A, -C(O)NR^BR^A, -NR^BC(O)R^A, -C(S)NR^BR^A, -NR^BC(S)R^A, -CO₂R^A, -OC(O)R^A, -C(O)SR^A, -SC(O)R^A, -C(S)OR^A, -OC(S)R^A, -C(S)SR^A, -SC(S)R^A, -S(O)₁₋₂OR^A, -OS(O)₁₋₂R^A, -S(O)₁₋₂NR^BR^A, -NR^BS(O)₁₋₂R^A, -OCO₂R^A, -OC(O)NR^BR^A, -NR^BCO₂R^A, -NR^BC(O)NR^BR^A, -SCO₂R^A, -OC(O)SR^A, -SC(O)SR^A, -SC(O)NR^BR^A, -NR^BC(O)SR^A, -OC(S)OR^A, -OC(S)NR^BR^A, -NR^BC(S)OR^A, -NR^BC(S)NR^BR^A,

-SC(S)OR^A, -OC(S)SR^A, -SC(S)SR^A, -SC(S)NR^BR^A, -NR^BC(S)SR^A,
 -NR^BC(NR^B)NR^BR^A, -NR^BS(O)₁₋₂NR^BR^A, unsubstituted phenyl, unsubstituted C₃-
 C₈ cycloalkyl, an unsubstituted five to six-membered heteroaryl, or an
 unsubstituted five to six-membered heterocycloalkyl; and

each R⁸ is independently optionally-substituted C₁-C₄ alkyl, -Cl, -F, -Br, -CN, -SF₅,
 -N₃, nitro, -SR^A, -S(O)₁₋₂R^A, -OR^A, -(C₀-C₃ alkyl)-OR^B, -NR^BR^A, -C(O)R^A,
 -C(O)NR^BR^A, -NR^BC(O)R^A, -C(S)NR^BR^A, -NR^BC(S)R^A, -CO₂R^A, -OC(O)R^A,
 -SO₃H, -C(O)SR^A, -SC(O)R^A, -C(S)OR^A, -OC(S)R^A, -C(S)SR^A, -SC(S)R^A,
 -S(O)₁₋₂OR^A, -OS(O)₁₋₂R^A, -S(O)₁₋₂NR^BR^A, -NR^BS(O)₁₋₂R^A, -OCO₂R^A,
 -OC(O)NR^BR^A, -NR^BCO₂R^A, -NR^BC(O)NR^BR^A, -SCO₂R^A, -OC(O)SR^A,
 -SC(O)SR^A, -SC(O)NR^BR^A, -NR^BC(O)SR^A, -OC(S)OR^A, -OC(S)NR^BR^A,
 -NR^BC(S)OR^A, -NR^BC(S)NR^BR^A, -SC(S)OR^A, -OC(S)SR^A, -SC(S)SR^A,
 -SC(S)NR^BR^A, -NR^BC(S)SR^A, -NR^BC(NR^B)NR^BR^A, -NR^BS(O)₁₋₂NR^BR^A;
 unsubstituted phenyl, unsubstituted C₃-C₈ cycloalkyl, an unsubstituted five to six-
 membered heteroaryl, or an unsubstituted five to six-membered heterocycloalkyl;

wherein each R^A is independently H or C₁-C₃ alkyl, and each R^B is independently
 H, C₁-C₃ alkyl, C₁-C₃ fluoroalkyl, C₁-C₃ hydroxyalkyl, -S(O)₁₋₂(C₁-C₃ alkyl),
 -C(O)(C₁-C₃ alkyl) or -CO₂(C₁-C₃ alkyl).

[0011] In another aspect, the present disclosure relates to pharmaceutical compositions comprising a compound (e.g., a compound of formula (I)) as described herein, or an enantiomer, diastereomer, racemate, tautomer, or metabolite thereof, or a pharmaceutically acceptable salt, solvate or hydrate of the compound, enantiomer, diastereomer, racemate, tautomer, or metabolite. In an embodiment, the pharmaceutical compositions comprise a pharmaceutically acceptable excipient, diluent, or carrier.

[0012] In another aspect, the present disclosure relates to a method for treating or preventing a disease, such as a disease associated with a cannabinoid receptor (e.g. CB1, CB2, 5HT1A, 5HT2A, GPR18, GPR55, GPR119, TRPV1, TPRV2, PPAR_γ, or a μ-opioid receptor), in a subject in need thereof. In an embodiment, the method includes administering to the subject a therapeutically effective amount of a compound as described herein, or an enantiomer, diastereomer, racemate, tautomer, or metabolite thereof, or a pharmaceutically acceptable salt, solvate or hydrate of the compound, enantiomer, diastereomer, racemate, tautomer, or metabolite. In an embodiment, the method includes administering to the subject a pharmaceutical composition as described herein.

[0013] In certain embodiments, the diseases that may be treated or prevented with the compounds or compositions as described herein include, but are not limited to attention-deficit/hyperactivity disorder (ADHD)/ attention-deficit disorder (ADD), alcohol use disorder, allergic asthma, amyotrophic lateral sclerosis (ALS), Alzheimer's, anorexia (e.g. human immunodeficiency virus (HIV)-related cachexia), anxiety disorders (e.g., social anxiety disorder, specific phobia, test anxiety, generalized anxiety disorder), arthritis, atherosclerosis, autism, bipolar disorder, burns, cancer, cancer pain, Charcot-Marie-Tooth disease, chronic inflammatory demyelinating polyneuropathies, chronic allograft nephropathy, cocaine use disorder, complex regional pain syndrome, chronic allograft nephropathy, depression, fibromyalgia, fragile X syndrome/fragile X-associated tremor and ataxia syndrome (FXTAS), frontotemporal dementias (behavioural variant), gingivitis pyrexia, glaucoma, glioblastoma, glomerulonephropathy, Huntington's disease, hypertrophic scars, inflammatory bowel disease (IBD)/ irritable bowel syndrome (IBS), inflammation, Inflammatory myopathies, ischemia, kidney fibrosis, keloids, leukodystrophies, liver fibrosis, liver cirrhosis, lung fibrosis, migraine, multiple sclerosis, myocardial infarction, nausea (e.g., chemotherapy-induced nausea and vomiting (CINV), motion sickness), neuropathic pain (e.g., postherpetic neuralgia, painful diabetic neuropathy), nightmare disorder, non-alcoholic fatty liver disease, obesity, obsessive-compulsive disorder, opioid sparing, opioid use disorder, osteoarthritis, osteoporosis, pain (e.g. acute or chronic pain), Parkinson's, post-concussion syndrome/traumatic brain injury, psychosis/schizophrenia, posttraumatic stress disorder (PTSD), regulation of bone mass, rapid eye movement (REM) sleep behaviour disorder, reperfusion injury, Rett syndrome, rheumatoid arthritis, skin conditions (e.g., acne, psoriatic arthritis), sleep disorders (e.g., insomnia, restless legs syndrome (RLS)), spinocerebellar ataxias, systemic fibrosis, systemic sclerosis, thermal injury, tobacco use disorder/nicotine dependence, Tourette's, tumors, and trigeminal neuralgia.

[0014] In another aspect, the present disclosure relates to use of a compound as described herein, or an enantiomer, diastereomer, racemate, tautomer, or metabolite thereof, or a pharmaceutically acceptable salt, solvate or hydrate of the compound, enantiomer, diastereomer, racemate, tautomer, or metabolite, for the treatment or prevention of a disease associated with cannabinoid receptor (e.g. CB1, CB2, 5HT1A, 5HT2A, GPR18, GPR55, GPR119, TRPV1, TRPV2, PPAR γ , or a μ -opioid receptor).

[0015] In another aspect, the present disclosure relates to use of a pharmaceutical composition as described herein for the treatment or prevention of a disease associated with cannabinoid

receptor (e.g. CB1, CB2, 5HT1A, 5HT2A, GPR18, GPR55, GPR119, TRPV1, TPRV2, PPAR γ , or a μ -opioid receptor).

[0016] In another aspect, the present disclosure relates to use of a compound as described herein, or an enantiomer, diastereomer, racemate, tautomer, or metabolite thereof, or a pharmaceutically acceptable salt, solvate or hydrate of the compound, enantiomer, diastereomer, racemate, tautomer, or metabolite, for selectively modulating the activity of a CB1 or CB2 receptor.

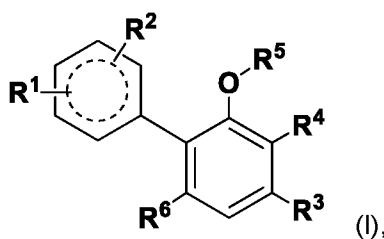
[0017] In another aspect, the present disclosure relates to use of a pharmaceutical composition as described herein, for selectively modulating the activity of a CB1 or CB2 receptor.

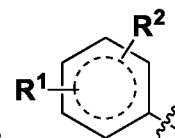
[0018] Other aspects and embodiments of the disclosure are evident in view of the detailed description provided herein.

DETAILED DESCRIPTION

[0019] The present disclosure provides compounds capable of acting as ligands to one or more cannabinoid receptors and/or prodrugs thereof. As used herein, “cannabinoid receptor” refers to a broad class of receptors that bind, interact with and/or are influenced functionally by cannabinoids or cannabinoid-like compounds. Without limitation, cannabinoid receptors may include CB1, CB2, 5HT1A, 5HT2A, GPR18, GPR55, GPR119, TRPV1, TPRV2, PPARs (e.g. PPAR γ) or μ -opioid receptors. In an embodiment, the present disclosure further relates to compounds, pharmaceutical compositions, methods and uses having the potential for treating or preventing one or more diseases associated with a cannabinoid receptor.

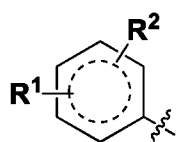
[0020] The compounds of the present disclosure can be defined generically as with respect to formula (I) as appropriate,



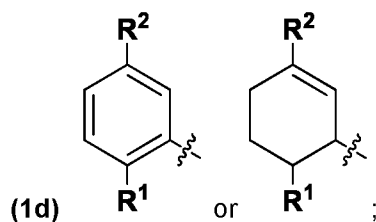
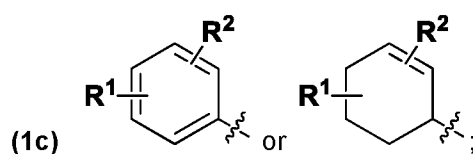
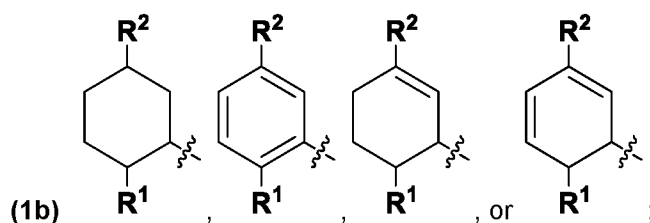
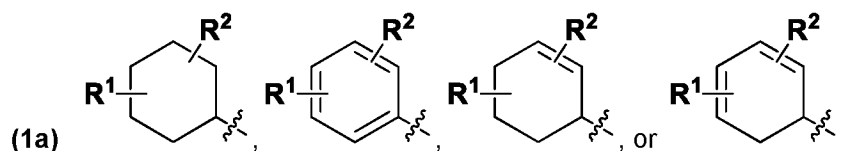


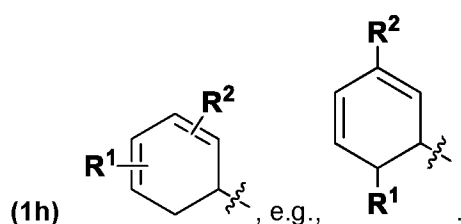
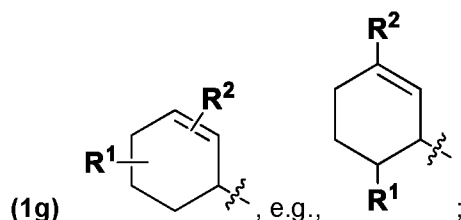
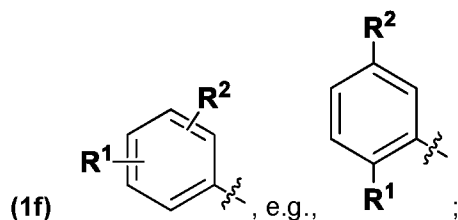
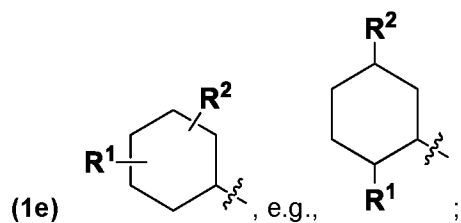
or in various subgenera compounds in which within the structural formula (I), the moiety, R^1 , R^2 , R^3 , R^5 , R^6 , R^4 , and R^{4a} , R^{4b} and R^{4c} are optionally independently selected from the groups (1a) to (1g), (1a) to (1h), (2a) to (2q), (3a) to (3s), (4a) to (4p), (5a) to (5c), (6a) to (6e), (7a) to (7e), and (8a) to (8gg), defined herein below (e.g., wherein the compound is of a structural formula as defined in any combination of the embodiments below):

[0021] In certain embodiments of the compounds as otherwise described herein, the



moiety is selected from the following groups (1a) – (1h):





[0022] In certain embodiments of the compounds as otherwise described herein, R^1 is selected from one of the following groups (2a) – (2q):

- (2a) hydrogen, halo, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, $-CO_2H$, $-(C_0-C_4 \text{ alkyl})-C(O)O(C_1-C_6 \text{ alkyl})$, $-OR^{1a}$, $-(C_1-C_4 \text{ alkyl})OR^{1a}$, $-SR^{1a}$, $-(C_1-C_4 \text{ alkyl})SR^{1a}$, $-NR^{1b}R^{1c}$, $-(C_1-C_4 \text{ alkyl})NR^{1b}R^{1c}$, $-(C_1-C_4 \text{ alkyl})C(O)NR^{1b}R^{1c}$, $-(C_0-C_4 \text{ alkyl})$ -aryl, $-(C_0-C_4 \text{ alkyl})$ -heteroaryl, $-(C_0-C_4 \text{ alkyl})$ -cycloalkyl, $-(C_0-C_4 \text{ alkyl})$ -heterocycloalkyl, or oxo;
- (2b) hydrogen, $-F$, $-Cl$, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, $-CO_2H$, $-(C_0-C_4 \text{ alkyl})-C(O)O(C_1-C_6 \text{ alkyl})$, $-(C_0-C_4 \text{ alkyl})$ -aryl, $-(C_0-C_4 \text{ alkyl})$ -heteroaryl, $-(C_0-C_4 \text{ alkyl})$ -cycloalkyl, $-(C_0-C_4 \text{ alkyl})$ -heterocycloalkyl, or oxo;
- (2c) hydrogen, $-F$, $-Cl$, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, $-CO_2H$, $-(C_0-C_2 \text{ alkyl})-C(O)O(C_1-C_6 \text{ alkyl})$, or oxo;

- (2d) hydrogen;
- (2e) hydrogen, C₁-C₄ alkyl or C₂-C₄ alkenyl;
- (2f) C₁-C₄ alkyl or C₂-C₄ alkenyl;
- (2g) C₁-C₄ alkyl optionally substituted with hydroxy;
- (2h) C₁-C₄ alkyl, e.g. methyl, ethyl, or propyl (such as isopropyl or n-propyl);
- (2i) C₂-C₄ alkenyl, e.g. isopropenyl;
- (2j) -CO₂H, -C(O)O(C₁-C₄ alkyl), or oxo;
- (2k) -CO₂H;
- (2l) oxo;
- (2m) -CH₂OH;
- (2n) -(C₀-C₄ alkyl)-aryl, -(C₀-C₄ alkyl)-heteroaryl, -(C₀-C₄ alkyl)-cycloalkyl, or -(C₀-C₄ alkyl)-heterocycloalkyl;
- (2o) -OR^{1a}, -(C₁-C₄ alkyl)OR^{1a}, -SR^{1a}, -(C₁-C₄ alkyl)SR^{1a}, -NR^{1b}R^{1c}, -(C₁-C₄ alkyl)NR^{1b}R^{1c}, or -(C₁-C₄ alkyl)C(O)NR^{1b}R^{1c};
- (2p) -OR^{1a}, -(C₁-C₄ alkyl)OR^{1a}, -NR^{1b}R^{1c}, -(C₁-C₄ alkyl)NR^{1b}R^{1c}, or -(C₁-C₄ alkyl)C(O)NR^{1b}R^{1c};
- (2q) as defined in (2o) and (2p), wherein R^{1a}, R^{1b}, and R^{1c} are independently hydrogen or C₁-C₄ alkyl.

[0023] In certain embodiments of the compounds as otherwise described herein, R² is selected from one of the following groups (3a) – (3s):

- (3a) hydrogen, halo, C₁-C₈ alkyl, C₂-C₈ alkenyl, -CO₂H, -(C₀-C₄ alkyl)-C(O)O(C₁-C₆ alkyl), -OR^{2a}, -(C₁-C₄ alkyl)OR^{2a}, -SR^{2a}, -(C₁-C₄ alkyl)SR^{2a}, -NR^{2b}R^{2c}, -(C₁-C₄ alkyl)NR^{2b}R^{2c}, -(C₁-C₄ alkyl)C(O)NR^{2b}R^{2c}, -(C₀-C₄ alkyl)-aryl, -(C₀-C₄ alkyl)-heteroaryl, -(C₀-C₄ alkyl)-cycloalkyl, -(C₀-C₄ alkyl)-heterocycloalkyl, or oxo;
- (3b) hydrogen, -F, -Cl, C₁-C₈ alkyl, C₂-C₈ alkenyl, -CO₂H, hydroxy, -(C₀-C₄ alkyl)-C(O)O(C₁-C₆ alkyl), -(C₀-C₄ alkyl)-aryl, -(C₀-C₄ alkyl)-heteroaryl, -(C₀-C₄ alkyl)-cycloalkyl, -(C₀-C₄ alkyl)-heterocycloalkyl, or oxo;
- (3c) hydrogen, -F, -Cl, C₁-C₆ alkyl, C₂-C₆ alkenyl, hydroxy, -CO₂H, -(C₀-C₂ alkyl)-C(O)O(C₁-C₆ alkyl) (e.g., -CO₂(C₁-C₄ alkyl)), or oxo;

- (3d) hydrogen;
- (3e) C₁-C₄ alkyl or C₂-C₄ alkenyl;
- (3f) C₁-C₄ alkyl optionally substituted with hydroxy;
- (3g) C₁-C₄ alkyl, e.g., methyl, ethyl, or propyl (such as isopropyl or n-propyl);
- (3h) C₂-C₄ alkenyl, e.g. isopropenyl;
- (3i) -CO₂H, -C(O)O(C₁-C₄ alkyl), or oxo;
- (3j) -CO₂H;
- (3k) oxo;
- (3l) -CH₂OH;
- (3m) -(C₀-C₄ alkyl)-aryl, -(C₀-C₄ alkyl)-heteroaryl, -(C₀-C₄ alkyl)-cycloalkyl, or -(C₀-C₄ alkyl)-heterocycloalkyl;
- (3n) -OR^{2a}, -(C₁-C₄ alkyl)OR^{2a}, -SR^{2a}, -(C₁-C₄ alkyl)SR^{2a}, -NR^{2b}R^{2c}, -(C₁-C₄ alkyl)NR^{2b}R^{2c}, or -(C₁-C₄ alkyl)C(O)NR^{2b}R^{2c};
- (3o) -OR^{2a}, -(C₁-C₄ alkyl)OR^{2a}, -NR^{2b}R^{2c}, -(C₁-C₄ alkyl)NR^{2b}R^{2c}, or -(C₁-C₄ alkyl)C(O)NR^{2b}R^{2c};
- (3p) -OR^{2a};
- (3q) -NR^{2b}R^{2c};
- (3r) as defined in (3n) – (3q), wherein R^{2a}, R^{2b}, and R^{2c} are independently hydrogen, C₁-C₄ alkyl, or -C(O)CH₃;
- (3s) as defined in (3n) – (3q), wherein R^{2a}, R^{2b}, and R^{2c} are independently hydrogen or C₁-C₄ alkyl.

[0024] In certain embodiments of the compounds as otherwise described herein, R³ is selected from one of the following groups (4a) – (4p):

- (4a) hydrogen, C₁-C₁₂ alkyl, C₂-C₁₂ alkenyl, C₂-C₁₂ alkynyl, -(OCH₂CH₂)₀₋₆OCH₃, -(C₀-C₄ alkyl)-aryl, -(C₀-C₄ alkyl)-heteroaryl, -(C₀-C₄ alkyl)-cycloalkyl or -(C₀-C₄ alkyl)-heterocycloalkyl;
- (4b) hydrogen, C₁-C₁₂ alkyl, -(C₀-C₄ alkyl)-heteroaryl, -(C₀-C₄ alkyl)-cycloalkyl or -(C₀-C₄ alkyl)-heterocycloalkyl;

- (4c) hydrogen, C₁-C₈ alkyl, -(C₁-C₄ alkyl)-heteroaryl or -(C₁-C₄ alkyl)-heterocycloalkyl;
- (4d) hydrogen, C₄-C₉ alkyl, -(C₁-C₂ alkyl)-heteroaryl or -(C₁-C₂ alkyl)-heterocycloalkyl;
- (4e) hydrogen or C₁-C₁₀ alkyl;
- (4f) hydrogen;
- (4g) C₂-C₉ alkyl, e.g., unsubstituted n-C₂-C₉ alkyl;
- (4h) C₄-C₆ alkyl, e.g., unsubstituted n-C₄-C₆ alkyl;
- (4i) n-pentyl;
- (4j) 1,1-dimethylheptyl;
- (4k) n-propyl;
- (4l) -(C₀-C₄ alkyl)-aryl, -(C₀-C₄ alkyl)-heteroaryl, -(C₀-C₄ alkyl)-cycloalkyl or -(C₀-C₄ alkyl)-heterocycloalkyl;
- (4m) -(C₀-C₄ alkyl)-heterocycloalkyl, wherein the heterocycloalkyl has 3-8 ring members and 1-3 heteroatoms that are nitrogen, oxygen or sulfur and is substituted with 0-4 R⁷;
- (4n) -(C₀-C₄ alkyl)-heterocycloalkyl, wherein the heterocycloalkyl has 3-8 ring members and 1-3 heteroatoms that are nitrogen, oxygen or sulfur and is substituted with 0-4 R⁷, wherein the heterocycloalkyl is piperidinyl, pyrrolidinyl, azetidiny, or aziridinyl;
- (4o) -(C₀-C₄ alkyl)-heterocycloalkyl, wherein the heterocycloalkyl has 3-8 ring members and 1-3 heteroatoms that are nitrogen, oxygen or sulfur and is substituted with 0-4 R⁷, wherein the heterocycloalkyl is azetidiny and is substituted with 1-2 R⁷ which are independently oxo, C₁-C₄ alkyl, Cl, F, Br, -C(O)R^A, or -CO₂R^A, wherein R^A is H or C₁-C₃ alkyl;
- (4p) -(C₀-C₄ alkyl)-heterocycloalkyl, wherein the heterocycloalkyl has 3-8 ring members and 1-3 heteroatoms that are nitrogen, oxygen or sulfur and is substituted with 0-4 R⁷, wherein R⁷ is -C(O)CH₃.

[0025] In certain embodiments of the compounds as otherwise described herein, R⁵ are independently selected from one of the following groups (5a) – (5c):

(5a) hydrogen, C₁-C₆ alkyl, -(C₁-C₄ alkyl)-O-(C₀-C₄ alkyl), -C(O)(C₁-C₄ alkyl), -C(O)O(C₁-C₄ alkyl), -C(O)NH₂, -C(O)NH(C₁-C₄ alkyl), or -C(O)N(C₁-C₄ alkyl)₂;

(5b) hydrogen, C₁-C₆ alkyl, or -(C₁-C₄ alkyl)-O-(C₀-C₄ alkyl);

(5c) hydrogen.

[0026] In certain embodiments of the compounds as otherwise described herein, R⁶ are independently selected from one of the following groups (6a) – (6e)

(6a) hydrogen;

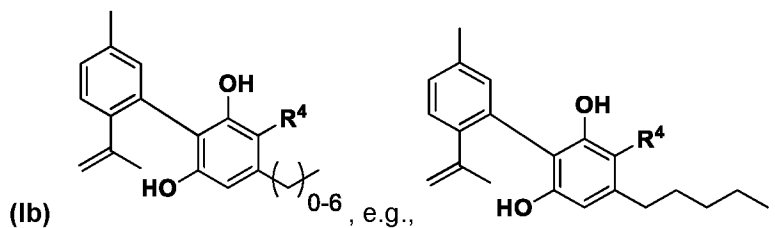
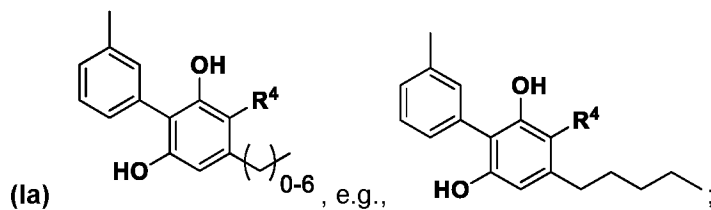
(6b) -OR^{6a};

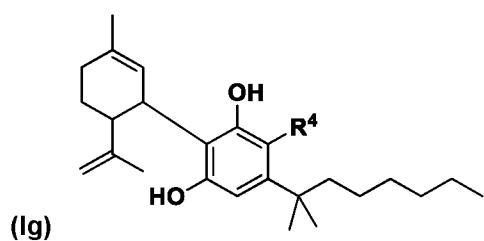
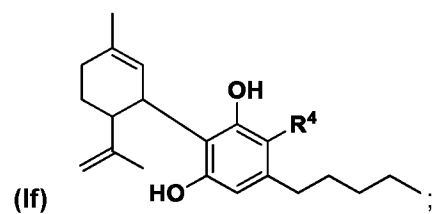
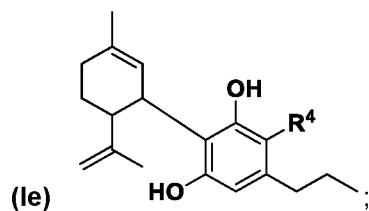
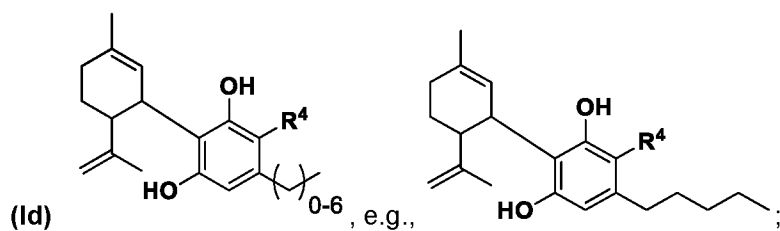
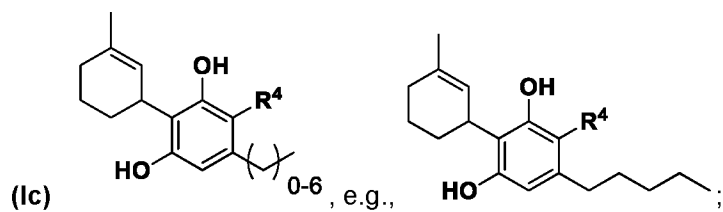
(6c) -OR^{6a}, wherein R^{6a} is hydrogen, C₁-C₆ alkyl, -(C₁-C₄ alkyl)-O-(C₀-C₄ alkyl), -C(O)(C₁-C₄ alkyl), -C(O)O(C₁-C₄ alkyl), -C(O)NH₂, -C(O)NH(C₁-C₄ alkyl), or -C(O)N(C₁-C₄ alkyl)₂;

(6d) -OR^{6a}, wherein R^{6a} is hydrogen, C₁-C₆ alkyl, or -(C₁-C₄ alkyl)-O-(C₀-C₄ alkyl);

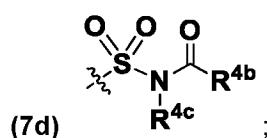
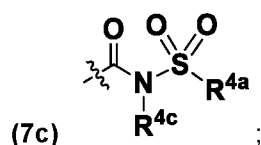
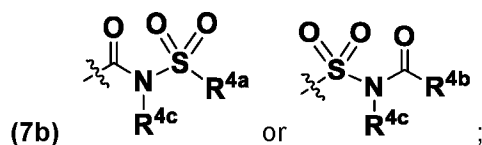
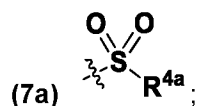
(6e) -OH.

[0027] In certain embodiments of the compounds as otherwise described herein, the compound has one of the following structural formulae (Ia) – (Ig):





[0028] In certain embodiments of the compounds as otherwise described herein, R^4 is selected from one of the following groups (7a) – (7e):



- (7e) sulfo, methylsulfonyl, cyclopropylsulfonyl, tert-butylsulfonyl, benzylsulfonyl, phenylsulfonyl, (4-nitrophenyl)sulfonyl, pyridin-3-ylsulfonyl, furan-2-ylsulfonyl, (1H-imidazol-4-yl)sulfonyl, oxetan-3-ylsulfonyl, perfluorophenylsulfonyl, (4-oxocyclohexyl)sulfonyl, (2-(2,5-dioxopyrrolidin-1-yl)ethyl)sulfonyl, (2-(dimethylamino)ethyl)sulfonyl, (1-acetylpiperidin-3-yl)sulfonyl, (2-chloropyrimidin-5-yl)sulfonyl, sulfamoyl, N-methylsulfamoyl, N,N-dimethylsulfamoyl, N-cyclopropylsulfamoyl, N-isopropylsulfamoyl, N-phenylsulfamoyl, N-benzylsulfamoyl, (4-methylpiperazin-1-yl)sulfonyl, piperidin-1-ylsulfonyl, morpholinylsulfonyl, N-(pyridin-3-yl)sulfamoyl, N-(pyrimidin-2-yl)sulfamoyl, N-(2-oxopropyl)sulfamoyl, (3-oxoazetidin-1-yl)sulfonyl, N-(oxetan-2-ylmethyl)sulfamoyl, (2-azaspiro[3.3]heptan-2-yl)sulfonyl, (2,6-diazaspiro[3.3]heptan-2-yl)sulfonyl, N-(1-carboxyethyl)sulfamoyl, N-(1-methoxy-1-oxopropan-2-yl)sulfamoyl, N-(3-morpholinopropanoyl)sulfamoyl, N-(3-carboxypropanoyl)sulfamoyl, N-(3-(4-methylpiperazin-1-yl)propanoyl)sulfamoyl, N-glycylsulfamoyl, N-(2-(2-methoxyethoxy)acetyl)sulfamoyl, N-seryl-sulfamoyl, N-alanyl-sulfamoyl, (3-amino-2-methylpropanoyl)sulfamoyl, N-acetyl-sulfamoyl, N-(3-oxobutanoyl)sulfamoyl, N-(2-(3-methyl-1H-1,2,4-triazol-5-yl)acetyl)sulfamoyl, N-(1H-1,2,4-triazole-5-carbonyl)sulfamoyl, N-(cyclobutanecarbonyl)sulfamoyl, N-benzoylsulfamoyl, N-nicotinoylsulfamoyl, N-(2-phenylacetyl)sulfamoyl, N-(2-(furan-2-yl)acetyl)sulfamoyl, N-(2-(oxazol-2-yl)acetyl)sulfamoyl, N-(2-(thiazol-2-

yl)acetyl)sulfamoyl, N-(2-(1H-benzo[d]imidazole-2-yl)acetyl)sulfamoyl, (phenylsulfonyl)carbamoyl, (cyclohexylsulfonyl)carbamoyl, (prop-1-en-1-ylsulfonyl)carbamoyl, ((1H-benzo[d]imidazol-2-yl)sulfonyl)carbamoyl.

[0029] In certain embodiments of the compounds as otherwise described herein, R^{4a}, R^{4b}, or R^{4c} is selected from one of the following groups (8a) – (8gg) as appropriate:

- (8a)** as defined in (7a) – (7c), wherein R^{4a} is C₁-C₈ alkyl, C₂-C₈ alkenyl, -OR^{4e}, -(C₁-C₄ alkyl)OR^{4e}, -(C₁-C₄ alkyl)-C(O)(C₁-C₄ alkyl), -(C₀-C₄ alkyl)-aryl, -(C₀-C₄ alkyl)-heteroaryl, -(C₀-C₄ alkyl)-cycloalkyl, -(C₀-C₄ alkyl)-heterocycloalkyl, -NR^{4d}R^{4e}, or -(C₁-C₄ alkyl)NR^{4d}R^{4e};
- (8b)** as defined in (7a) – (7c), wherein R^{4a} is C₁-C₈ alkyl, C₂-C₈ alkenyl, or -OR^{4e};
- (8c)** as defined in (7a) – (7c), wherein R^{4a} is C₂-C₆ alkenyl (e.g., propenyl or 3-methoxyprop-1-en-1-yl);
- (8d)** as defined in (7a) – (7c), wherein R^{4a} is C₁-C₄ alkyl (e.g., methyl or *tert*-butyl);
- (8e)** as defined in (7a) – (7c), wherein R^{4a} is -OR^{4e} (e.g., -OH, -ONa, or -OCH₂CH₃);
- (8f)** as defined in (7a) – (7c), wherein R^{4a} is C₁-C₈ alkyl, C₂-C₈ alkenyl, -(C₀-C₄ alkyl)-aryl, -(C₀-C₄ alkyl)-heteroaryl, -(C₀-C₄ alkyl)-cycloalkyl, or -(C₀-C₄ alkyl)-heterocycloalkyl;
- (8g)** as defined in (7a) – (7c), wherein R^{4a} is -(C₀-C₄ alkyl)-aryl, -(C₀-C₄ alkyl)-heteroaryl, -(C₀-C₄ alkyl)-cycloalkyl, or -(C₀-C₄ alkyl)-heterocycloalkyl;
- (8h)** as defined in (7a) – (7c), wherein R^{4a} is monocyclic -(C₀-C₁ alkyl)-aryl (e.g., phenyl or benzyl), monocyclic or bicyclic -(C₀-C₁ alkyl)-heteroaryl (e.g., pyridyl, triazolyl, oxazolyl, furanyl, imidazolyl, pyrimidinyl, or benzimidazolyl), monocyclic -(C₀-C₁ alkyl)-cycloalkyl (e.g. cyclopropyl, cyclopropanyl or cyclohexyl) or monocyclic -(C₀-C₂ alkyl)-heterocycloalkyl (e.g., oxetanylmethyl, azetidiny, azaspiro[3.3]heptanyl, diazaspiro[3.3]heptanyl, oxetanyl, morpholinyl, piperazinyl, pyrrolidinyl, or piperidinyl), wherein each is substituted with 0-6 R⁷ and/or 0-3 R⁸;
- (8i)** as defined in (7a) – (7c), wherein R^{4a} is monocyclic -(C₀-C₁ alkyl)-aryl (e.g., phenyl or benzyl) or monocyclic -(C₀-C₁ alkyl)-cycloalkyl (e.g. cyclopropyl, cyclopropanyl or cyclohexyl), wherein each is substituted with 0-6 R⁷ and/or 0-3 R⁸;

- (8j)** as defined in (7a) – (7c), wherein R^{4a} is monocyclic or bicyclic $-(C_0-C_1$ alkyl)-heteroaryl (e.g., pyridyl, triazolyl, oxazolyl, furanyl, imidazolyl, pyrimidinyl, or benzimidazolyl) or monocyclic $-(C_0-C_2$ alkyl)-heterocycloalkyl (e.g., oxetanylmethyl, azetidiny, azaspiro[3.3]heptanyl, diazaspiro[3.3]heptanyl, oxetanyl, morpholinyl, piperazinyl, pyrrolidinyl, or piperidinyl), wherein each is substituted with 0-6 R^7 and/or 0-3 R^8 ;
- (8k)** as defined in (8h) – (8j), wherein R^8 is independently C_1-C_4 alkyl, -F, -Cl, nitro, amino, methoxymethyl, cyclopropyl, phenyl, pyridyl, or $-NR^B C(O)R^A$, wherein R^B is hydrogen or methyl and R^A is hydrogen or C_1-C_4 alkyl;
- (8l)** as defined in (8h) – (8k), wherein each R^7 is independently C_1-C_4 alkyl, methoxymethyl, -F, -Cl, hydroxy, oxo, cyclopropyl, phenyl, or pyridyl;
- (8m)** as defined in (7a) – (7c), wherein R^{4a} is $-(C_1-C_4$ alkyl) $NR^{4d}R^{4e}$ (e.g., wherein R^{4d} and R^{4e} are independently H or C_1-C_4 alkyl, such as (dimethylamino)ethyl, aminopropan-2-yl, aminoethyl or 1-amino-2-hydroxyethyl);
- (8n)** as defined in (7a) – (7c), wherein R^{4a} is $-NR^{4d}R^{4e}$;
- (8o)** as defined in (7a) – (7c), wherein R^{4a} is $NR^{4d}R^{4e}$, wherein R^{4d} is hydrogen, C_1-C_4 alkyl, $-(C_1-C_4$ alkyl)- $C(O)O(R^{4e})$, $-(C_0-C_2$ alkyl)-aryl, $-(C_0-C_2$ alkyl)-heteroaryl, $-(C_0-C_2$ alkyl)-cycloalkyl, or $-(C_0-C_2$ alkyl)-heterocycloalkyl and R^{4e} is hydrogen or C_1-C_4 alkyl;
- (8p)** as defined in (7a) – (7c), wherein R^{4a} is $-NR^{4d}R^{4e}$, wherein R^{4d} is hydrogen or C_1-C_4 alkyl and R^{4e} is hydrogen or methyl;
- (8q)** as defined in (7a) – (7c), wherein R^{4a} is $-NR^{4d}R^{4e}$, wherein R^{4d} is $-(C_0-C_1$ alkyl)-aryl, $-(C_0-C_1$ alkyl)-heteroaryl, $-(C_0-C_1$ alkyl)-cycloalkyl, or $-(C_0-C_1$ alkyl)-heterocycloalkyl and R^{4e} is hydrogen or methyl;
- (8r)** as defined in (7b) or (7d), wherein R^{4b} is C_1-C_8 alkyl, C_2-C_8 alkenyl, $-CH_2-(OCH_2CH_2)_{0-6}O(C_1-C_6$ alkyl), $-(C_1-C_4$ alkyl)- $C(O)O(R^{4e})$, $-(C_1-C_4$ alkyl) OR^{4e} , $-(C_1-C_4$ alkyl)- $C(O)(C_1-C_4$ alkyl), $-(C_0-C_4$ alkyl)-aryl, $-(C_0-C_4$ alkyl)-heteroaryl, $-(C_0-C_4$ alkyl)-cycloalkyl, $-(C_0-C_4$ alkyl)-heterocycloalkyl, or $-(C_1-C_4$ alkyl) $NR^{4d}R^{4e}$;
- (8s)** as defined in (7b) or (7d), wherein R^{4b} is C_1-C_8 alkyl, C_2-C_8 alkenyl, or $-(C_1-C_4$ alkyl) OR^{4e} ;
- (8t)** as defined in (7b) or (7d), wherein R^{4b} is C_1-C_4 alkyl, e.g., methyl;

- (8u)** as defined in (7b) or (7d), wherein R^{4b} is $-\text{CH}_2-(\text{OCH}_2\text{CH}_2)_{0-4}\text{O}(\text{C}_1-\text{C}_6 \text{ alkyl})$, $-(\text{C}_1-\text{C}_4 \text{ alkyl})-\text{C}(\text{O})\text{O}(\text{R}^{4e})$ (e.g., $-(\text{C}_1-\text{C}_4 \text{ alkyl})-\text{C}(\text{O})\text{OH}$), or $-(\text{C}_1-\text{C}_4 \text{ alkyl})-\text{C}(\text{O})(\text{C}_1-\text{C}_4 \text{ alkyl})$ (e.g., $-\text{CH}_2\text{C}(\text{O})\text{CH}_3$);
- (8v)** as defined in (7b) or (7d), wherein R^{4b} is $\text{C}_1-\text{C}_8 \text{ alkyl}$, $\text{C}_2-\text{C}_8 \text{ alkenyl}$, $-(\text{C}_0-\text{C}_4 \text{ alkyl})-\text{aryl}$, $-(\text{C}_0-\text{C}_4 \text{ alkyl})-\text{heteroaryl}$, $-(\text{C}_0-\text{C}_4 \text{ alkyl})-\text{cycloalkyl}$, or $-(\text{C}_0-\text{C}_4 \text{ alkyl})-\text{heterocycloalkyl}$;
- (8w)** as defined in (7b) or (7d), wherein R^{4b} is $-(\text{C}_0-\text{C}_4 \text{ alkyl})-\text{aryl}$, $-(\text{C}_0-\text{C}_4 \text{ alkyl})-\text{heteroaryl}$, $-(\text{C}_0-\text{C}_4 \text{ alkyl})-\text{cycloalkyl}$, or $-(\text{C}_0-\text{C}_4 \text{ alkyl})-\text{heterocycloalkyl}$;
- (8x)** as defined in (7b) or (7d), wherein R^{4b} is monocyclic $-(\text{C}_0-\text{C}_1 \text{ alkyl})-\text{aryl}$ (e.g., phenyl or benzyl), monocyclic or bicyclic $-(\text{C}_0-\text{C}_1 \text{ alkyl})-\text{heteroaryl}$ (e.g., pyridyl, triazolyl, oxazolyl, furanyl, imidazolyl, pyrimidinyl, or benzimidazolyl), monocyclic $-(\text{C}_0-\text{C}_1 \text{ alkyl})-\text{cycloalkyl}$ (e.g. cyclopropyl, cyclopropanyl or cyclohexyl) or monocyclic $-(\text{C}_0-\text{C}_2 \text{ alkyl})-\text{heterocycloalkyl}$ (e.g., oxetanylmethyl, azetidiny, azaspiro[3.3]heptanyl, diazaspiro[3.3]heptanyl, oxetanyl, morpholinyl, piperazinyl, pyrrolidinyl, or piperidinyl), wherein each is substituted with 0-6 R^7 and/or 0-3 R^8 ;
- (8y)** as defined in (7b) or (7d), wherein R^{4b} is monocyclic $-(\text{C}_0-\text{C}_1 \text{ alkyl})-\text{aryl}$ (e.g., phenyl or benzyl) or monocyclic $-(\text{C}_0-\text{C}_1 \text{ alkyl})-\text{cycloalkyl}$ (e.g. cyclopropyl, cyclopropanyl or cyclohexyl), wherein each is substituted with 0-6 R^7 and/or 0-3 R^8 ;
- (8z)** as defined in (7b) or (7d), wherein R^{4b} is monocyclic or bicyclic $-(\text{C}_0-\text{C}_1 \text{ alkyl})-\text{heteroaryl}$ (e.g., pyridyl, triazolyl, oxazolyl, furanyl, imidazolyl, pyrimidinyl, or benzimidazolyl) or monocyclic $-(\text{C}_0-\text{C}_2 \text{ alkyl})-\text{heterocycloalkyl}$ (e.g., oxetanylmethyl, azetidiny, azaspiro[3.3]heptanyl, diazaspiro[3.3]heptanyl, oxetanyl, morpholinyl, piperazinyl, pyrrolidinyl, or piperidinyl), wherein each is substituted with 0-6 R^7 and/or 0-3 R^8 ;
- (8aa)** as defined in (8v) – (8z), wherein each R^8 is independently $\text{C}_1-\text{C}_4 \text{ alkyl}$, $-\text{F}$, $-\text{Cl}$, nitro, amino, methoxymethyl, cyclopropyl, phenyl, pyridyl, or $-\text{NR}^B\text{C}(\text{O})\text{R}^A$, wherein R^B is hydrogen or methyl and R^A is hydrogen or $\text{C}_1-\text{C}_4 \text{ alkyl}$;
- (8bb)** as defined in (8v) – (8aa), wherein each R^7 is independently $\text{C}_1-\text{C}_4 \text{ alkyl}$, methoxymethyl, $-\text{F}$, $-\text{Cl}$, hydroxy, oxo, cyclopropyl, phenyl, or pyridyl;

(8cc) as defined in (7b) or (7d), wherein R^{4b} is $-(C_1-C_4 \text{ alkyl})NR^{4d}R^{4e}$ (e.g., wherein R^{4d} and R^{4e} are independently H or C_1-C_4 alkyl, such as (dimethylamino)ethyl, aminopropan-2-yl, aminoethyl or 1-amino-2-hydroxyethyl);

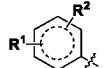
(8dd) as defined in (7b) – (7d) or (8a) – (8y), wherein R^{4c} is hydrogen;

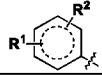
(8ee) as defined in (7b) – (7d) or (8a) – (8y), wherein R^{4c} is C_1-C_4 alkyl, e.g., methyl.

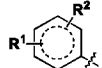
(8ff) as defined in (8a), (8m), (8r), or (8cc), wherein R^{4d} is hydrogen or C_1-C_6 alkyl (e.g., methyl, ethyl, or propyl).

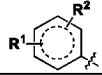
(8gg) as defined in (8a), (8m), (8r), or (8cc), wherein R^{4e} is hydrogen or methyl.

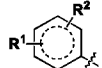
[0030] Various particular embodiment nos. 1-969 of compounds of the present disclosure include compounds of formula (I), each as defined in each of the following rows (or enantiomers, diastereomers, racemates, tautomers, or metabolites thereof, or pharmaceutically acceptable salts, solvates or hydrates of the compounds, enantiomers, diastereomers, racemates, tautomers, or metabolites), wherein each entry is a group number as defined above:

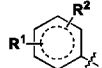
Embodiment		R^1	R^2	R^3	R^5	R^6	R^4	R^{4a}	R^{4b}	R^{4c}
1	(1a)-(1h)	(2d)	(3c)	(4a)	(5b)	(6d)	(7a)	(8a)	-	-
2	(1a)-(1h)	(2d)	(3c)	(4a)	(5b)	(6d)	(7a)	(8b), (8g)	-	-
3	(1a)-(1h)	(2d)	(3c)	(4a)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
4	(1a)-(1h)	(2d)	(3c)	(4a)	(5b)	(6d)	(7c)	(8b), (8g)	-	(8dd)
5	(1a)-(1h)	(2d)	(3c)	(4a)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
6	(1a)-(1h)	(2d)	(3c)	(4a)	(5b)	(6d)	(7d)	-	(8s), (8w)	(8dd)
7	(1a)-(1h)	(2d)	(3c)	(4a)	(5b)	(6e)	(7a)	(8a)	-	-
8	(1a)-(1h)	(2d)	(3c)	(4a)	(5b)	(6e)	(7a)	(8b), (8g)	-	-
9	(1a)-(1h)	(2d)	(3c)	(4a)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
10	(1a)-(1h)	(2d)	(3c)	(4a)	(5b)	(6e)	(7c)	(8b), (8g)	-	(8dd)
11	(1a)-(1h)	(2d)	(3c)	(4a)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
12	(1a)-(1h)	(2d)	(3c)	(4a)	(5b)	(6e)	(7d)	-	(8s), (8w)	(8dd)
13	(1a)-(1h)	(2d)	(3c)	(4a)	(5c)	(6d)	(7a)	(8a)	-	-
14	(1a)-(1h)	(2d)	(3c)	(4a)	(5c)	(6d)	(7a)	(8b), (8g)	-	-
15	(1a)-(1h)	(2d)	(3c)	(4a)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
16	(1a)-(1h)	(2d)	(3c)	(4a)	(5c)	(6d)	(7c)	(8b), (8g)	-	(8dd)
17	(1a)-(1h)	(2d)	(3c)	(4a)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
18	(1a)-(1h)	(2d)	(3c)	(4a)	(5c)	(6d)	(7d)	-	(8s), (8w)	(8dd)
19	(1a)-(1h)	(2d)	(3c)	(4a)	(5c)	(6e)	(7a)	(8a)	-	-
20	(1a)-(1h)	(2d)	(3c)	(4a)	(5c)	(6e)	(7a)	(8b), (8g)	-	-
21	(1a)-(1h)	(2d)	(3c)	(4a)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
22	(1a)-(1h)	(2d)	(3c)	(4a)	(5c)	(6e)	(7c)	(8b), (8g)	-	(8dd)

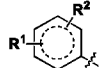
Embo- diment		R ¹	R ²	R ³	R ⁵	R ⁶	R ⁴	R ^{4a}	R ^{4b}	R ^{4c}
23	(1a)-(1h)	(2d)	(3c)	(4a)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
24	(1a)-(1h)	(2d)	(3c)	(4a)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
25	(1a)-(1h)	(2d)	(3c)	(4d)	(5b)	(6d)	(7a)	(8a)	-	-
26	(1a)-(1h)	(2d)	(3c)	(4d)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
27	(1a)-(1h)	(2d)	(3c)	(4d)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
28	(1a)-(1h)	(2d)	(3c)	(4d)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
29	(1a)-(1h)	(2d)	(3c)	(4d)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
30	(1a)-(1h)	(2d)	(3c)	(4d)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
31	(1a)-(1h)	(2d)	(3c)	(4d)	(5b)	(6e)	(7a)	(8a)	-	-
32	(1a)-(1h)	(2d)	(3c)	(4d)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
33	(1a)-(1h)	(2d)	(3c)	(4d)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
34	(1a)-(1h)	(2d)	(3c)	(4d)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
35	(1a)-(1h)	(2d)	(3c)	(4d)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
36	(1a)-(1h)	(2d)	(3c)	(4d)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
37	(1a)-(1h)	(2d)	(3c)	(4d)	(5c)	(6d)	(7a)	(8a)	-	-
38	(1a)-(1h)	(2d)	(3c)	(4d)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
39	(1a)-(1h)	(2d)	(3c)	(4d)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
40	(1a)-(1h)	(2d)	(3c)	(4d)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
41	(1a)-(1h)	(2d)	(3c)	(4d)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
42	(1a)-(1h)	(2d)	(3c)	(4d)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
43	(1a)-(1h)	(2d)	(3c)	(4d)	(5c)	(6e)	(7a)	(8a)	-	-
44	(1a)-(1h)	(2d)	(3c)	(4d)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
45	(1a)-(1h)	(2d)	(3c)	(4d)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
46	(1a)-(1h)	(2d)	(3c)	(4d)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
47	(1a)-(1h)	(2d)	(3c)	(4d)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
48	(1a)-(1h)	(2d)	(3c)	(4d)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
49	(1a)-(1h)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7a)	(8a)	-	-
50	(1a)-(1h)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
51	(1a)-(1h)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
52	(1a)-(1h)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
53	(1a)-(1h)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
54	(1a)-(1h)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
55	(1a)-(1h)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7a)	(8a)	-	-
56	(1a)-(1h)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
57	(1a)-(1h)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
58	(1a)-(1h)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
59	(1a)-(1h)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
60	(1a)-(1h)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
61	(1a)-(1h)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7a)	(8a)	-	-
62	(1a)-(1h)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
63	(1a)-(1h)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
64	(1a)-(1h)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
65	(1a)-(1h)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7d)	-	(8r)	(8dd)

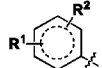
Embo- diment		R ¹	R ²	R ³	R ⁵	R ⁶	R ⁴	R ^{4a}	R ^{4b}	R ^{4c}
66	(1a)-(1h)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
67	(1a)-(1h)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7a)	(8a)	-	-
68	(1a)-(1h)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
69	(1a)-(1h)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
70	(1a)-(1h)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
71	(1a)-(1h)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
72	(1a)-(1h)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
73	(1a)-(1h)	(2d)	(3g)	(4a)	(5b)	(6d)	(7a)	(8a)	-	-
74	(1a)-(1h)	(2d)	(3g)	(4a)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
75	(1a)-(1h)	(2d)	(3g)	(4a)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
76	(1a)-(1h)	(2d)	(3g)	(4a)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
77	(1a)-(1h)	(2d)	(3g)	(4a)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
78	(1a)-(1h)	(2d)	(3g)	(4a)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
79	(1a)-(1h)	(2d)	(3g)	(4a)	(5b)	(6e)	(7a)	(8a)	-	-
80	(1a)-(1h)	(2d)	(3g)	(4a)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
81	(1a)-(1h)	(2d)	(3g)	(4a)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
82	(1a)-(1h)	(2d)	(3g)	(4a)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
83	(1a)-(1h)	(2d)	(3g)	(4a)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
84	(1a)-(1h)	(2d)	(3g)	(4a)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
85	(1a)-(1h)	(2d)	(3g)	(4a)	(5c)	(6d)	(7a)	(8a)	-	-
86	(1a)-(1h)	(2d)	(3g)	(4a)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
87	(1a)-(1h)	(2d)	(3g)	(4a)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
88	(1a)-(1h)	(2d)	(3g)	(4a)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
89	(1a)-(1h)	(2d)	(3g)	(4a)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
90	(1a)-(1h)	(2d)	(3g)	(4a)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
91	(1a)-(1h)	(2d)	(3g)	(4a)	(5c)	(6e)	(7a)	(8a)	-	-
92	(1a)-(1h)	(2d)	(3g)	(4a)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
93	(1a)-(1h)	(2d)	(3g)	(4a)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
94	(1a)-(1h)	(2d)	(3g)	(4a)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
95	(1a)-(1h)	(2d)	(3g)	(4a)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
96	(1a)-(1h)	(2d)	(3g)	(4a)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
97	(1a)-(1h)	(2d)	(3g)	(4d)	(5b)	(6d)	(7a)	(8a)	-	-
98	(1a)-(1h)	(2d)	(3g)	(4d)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
99	(1a)-(1h)	(2d)	(3g)	(4d)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
100	(1a)-(1h)	(2d)	(3g)	(4d)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
101	(1a)-(1h)	(2d)	(3g)	(4d)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
102	(1a)-(1h)	(2d)	(3g)	(4d)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
103	(1a)-(1h)	(2d)	(3g)	(4d)	(5b)	(6e)	(7a)	(8a)	-	-
104	(1a)-(1h)	(2d)	(3g)	(4d)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
105	(1a)-(1h)	(2d)	(3g)	(4d)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
106	(1a)-(1h)	(2d)	(3g)	(4d)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
107	(1a)-(1h)	(2d)	(3g)	(4d)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
108	(1a)-(1h)	(2d)	(3g)	(4d)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)

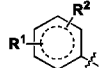
Embo- diment		R ¹	R ²	R ³	R ⁵	R ⁶	R ⁴	R ^{4a}	R ^{4b}	R ^{4c}
109	(1a)-(1h)	(2d)	(3g)	(4d)	(5c)	(6d)	(7a)	(8a)	-	-
110	(1a)-(1h)	(2d)	(3g)	(4d)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
111	(1a)-(1h)	(2d)	(3g)	(4d)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
112	(1a)-(1h)	(2d)	(3g)	(4d)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
113	(1a)-(1h)	(2d)	(3g)	(4d)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
114	(1a)-(1h)	(2d)	(3g)	(4d)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
115	(1a)-(1h)	(2d)	(3g)	(4d)	(5c)	(6e)	(7a)	(8a)	-	-
116	(1a)-(1h)	(2d)	(3g)	(4d)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
117	(1a)-(1h)	(2d)	(3g)	(4d)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
118	(1a)-(1h)	(2d)	(3g)	(4d)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
119	(1a)-(1h)	(2d)	(3g)	(4d)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
120	(1a)-(1h)	(2d)	(3g)	(4d)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
121	(1a)-(1h)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7a)	(8a)	-	-
122	(1a)-(1h)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
123	(1a)-(1h)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
124	(1a)-(1h)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
125	(1a)-(1h)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
126	(1a)-(1h)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
127	(1a)-(1h)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7a)	(8a)	-	-
128	(1a)-(1h)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
129	(1a)-(1h)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
130	(1a)-(1h)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
131	(1a)-(1h)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
132	(1a)-(1h)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
133	(1a)-(1h)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7a)	(8a)	-	-
134	(1a)-(1h)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
135	(1a)-(1h)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
136	(1a)-(1h)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
137	(1a)-(1h)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
138	(1a)-(1h)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
139	(1a)-(1h)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7a)	(8a)	-	-
140	(1a)-(1h)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
141	(1a)-(1h)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
142	(1a)-(1h)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
143	(1a)-(1h)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
144	(1a)-(1h)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
145	(1a)-(1h)	(2e)	(3c)	(4a)	(5b)	(6d)	(7a)	(8a)	-	-
146	(1a)-(1h)	(2e)	(3c)	(4a)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
147	(1a)-(1h)	(2e)	(3c)	(4a)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
148	(1a)-(1h)	(2e)	(3c)	(4a)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
149	(1a)-(1h)	(2e)	(3c)	(4a)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
150	(1a)-(1h)	(2e)	(3c)	(4a)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
151	(1a)-(1h)	(2e)	(3c)	(4a)	(5b)	(6e)	(7a)	(8a)	-	-

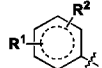
Embo- diment		R ¹	R ²	R ³	R ⁵	R ⁶	R ⁴	R ^{4a}	R ^{4b}	R ^{4c}
152	(1a)-(1h)	(2e)	(3c)	(4a)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
153	(1a)-(1h)	(2e)	(3c)	(4a)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
154	(1a)-(1h)	(2e)	(3c)	(4a)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
155	(1a)-(1h)	(2e)	(3c)	(4a)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
156	(1a)-(1h)	(2e)	(3c)	(4a)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
157	(1a)-(1h)	(2e)	(3c)	(4a)	(5c)	(6d)	(7a)	(8a)	-	-
158	(1a)-(1h)	(2e)	(3c)	(4a)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
159	(1a)-(1h)	(2e)	(3c)	(4a)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
160	(1a)-(1h)	(2e)	(3c)	(4a)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
161	(1a)-(1h)	(2e)	(3c)	(4a)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
162	(1a)-(1h)	(2e)	(3c)	(4a)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
163	(1a)-(1h)	(2e)	(3c)	(4a)	(5c)	(6e)	(7a)	(8a)	-	-
164	(1a)-(1h)	(2e)	(3c)	(4a)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
165	(1a)-(1h)	(2e)	(3c)	(4a)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
166	(1a)-(1h)	(2e)	(3c)	(4a)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
167	(1a)-(1h)	(2e)	(3c)	(4a)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
168	(1a)-(1h)	(2e)	(3c)	(4a)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
169	(1a)-(1h)	(2e)	(3c)	(4d)	(5b)	(6d)	(7a)	(8a)	-	-
170	(1a)-(1h)	(2e)	(3c)	(4d)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
171	(1a)-(1h)	(2e)	(3c)	(4d)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
172	(1a)-(1h)	(2e)	(3c)	(4d)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
173	(1a)-(1h)	(2e)	(3c)	(4d)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
174	(1a)-(1h)	(2e)	(3c)	(4d)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
175	(1a)-(1h)	(2e)	(3c)	(4d)	(5b)	(6e)	(7a)	(8a)	-	-
176	(1a)-(1h)	(2e)	(3c)	(4d)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
177	(1a)-(1h)	(2e)	(3c)	(4d)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
178	(1a)-(1h)	(2e)	(3c)	(4d)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
179	(1a)-(1h)	(2e)	(3c)	(4d)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
180	(1a)-(1h)	(2e)	(3c)	(4d)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
181	(1a)-(1h)	(2e)	(3c)	(4d)	(5c)	(6d)	(7a)	(8a)	-	-
182	(1a)-(1h)	(2e)	(3c)	(4d)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
183	(1a)-(1h)	(2e)	(3c)	(4d)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
184	(1a)-(1h)	(2e)	(3c)	(4d)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
185	(1a)-(1h)	(2e)	(3c)	(4d)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
186	(1a)-(1h)	(2e)	(3c)	(4d)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
187	(1a)-(1h)	(2e)	(3c)	(4d)	(5c)	(6e)	(7a)	(8a)	-	-
188	(1a)-(1h)	(2e)	(3c)	(4d)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
189	(1a)-(1h)	(2e)	(3c)	(4d)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
190	(1a)-(1h)	(2e)	(3c)	(4d)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
191	(1a)-(1h)	(2e)	(3c)	(4d)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
192	(1a)-(1h)	(2e)	(3c)	(4d)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
193	(1a)-(1h)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7a)	(8a)	-	-
194	(1a)-(1h)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7a)	(8b),(8g)	-	-

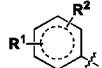
Embo- diment		R ¹	R ²	R ³	R ⁵	R ⁶	R ⁴	R ^{4a}	R ^{4b}	R ^{4c}
195	(1a)-(1h)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
196	(1a)-(1h)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
197	(1a)-(1h)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
198	(1a)-(1h)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
199	(1a)-(1h)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7a)	(8a)	-	-
200	(1a)-(1h)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
201	(1a)-(1h)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
202	(1a)-(1h)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
203	(1a)-(1h)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
204	(1a)-(1h)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
205	(1a)-(1h)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7a)	(8a)	-	-
206	(1a)-(1h)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
207	(1a)-(1h)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
208	(1a)-(1h)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
209	(1a)-(1h)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
210	(1a)-(1h)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
211	(1a)-(1h)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7a)	(8a)	-	-
212	(1a)-(1h)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
213	(1a)-(1h)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
214	(1a)-(1h)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
215	(1a)-(1h)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
216	(1a)-(1h)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
217	(1a)-(1h)	(2e)	(3g)	(4a)	(5b)	(6d)	(7a)	(8a)	-	-
218	(1a)-(1h)	(2e)	(3g)	(4a)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
219	(1a)-(1h)	(2e)	(3g)	(4a)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
220	(1a)-(1h)	(2e)	(3g)	(4a)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
221	(1a)-(1h)	(2e)	(3g)	(4a)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
222	(1a)-(1h)	(2e)	(3g)	(4a)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
223	(1a)-(1h)	(2e)	(3g)	(4a)	(5b)	(6e)	(7a)	(8a)	-	-
224	(1a)-(1h)	(2e)	(3g)	(4a)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
225	(1a)-(1h)	(2e)	(3g)	(4a)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
226	(1a)-(1h)	(2e)	(3g)	(4a)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
227	(1a)-(1h)	(2e)	(3g)	(4a)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
228	(1a)-(1h)	(2e)	(3g)	(4a)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
229	(1a)-(1h)	(2e)	(3g)	(4a)	(5c)	(6d)	(7a)	(8a)	-	-
230	(1a)-(1h)	(2e)	(3g)	(4a)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
231	(1a)-(1h)	(2e)	(3g)	(4a)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
232	(1a)-(1h)	(2e)	(3g)	(4a)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
233	(1a)-(1h)	(2e)	(3g)	(4a)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
234	(1a)-(1h)	(2e)	(3g)	(4a)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
235	(1a)-(1h)	(2e)	(3g)	(4a)	(5c)	(6e)	(7a)	(8a)	-	-
236	(1a)-(1h)	(2e)	(3g)	(4a)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
237	(1a)-(1h)	(2e)	(3g)	(4a)	(5c)	(6e)	(7c)	(8a)	-	(8dd)

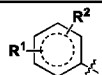
Embo- diment		R ¹	R ²	R ³	R ⁵	R ⁶	R ⁴	R ^{4a}	R ^{4b}	R ^{4c}
238	(1a)-(1h)	(2e)	(3g)	(4a)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
239	(1a)-(1h)	(2e)	(3g)	(4a)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
240	(1a)-(1h)	(2e)	(3g)	(4a)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
241	(1a)-(1h)	(2e)	(3g)	(4d)	(5b)	(6d)	(7a)	(8a)	-	-
242	(1a)-(1h)	(2e)	(3g)	(4d)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
243	(1a)-(1h)	(2e)	(3g)	(4d)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
244	(1a)-(1h)	(2e)	(3g)	(4d)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
245	(1a)-(1h)	(2e)	(3g)	(4d)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
246	(1a)-(1h)	(2e)	(3g)	(4d)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
247	(1a)-(1h)	(2e)	(3g)	(4d)	(5b)	(6e)	(7a)	(8a)	-	-
248	(1a)-(1h)	(2e)	(3g)	(4d)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
249	(1a)-(1h)	(2e)	(3g)	(4d)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
250	(1a)-(1h)	(2e)	(3g)	(4d)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
251	(1a)-(1h)	(2e)	(3g)	(4d)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
252	(1a)-(1h)	(2e)	(3g)	(4d)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
253	(1a)-(1h)	(2e)	(3g)	(4d)	(5c)	(6d)	(7a)	(8a)	-	-
254	(1a)-(1h)	(2e)	(3g)	(4d)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
255	(1a)-(1h)	(2e)	(3g)	(4d)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
256	(1a)-(1h)	(2e)	(3g)	(4d)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
257	(1a)-(1h)	(2e)	(3g)	(4d)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
258	(1a)-(1h)	(2e)	(3g)	(4d)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
259	(1a)-(1h)	(2e)	(3g)	(4d)	(5c)	(6e)	(7a)	(8a)	-	-
260	(1a)-(1h)	(2e)	(3g)	(4d)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
261	(1a)-(1h)	(2e)	(3g)	(4d)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
262	(1a)-(1h)	(2e)	(3g)	(4d)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
263	(1a)-(1h)	(2e)	(3g)	(4d)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
264	(1a)-(1h)	(2e)	(3g)	(4d)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
265	(1a)-(1h)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7a)	(8a)	-	-
266	(1a)-(1h)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
267	(1a)-(1h)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
268	(1a)-(1h)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
269	(1a)-(1h)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
270	(1a)-(1h)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
271	(1a)-(1h)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7a)	(8a)	-	-
272	(1a)-(1h)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
273	(1a)-(1h)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
274	(1a)-(1h)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
275	(1a)-(1h)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
276	(1a)-(1h)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
277	(1a)-(1h)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7a)	(8a)	-	-
278	(1a)-(1h)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
279	(1a)-(1h)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
280	(1a)-(1h)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)

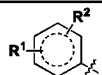
Embo- diment		R ¹	R ²	R ³	R ⁵	R ⁶	R ⁴	R ^{4a}	R ^{4b}	R ^{4c}
281	(1a)-(1h)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
282	(1a)-(1h)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
283	(1a)-(1h)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7a)	(8a)	-	-
284	(1a)-(1h)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
285	(1a)-(1h)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
286	(1a)-(1h)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
287	(1a)-(1h)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
288	(1a)-(1h)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
289	(1a)-(1h)	(2i)	(3c)	(4a)	(5b)	(6d)	(7a)	(8a)	-	-
290	(1a)-(1h)	(2i)	(3c)	(4a)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
291	(1a)-(1h)	(2i)	(3c)	(4a)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
292	(1a)-(1h)	(2i)	(3c)	(4a)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
293	(1a)-(1h)	(2i)	(3c)	(4a)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
294	(1a)-(1h)	(2i)	(3c)	(4a)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
295	(1a)-(1h)	(2i)	(3c)	(4a)	(5b)	(6e)	(7a)	(8a)	-	-
296	(1a)-(1h)	(2i)	(3c)	(4a)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
297	(1a)-(1h)	(2i)	(3c)	(4a)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
298	(1a)-(1h)	(2i)	(3c)	(4a)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
299	(1a)-(1h)	(2i)	(3c)	(4a)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
300	(1a)-(1h)	(2i)	(3c)	(4a)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
301	(1a)-(1h)	(2i)	(3c)	(4a)	(5c)	(6d)	(7a)	(8a)	-	-
302	(1a)-(1h)	(2i)	(3c)	(4a)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
303	(1a)-(1h)	(2i)	(3c)	(4a)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
304	(1a)-(1h)	(2i)	(3c)	(4a)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
305	(1a)-(1h)	(2i)	(3c)	(4a)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
306	(1a)-(1h)	(2i)	(3c)	(4a)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
307	(1a)-(1h)	(2i)	(3c)	(4a)	(5c)	(6e)	(7a)	(8a)	-	-
308	(1a)-(1h)	(2i)	(3c)	(4a)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
309	(1a)-(1h)	(2i)	(3c)	(4a)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
310	(1a)-(1h)	(2i)	(3c)	(4a)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
311	(1a)-(1h)	(2i)	(3c)	(4a)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
312	(1a)-(1h)	(2i)	(3c)	(4a)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
313	(1a)-(1h)	(2i)	(3c)	(4d)	(5b)	(6d)	(7a)	(8a)	-	-
314	(1a)-(1h)	(2i)	(3c)	(4d)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
315	(1a)-(1h)	(2i)	(3c)	(4d)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
316	(1a)-(1h)	(2i)	(3c)	(4d)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
317	(1a)-(1h)	(2i)	(3c)	(4d)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
318	(1a)-(1h)	(2i)	(3c)	(4d)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
319	(1a)-(1h)	(2i)	(3c)	(4d)	(5b)	(6e)	(7a)	(8a)	-	-
320	(1a)-(1h)	(2i)	(3c)	(4d)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
321	(1a)-(1h)	(2i)	(3c)	(4d)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
322	(1a)-(1h)	(2i)	(3c)	(4d)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
323	(1a)-(1h)	(2i)	(3c)	(4d)	(5b)	(6e)	(7d)	-	(8r)	(8dd)

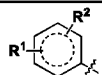
Embo- diment		R ¹	R ²	R ³	R ⁵	R ⁶	R ⁴	R ^{4a}	R ^{4b}	R ^{4c}
324	(1a)-(1h)	(2i)	(3c)	(4d)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
325	(1a)-(1h)	(2i)	(3c)	(4d)	(5c)	(6d)	(7a)	(8a)	-	-
326	(1a)-(1h)	(2i)	(3c)	(4d)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
327	(1a)-(1h)	(2i)	(3c)	(4d)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
328	(1a)-(1h)	(2i)	(3c)	(4d)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
329	(1a)-(1h)	(2i)	(3c)	(4d)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
330	(1a)-(1h)	(2i)	(3c)	(4d)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
331	(1a)-(1h)	(2i)	(3c)	(4d)	(5c)	(6e)	(7a)	(8a)	-	-
332	(1a)-(1h)	(2i)	(3c)	(4d)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
333	(1a)-(1h)	(2i)	(3c)	(4d)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
334	(1a)-(1h)	(2i)	(3c)	(4d)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
335	(1a)-(1h)	(2i)	(3c)	(4d)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
336	(1a)-(1h)	(2i)	(3c)	(4d)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
337	(1a)-(1h)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7a)	(8a)	-	-
338	(1a)-(1h)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
339	(1a)-(1h)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
340	(1a)-(1h)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
341	(1a)-(1h)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
342	(1a)-(1h)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
343	(1a)-(1h)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7a)	(8a)	-	-
344	(1a)-(1h)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
345	(1a)-(1h)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
346	(1a)-(1h)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
347	(1a)-(1h)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
348	(1a)-(1h)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
349	(1a)-(1h)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7a)	(8a)	-	-
350	(1a)-(1h)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
351	(1a)-(1h)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
352	(1a)-(1h)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
353	(1a)-(1h)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
354	(1a)-(1h)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
355	(1a)-(1h)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7a)	(8a)	-	-
356	(1a)-(1h)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
357	(1a)-(1h)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
358	(1a)-(1h)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
359	(1a)-(1h)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
360	(1a)-(1h)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
361	(1a)-(1h)	(2i)	(3g)	(4a)	(5b)	(6d)	(7a)	(8a)	-	-
362	(1a)-(1h)	(2i)	(3g)	(4a)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
363	(1a)-(1h)	(2i)	(3g)	(4a)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
364	(1a)-(1h)	(2i)	(3g)	(4a)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
365	(1a)-(1h)	(2i)	(3g)	(4a)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
366	(1a)-(1h)	(2i)	(3g)	(4a)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)

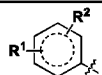
Embo- diment		R ¹	R ²	R ³	R ⁵	R ⁶	R ⁴	R ^{4a}	R ^{4b}	R ^{4c}
367	(1a)-(1h)	(2i)	(3g)	(4a)	(5b)	(6e)	(7a)	(8a)	-	-
368	(1a)-(1h)	(2i)	(3g)	(4a)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
369	(1a)-(1h)	(2i)	(3g)	(4a)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
370	(1a)-(1h)	(2i)	(3g)	(4a)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
371	(1a)-(1h)	(2i)	(3g)	(4a)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
372	(1a)-(1h)	(2i)	(3g)	(4a)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
373	(1a)-(1h)	(2i)	(3g)	(4a)	(5c)	(6d)	(7a)	(8a)	-	-
374	(1a)-(1h)	(2i)	(3g)	(4a)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
375	(1a)-(1h)	(2i)	(3g)	(4a)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
376	(1a)-(1h)	(2i)	(3g)	(4a)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
377	(1a)-(1h)	(2i)	(3g)	(4a)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
378	(1a)-(1h)	(2i)	(3g)	(4a)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
379	(1a)-(1h)	(2i)	(3g)	(4a)	(5c)	(6e)	(7a)	(8a)	-	-
380	(1a)-(1h)	(2i)	(3g)	(4a)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
381	(1a)-(1h)	(2i)	(3g)	(4a)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
382	(1a)-(1h)	(2i)	(3g)	(4a)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
383	(1a)-(1h)	(2i)	(3g)	(4a)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
384	(1a)-(1h)	(2i)	(3g)	(4a)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
385	(1a)-(1h)	(2i)	(3g)	(4d)	(5b)	(6d)	(7a)	(8a)	-	-
386	(1a)-(1h)	(2i)	(3g)	(4d)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
387	(1a)-(1h)	(2i)	(3g)	(4d)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
388	(1a)-(1h)	(2i)	(3g)	(4d)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
389	(1a)-(1h)	(2i)	(3g)	(4d)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
390	(1a)-(1h)	(2i)	(3g)	(4d)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
391	(1a)-(1h)	(2i)	(3g)	(4d)	(5b)	(6e)	(7a)	(8a)	-	-
392	(1a)-(1h)	(2i)	(3g)	(4d)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
393	(1a)-(1h)	(2i)	(3g)	(4d)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
394	(1a)-(1h)	(2i)	(3g)	(4d)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
395	(1a)-(1h)	(2i)	(3g)	(4d)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
396	(1a)-(1h)	(2i)	(3g)	(4d)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
397	(1a)-(1h)	(2i)	(3g)	(4d)	(5c)	(6d)	(7a)	(8a)	-	-
398	(1a)-(1h)	(2i)	(3g)	(4d)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
399	(1a)-(1h)	(2i)	(3g)	(4d)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
400	(1a)-(1h)	(2i)	(3g)	(4d)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
401	(1a)-(1h)	(2i)	(3g)	(4d)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
402	(1a)-(1h)	(2i)	(3g)	(4d)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
403	(1a)-(1h)	(2i)	(3g)	(4d)	(5c)	(6e)	(7a)	(8a)	-	-
404	(1a)-(1h)	(2i)	(3g)	(4d)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
405	(1a)-(1h)	(2i)	(3g)	(4d)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
406	(1a)-(1h)	(2i)	(3g)	(4d)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
407	(1a)-(1h)	(2i)	(3g)	(4d)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
408	(1a)-(1h)	(2i)	(3g)	(4d)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
409	(1a)-(1h)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7a)	(8a)	-	-

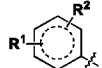
Embo- diment		R ¹	R ²	R ³	R ⁵	R ⁶	R ⁴	R ^{4a}	R ^{4b}	R ^{4c}
410	(1a)-(1h)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
411	(1a)-(1h)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
412	(1a)-(1h)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
413	(1a)-(1h)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
414	(1a)-(1h)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
415	(1a)-(1h)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7a)	(8a)	-	-
416	(1a)-(1h)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
417	(1a)-(1h)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
418	(1a)-(1h)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
419	(1a)-(1h)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
420	(1a)-(1h)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
421	(1a)-(1h)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7a)	(8a)	-	-
422	(1a)-(1h)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
423	(1a)-(1h)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
424	(1a)-(1h)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
425	(1a)-(1h)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
426	(1a)-(1h)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
427	(1a)-(1h)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7a)	(8a)	-	-
428	(1a)-(1h)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
429	(1a)-(1h)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
430	(1a)-(1h)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
431	(1a)-(1h)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
432	(1a)-(1h)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
433	(1g)	(2d)	(3c)	(4a)	(5b)	(6d)	(7a)	(8a)	-	-
434	(1g)	(2d)	(3c)	(4a)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
435	(1g)	(2d)	(3c)	(4a)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
436	(1g)	(2d)	(3c)	(4a)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
437	(1g)	(2d)	(3c)	(4a)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
438	(1g)	(2d)	(3c)	(4a)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
439	(1g)	(2d)	(3c)	(4a)	(5b)	(6e)	(7a)	(8a)	-	-
440	(1g)	(2d)	(3c)	(4a)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
441	(1g)	(2d)	(3c)	(4a)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
442	(1g)	(2d)	(3c)	(4a)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
443	(1g)	(2d)	(3c)	(4a)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
444	(1g)	(2d)	(3c)	(4a)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
445	(1g)	(2d)	(3c)	(4a)	(5c)	(6d)	(7a)	(8a)	-	-
446	(1g)	(2d)	(3c)	(4a)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
447	(1g)	(2d)	(3c)	(4a)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
448	(1g)	(2d)	(3c)	(4a)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
449	(1g)	(2d)	(3c)	(4a)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
450	(1g)	(2d)	(3c)	(4a)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
451	(1g)	(2d)	(3c)	(4a)	(5c)	(6e)	(7a)	(8a)	-	-
452	(1g)	(2d)	(3c)	(4a)	(5c)	(6e)	(7a)	(8b),(8g)	-	-

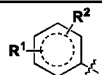
Embo- diment		R ¹	R ²	R ³	R ⁵	R ⁶	R ⁴	R ^{4a}	R ^{4b}	R ^{4c}
453	(1g)	(2d)	(3c)	(4a)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
454	(1g)	(2d)	(3c)	(4a)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
455	(1g)	(2d)	(3c)	(4a)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
456	(1g)	(2d)	(3c)	(4a)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
457	(1g)	(2d)	(3c)	(4d)	(5b)	(6d)	(7a)	(8a)	-	-
458	(1g)	(2d)	(3c)	(4d)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
459	(1g)	(2d)	(3c)	(4d)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
460	(1g)	(2d)	(3c)	(4d)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
461	(1g)	(2d)	(3c)	(4d)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
462	(1g)	(2d)	(3c)	(4d)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
463	(1g)	(2d)	(3c)	(4d)	(5b)	(6e)	(7a)	(8a)	-	-
464	(1g)	(2d)	(3c)	(4d)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
465	(1g)	(2d)	(3c)	(4d)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
466	(1g)	(2d)	(3c)	(4d)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
467	(1g)	(2d)	(3c)	(4d)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
468	(1g)	(2d)	(3c)	(4d)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
469	(1g)	(2d)	(3c)	(4d)	(5c)	(6d)	(7a)	(8a)	-	-
470	(1g)	(2d)	(3c)	(4d)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
471	(1g)	(2d)	(3c)	(4d)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
472	(1g)	(2d)	(3c)	(4d)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
473	(1g)	(2d)	(3c)	(4d)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
474	(1g)	(2d)	(3c)	(4d)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
475	(1g)	(2d)	(3c)	(4d)	(5c)	(6e)	(7a)	(8a)	-	-
476	(1g)	(2d)	(3c)	(4d)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
477	(1g)	(2d)	(3c)	(4d)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
478	(1g)	(2d)	(3c)	(4d)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
479	(1g)	(2d)	(3c)	(4d)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
480	(1g)	(2d)	(3c)	(4d)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
481	(1g)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7a)	(8a)	-	-
482	(1g)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
483	(1g)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
484	(1g)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
485	(1g)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
486	(1g)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
487	(1g)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7a)	(8a)	-	-
488	(1g)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
489	(1g)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
490	(1g)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
491	(1g)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
492	(1g)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
493	(1g)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7a)	(8a)	-	-
494	(1g)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
495	(1g)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7c)	(8a)	-	(8dd)

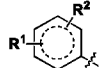
Embo- diment		R ¹	R ²	R ³	R ⁵	R ⁶	R ⁴	R ^{4a}	R ^{4b}	R ^{4c}
496	(1g)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
497	(1g)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
498	(1g)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
499	(1g)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7a)	(8a)	-	-
500	(1g)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
501	(1g)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
502	(1g)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
503	(1g)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
504	(1g)	(2d)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
505	(1g)	(2d)	(3g)	(4a)	(5b)	(6d)	(7a)	(8a)	-	-
506	(1g)	(2d)	(3g)	(4a)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
507	(1g)	(2d)	(3g)	(4a)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
508	(1g)	(2d)	(3g)	(4a)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
509	(1g)	(2d)	(3g)	(4a)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
510	(1g)	(2d)	(3g)	(4a)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
511	(1g)	(2d)	(3g)	(4a)	(5b)	(6e)	(7a)	(8a)	-	-
512	(1g)	(2d)	(3g)	(4a)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
513	(1g)	(2d)	(3g)	(4a)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
514	(1g)	(2d)	(3g)	(4a)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
515	(1g)	(2d)	(3g)	(4a)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
516	(1g)	(2d)	(3g)	(4a)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
517	(1g)	(2d)	(3g)	(4a)	(5c)	(6d)	(7a)	(8a)	-	-
518	(1g)	(2d)	(3g)	(4a)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
519	(1g)	(2d)	(3g)	(4a)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
520	(1g)	(2d)	(3g)	(4a)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
521	(1g)	(2d)	(3g)	(4a)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
522	(1g)	(2d)	(3g)	(4a)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
523	(1g)	(2d)	(3g)	(4a)	(5c)	(6e)	(7a)	(8a)	-	-
524	(1g)	(2d)	(3g)	(4a)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
525	(1g)	(2d)	(3g)	(4a)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
526	(1g)	(2d)	(3g)	(4a)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
527	(1g)	(2d)	(3g)	(4a)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
528	(1g)	(2d)	(3g)	(4a)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
529	(1g)	(2d)	(3g)	(4d)	(5b)	(6d)	(7a)	(8a)	-	-
530	(1g)	(2d)	(3g)	(4d)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
531	(1g)	(2d)	(3g)	(4d)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
532	(1g)	(2d)	(3g)	(4d)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
533	(1g)	(2d)	(3g)	(4d)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
534	(1g)	(2d)	(3g)	(4d)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
535	(1g)	(2d)	(3g)	(4d)	(5b)	(6e)	(7a)	(8a)	-	-
536	(1g)	(2d)	(3g)	(4d)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
537	(1g)	(2d)	(3g)	(4d)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
538	(1g)	(2d)	(3g)	(4d)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)

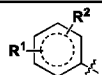
Embo- diment		R ¹	R ²	R ³	R ⁵	R ⁶	R ⁴	R ^{4a}	R ^{4b}	R ^{4c}
539	(1g)	(2d)	(3g)	(4d)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
540	(1g)	(2d)	(3g)	(4d)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
541	(1g)	(2d)	(3g)	(4d)	(5c)	(6d)	(7a)	(8a)	-	-
542	(1g)	(2d)	(3g)	(4d)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
543	(1g)	(2d)	(3g)	(4d)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
544	(1g)	(2d)	(3g)	(4d)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
545	(1g)	(2d)	(3g)	(4d)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
546	(1g)	(2d)	(3g)	(4d)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
547	(1g)	(2d)	(3g)	(4d)	(5c)	(6e)	(7a)	(8a)	-	-
548	(1g)	(2d)	(3g)	(4d)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
549	(1g)	(2d)	(3g)	(4d)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
550	(1g)	(2d)	(3g)	(4d)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
551	(1g)	(2d)	(3g)	(4d)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
552	(1g)	(2d)	(3g)	(4d)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
553	(1g)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7a)	(8a)	-	-
554	(1g)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
555	(1g)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
556	(1g)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
557	(1g)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
558	(1g)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
559	(1g)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7a)	(8a)	-	-
560	(1g)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
561	(1g)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
562	(1g)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
563	(1g)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
564	(1g)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
565	(1g)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7a)	(8a)	-	-
566	(1g)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
567	(1g)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
568	(1g)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
569	(1g)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
570	(1g)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
571	(1g)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7a)	(8a)	-	-
572	(1g)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
573	(1g)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
574	(1g)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
575	(1g)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
576	(1g)	(2d)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
577	(1g)	(2e)	(3c)	(4a)	(5b)	(6d)	(7a)	(8a)	-	-
578	(1g)	(2e)	(3c)	(4a)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
579	(1g)	(2e)	(3c)	(4a)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
580	(1g)	(2e)	(3c)	(4a)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
581	(1g)	(2e)	(3c)	(4a)	(5b)	(6d)	(7d)	-	(8r)	(8dd)

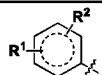
Embo- diment		R ¹	R ²	R ³	R ⁵	R ⁶	R ⁴	R ^{4a}	R ^{4b}	R ^{4c}
582	(1g)	(2e)	(3c)	(4a)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
583	(1g)	(2e)	(3c)	(4a)	(5b)	(6e)	(7a)	(8a)	-	-
584	(1g)	(2e)	(3c)	(4a)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
585	(1g)	(2e)	(3c)	(4a)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
586	(1g)	(2e)	(3c)	(4a)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
587	(1g)	(2e)	(3c)	(4a)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
588	(1g)	(2e)	(3c)	(4a)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
589	(1g)	(2e)	(3c)	(4a)	(5c)	(6d)	(7a)	(8a)	-	-
590	(1g)	(2e)	(3c)	(4a)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
591	(1g)	(2e)	(3c)	(4a)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
592	(1g)	(2e)	(3c)	(4a)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
593	(1g)	(2e)	(3c)	(4a)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
594	(1g)	(2e)	(3c)	(4a)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
595	(1g)	(2e)	(3c)	(4a)	(5c)	(6e)	(7a)	(8a)	-	-
596	(1g)	(2e)	(3c)	(4a)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
597	(1g)	(2e)	(3c)	(4a)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
598	(1g)	(2e)	(3c)	(4a)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
599	(1g)	(2e)	(3c)	(4a)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
600	(1g)	(2e)	(3c)	(4a)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
601	(1g)	(2e)	(3c)	(4d)	(5b)	(6d)	(7a)	(8a)	-	-
602	(1g)	(2e)	(3c)	(4d)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
603	(1g)	(2e)	(3c)	(4d)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
604	(1g)	(2e)	(3c)	(4d)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
605	(1g)	(2e)	(3c)	(4d)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
606	(1g)	(2e)	(3c)	(4d)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
607	(1g)	(2e)	(3c)	(4d)	(5b)	(6e)	(7a)	(8a)	-	-
608	(1g)	(2e)	(3c)	(4d)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
609	(1g)	(2e)	(3c)	(4d)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
610	(1g)	(2e)	(3c)	(4d)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
611	(1g)	(2e)	(3c)	(4d)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
612	(1g)	(2e)	(3c)	(4d)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
613	(1g)	(2e)	(3c)	(4d)	(5c)	(6d)	(7a)	(8a)	-	-
614	(1g)	(2e)	(3c)	(4d)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
615	(1g)	(2e)	(3c)	(4d)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
616	(1g)	(2e)	(3c)	(4d)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
617	(1g)	(2e)	(3c)	(4d)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
618	(1g)	(2e)	(3c)	(4d)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
619	(1g)	(2e)	(3c)	(4d)	(5c)	(6e)	(7a)	(8a)	-	-
620	(1g)	(2e)	(3c)	(4d)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
621	(1g)	(2e)	(3c)	(4d)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
622	(1g)	(2e)	(3c)	(4d)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
623	(1g)	(2e)	(3c)	(4d)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
624	(1g)	(2e)	(3c)	(4d)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)

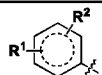
Embo- diment		R ¹	R ²	R ³	R ⁵	R ⁶	R ⁴	R ^{4a}	R ^{4b}	R ^{4c}
625	(1g)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7a)	(8a)	-	-
626	(1g)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
627	(1g)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
628	(1g)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
629	(1g)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
630	(1g)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
631	(1g)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7a)	(8a)	-	-
632	(1g)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
633	(1g)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
634	(1g)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
635	(1g)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
636	(1g)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
637	(1g)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7a)	(8a)	-	-
638	(1g)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
639	(1g)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
640	(1g)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
641	(1g)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
642	(1g)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
643	(1g)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7a)	(8a)	-	-
644	(1g)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
645	(1g)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
646	(1g)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
647	(1g)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
648	(1g)	(2e)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
649	(1g)	(2e)	(3g)	(4a)	(5b)	(6d)	(7a)	(8a)	-	-
650	(1g)	(2e)	(3g)	(4a)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
651	(1g)	(2e)	(3g)	(4a)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
652	(1g)	(2e)	(3g)	(4a)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
653	(1g)	(2e)	(3g)	(4a)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
654	(1g)	(2e)	(3g)	(4a)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
655	(1g)	(2e)	(3g)	(4a)	(5b)	(6e)	(7a)	(8a)	-	-
656	(1g)	(2e)	(3g)	(4a)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
657	(1g)	(2e)	(3g)	(4a)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
658	(1g)	(2e)	(3g)	(4a)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
659	(1g)	(2e)	(3g)	(4a)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
660	(1g)	(2e)	(3g)	(4a)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
661	(1g)	(2e)	(3g)	(4a)	(5c)	(6d)	(7a)	(8a)	-	-
662	(1g)	(2e)	(3g)	(4a)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
663	(1g)	(2e)	(3g)	(4a)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
664	(1g)	(2e)	(3g)	(4a)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
665	(1g)	(2e)	(3g)	(4a)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
666	(1g)	(2e)	(3g)	(4a)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
667	(1g)	(2e)	(3g)	(4a)	(5c)	(6e)	(7a)	(8a)	-	-

Embo- diment		R ¹	R ²	R ³	R ⁵	R ⁶	R ⁴	R ^{4a}	R ^{4b}	R ^{4c}
668	(1g)	(2e)	(3g)	(4a)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
669	(1g)	(2e)	(3g)	(4a)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
670	(1g)	(2e)	(3g)	(4a)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
671	(1g)	(2e)	(3g)	(4a)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
672	(1g)	(2e)	(3g)	(4a)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
673	(1g)	(2e)	(3g)	(4d)	(5b)	(6d)	(7a)	(8a)	-	-
674	(1g)	(2e)	(3g)	(4d)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
675	(1g)	(2e)	(3g)	(4d)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
676	(1g)	(2e)	(3g)	(4d)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
677	(1g)	(2e)	(3g)	(4d)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
678	(1g)	(2e)	(3g)	(4d)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
679	(1g)	(2e)	(3g)	(4d)	(5b)	(6e)	(7a)	(8a)	-	-
680	(1g)	(2e)	(3g)	(4d)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
681	(1g)	(2e)	(3g)	(4d)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
682	(1g)	(2e)	(3g)	(4d)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
683	(1g)	(2e)	(3g)	(4d)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
684	(1g)	(2e)	(3g)	(4d)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
685	(1g)	(2e)	(3g)	(4d)	(5c)	(6d)	(7a)	(8a)	-	-
686	(1g)	(2e)	(3g)	(4d)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
687	(1g)	(2e)	(3g)	(4d)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
688	(1g)	(2e)	(3g)	(4d)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
689	(1g)	(2e)	(3g)	(4d)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
690	(1g)	(2e)	(3g)	(4d)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
691	(1g)	(2e)	(3g)	(4d)	(5c)	(6e)	(7a)	(8a)	-	-
692	(1g)	(2e)	(3g)	(4d)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
693	(1g)	(2e)	(3g)	(4d)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
694	(1g)	(2e)	(3g)	(4d)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
695	(1g)	(2e)	(3g)	(4d)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
696	(1g)	(2e)	(3g)	(4d)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
697	(1g)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7a)	(8a)	-	-
698	(1g)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
699	(1g)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
700	(1g)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
701	(1g)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
702	(1g)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
703	(1g)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7a)	(8a)	-	-
704	(1g)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
705	(1g)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
706	(1g)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
707	(1g)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
708	(1g)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
709	(1g)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7a)	(8a)	-	-
710	(1g)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7a)	(8b),(8g)	-	-

Embo- diment		R ¹	R ²	R ³	R ⁵	R ⁶	R ⁴	R ^{4a}	R ^{4b}	R ^{4c}
711	(1g)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
712	(1g)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
713	(1g)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
714	(1g)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
715	(1g)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7a)	(8a)	-	-
716	(1g)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
717	(1g)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
718	(1g)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
719	(1g)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
720	(1g)	(2e)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
721	(1g)	(2i)	(3c)	(4a)	(5b)	(6d)	(7a)	(8a)	-	-
722	(1g)	(2i)	(3c)	(4a)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
723	(1g)	(2i)	(3c)	(4a)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
724	(1g)	(2i)	(3c)	(4a)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
725	(1g)	(2i)	(3c)	(4a)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
726	(1g)	(2i)	(3c)	(4a)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
727	(1g)	(2i)	(3c)	(4a)	(5b)	(6e)	(7a)	(8a)	-	-
728	(1g)	(2i)	(3c)	(4a)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
729	(1g)	(2i)	(3c)	(4a)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
730	(1g)	(2i)	(3c)	(4a)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
731	(1g)	(2i)	(3c)	(4a)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
732	(1g)	(2i)	(3c)	(4a)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
733	(1g)	(2i)	(3c)	(4a)	(5c)	(6d)	(7a)	(8a)	-	-
734	(1g)	(2i)	(3c)	(4a)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
735	(1g)	(2i)	(3c)	(4a)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
736	(1g)	(2i)	(3c)	(4a)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
737	(1g)	(2i)	(3c)	(4a)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
738	(1g)	(2i)	(3c)	(4a)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
739	(1g)	(2i)	(3c)	(4a)	(5c)	(6e)	(7a)	(8a)	-	-
740	(1g)	(2i)	(3c)	(4a)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
741	(1g)	(2i)	(3c)	(4a)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
742	(1g)	(2i)	(3c)	(4a)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
743	(1g)	(2i)	(3c)	(4a)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
744	(1g)	(2i)	(3c)	(4a)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
745	(1g)	(2i)	(3c)	(4d)	(5b)	(6d)	(7a)	(8a)	-	-
746	(1g)	(2i)	(3c)	(4d)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
747	(1g)	(2i)	(3c)	(4d)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
748	(1g)	(2i)	(3c)	(4d)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
749	(1g)	(2i)	(3c)	(4d)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
750	(1g)	(2i)	(3c)	(4d)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
751	(1g)	(2i)	(3c)	(4d)	(5b)	(6e)	(7a)	(8a)	-	-
752	(1g)	(2i)	(3c)	(4d)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
753	(1g)	(2i)	(3c)	(4d)	(5b)	(6e)	(7c)	(8a)	-	(8dd)

Embo- diment		R ¹	R ²	R ³	R ⁵	R ⁶	R ⁴	R ^{4a}	R ^{4b}	R ^{4c}
754	(1g)	(2i)	(3c)	(4d)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
755	(1g)	(2i)	(3c)	(4d)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
756	(1g)	(2i)	(3c)	(4d)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
757	(1g)	(2i)	(3c)	(4d)	(5c)	(6d)	(7a)	(8a)	-	-
758	(1g)	(2i)	(3c)	(4d)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
759	(1g)	(2i)	(3c)	(4d)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
760	(1g)	(2i)	(3c)	(4d)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
761	(1g)	(2i)	(3c)	(4d)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
762	(1g)	(2i)	(3c)	(4d)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
763	(1g)	(2i)	(3c)	(4d)	(5c)	(6e)	(7a)	(8a)	-	-
764	(1g)	(2i)	(3c)	(4d)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
765	(1g)	(2i)	(3c)	(4d)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
766	(1g)	(2i)	(3c)	(4d)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
767	(1g)	(2i)	(3c)	(4d)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
768	(1g)	(2i)	(3c)	(4d)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
769	(1g)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7a)	(8a)	-	-
770	(1g)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
771	(1g)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
772	(1g)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
773	(1g)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
774	(1g)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
775	(1g)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7a)	(8a)	-	-
776	(1g)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
777	(1g)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
778	(1g)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
779	(1g)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
780	(1g)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
781	(1g)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7a)	(8a)	-	-
782	(1g)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
783	(1g)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
784	(1g)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
785	(1g)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
786	(1g)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
787	(1g)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7a)	(8a)	-	-
788	(1g)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
789	(1g)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
790	(1g)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
791	(1g)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
792	(1g)	(2i)	(3c)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
793	(1g)	(2i)	(3g)	(4a)	(5b)	(6d)	(7a)	(8a)	-	-
794	(1g)	(2i)	(3g)	(4a)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
795	(1g)	(2i)	(3g)	(4a)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
796	(1g)	(2i)	(3g)	(4a)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)

Embo- diment		R ¹	R ²	R ³	R ⁵	R ⁶	R ⁴	R ^{4a}	R ^{4b}	R ^{4c}
797	(1g)	(2i)	(3g)	(4a)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
798	(1g)	(2i)	(3g)	(4a)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
799	(1g)	(2i)	(3g)	(4a)	(5b)	(6e)	(7a)	(8a)	-	-
800	(1g)	(2i)	(3g)	(4a)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
801	(1g)	(2i)	(3g)	(4a)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
802	(1g)	(2i)	(3g)	(4a)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
803	(1g)	(2i)	(3g)	(4a)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
804	(1g)	(2i)	(3g)	(4a)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
805	(1g)	(2i)	(3g)	(4a)	(5c)	(6d)	(7a)	(8a)	-	-
806	(1g)	(2i)	(3g)	(4a)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
807	(1g)	(2i)	(3g)	(4a)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
808	(1g)	(2i)	(3g)	(4a)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
809	(1g)	(2i)	(3g)	(4a)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
810	(1g)	(2i)	(3g)	(4a)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
811	(1g)	(2i)	(3g)	(4a)	(5c)	(6e)	(7a)	(8a)	-	-
812	(1g)	(2i)	(3g)	(4a)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
813	(1g)	(2i)	(3g)	(4a)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
814	(1g)	(2i)	(3g)	(4a)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
815	(1g)	(2i)	(3g)	(4a)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
816	(1g)	(2i)	(3g)	(4a)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
817	(1g)	(2i)	(3g)	(4d)	(5b)	(6d)	(7a)	(8a)	-	-
818	(1g)	(2i)	(3g)	(4d)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
819	(1g)	(2i)	(3g)	(4d)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
820	(1g)	(2i)	(3g)	(4d)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
821	(1g)	(2i)	(3g)	(4d)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
822	(1g)	(2i)	(3g)	(4d)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
823	(1g)	(2i)	(3g)	(4d)	(5b)	(6e)	(7a)	(8a)	-	-
824	(1g)	(2i)	(3g)	(4d)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
825	(1g)	(2i)	(3g)	(4d)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
826	(1g)	(2i)	(3g)	(4d)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
827	(1g)	(2i)	(3g)	(4d)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
828	(1g)	(2i)	(3g)	(4d)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
829	(1g)	(2i)	(3g)	(4d)	(5c)	(6d)	(7a)	(8a)	-	-
830	(1g)	(2i)	(3g)	(4d)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
831	(1g)	(2i)	(3g)	(4d)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
832	(1g)	(2i)	(3g)	(4d)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
833	(1g)	(2i)	(3g)	(4d)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
834	(1g)	(2i)	(3g)	(4d)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
835	(1g)	(2i)	(3g)	(4d)	(5c)	(6e)	(7a)	(8a)	-	-
836	(1g)	(2i)	(3g)	(4d)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
837	(1g)	(2i)	(3g)	(4d)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
838	(1g)	(2i)	(3g)	(4d)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
839	(1g)	(2i)	(3g)	(4d)	(5c)	(6e)	(7d)	-	(8r)	(8dd)

Embodiment		R ¹	R ²	R ³	R ⁵	R ⁶	R ⁴	R ^{4a}	R ^{4b}	R ^{4c}
840	(1g)	(2i)	(3g)	(4d)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)
841	(1g)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7a)	(8a)	-	-
842	(1g)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7a)	(8b),(8g)	-	-
843	(1g)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7c)	(8a)	-	(8dd)
844	(1g)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7c)	(8b),(8g)	-	(8dd)
845	(1g)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7d)	-	(8r)	(8dd)
846	(1g)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6d)	(7d)	-	(8s),(8w)	(8dd)
847	(1g)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7a)	(8a)	-	-
848	(1g)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7a)	(8b),(8g)	-	-
849	(1g)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7c)	(8a)	-	(8dd)
850	(1g)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7c)	(8b),(8g)	-	(8dd)
851	(1g)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7d)	-	(8r)	(8dd)
852	(1g)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5b)	(6e)	(7d)	-	(8s),(8w)	(8dd)
853	(1g)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7a)	(8a)	-	-
854	(1g)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7a)	(8b),(8g)	-	-
855	(1g)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7c)	(8a)	-	(8dd)
856	(1g)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7c)	(8b),(8g)	-	(8dd)
857	(1g)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7d)	-	(8r)	(8dd)
858	(1g)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6d)	(7d)	-	(8s),(8w)	(8dd)
859	(1g)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7a)	(8a)	-	-
860	(1g)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7a)	(8b),(8g)	-	-
861	(1g)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7c)	(8a)	-	(8dd)
862	(1g)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7c)	(8b),(8g)	-	(8dd)
863	(1g)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7d)	-	(8r)	(8dd)
864	(1g)	(2i)	(3g)	(4g),(4i),(4j),(4k)	(5c)	(6e)	(7d)	-	(8s),(8w)	(8dd)

Embodiment	Structural Formula	R ⁴	R ^{4a}	R ^{4b}	R ^{4c}
865	(la)	(7a)	(8a)	-	-
866	(la)	(7a)	(8b),(8g)	-	-
867	(la)	(7c)	(8a)	-	(8dd)
868	(la)	(7c)	(8b),(8g)	-	(8dd)
869	(la)	(7d)	-	(8r)	(8dd)
870	(la)	(7d)	-	(8s),(8w)	(8dd)
871	(lb)	(7a)	(8a)	-	-
872	(lb)	(7a)	(8b),(8g)	-	-
873	(lb)	(7c)	(8a)	-	(8dd)
874	(lb)	(7c)	(8b),(8g)	-	(8dd)
875	(lb)	(7d)	-	(8r)	(8dd)
876	(lb)	(7d)	-	(8s),(8w)	(8dd)
877	(lc)	(7a)	(8a)	-	-
878	(lc)	(7a)	(8b),(8g)	-	-
879	(lc)	(7c)	(8a)	-	(8dd)

Embodiment	Structural Formula	R ⁴	R ^{4a}	R ^{4b}	R ^{4c}
880	(lc)	(7c)	(8b),(8g)	-	(8dd)
881	(lc)	(7d)	-	(8r)	(8dd)
882	(lc)	(7d)	-	(8s),(8w)	(8dd)
883	(ld)	(7a)	(8a)	-	-
884	(ld)	(7a)	(8b),(8g)	-	-
885	(ld)	(7c)	(8a)	-	(8dd)
886	(ld)	(7c)	(8b),(8g)	-	(8dd)
887	(ld)	(7d)	-	(8r)	(8dd)
888	(ld)	(7d)	-	(8s),(8w)	(8dd)
889	(le)	(7a)	(8a)	-	-
890	(le)	(7a)	(8b),(8g)	-	-
891	(le)	(7c)	(8a)	-	(8dd)
892	(le)	(7c)	(8b),(8g)	-	(8dd)
893	(le)	(7d)	-	(8r)	(8dd)
894	(le)	(7d)	-	(8s),(8w)	(8dd)
895	(lf)	(7a)	(8a)	-	-
896	(lf)	(7a)	(8b),(8g)	-	-
897	(lf)	(7c)	(8a)	-	(8dd)
898	(lf)	(7c)	(8b),(8g)	-	(8dd)
899	(lf)	(7d)	-	(8r)	(8dd)
900	(lf)	(7d)	-	(8s),(8w)	(8dd)
901	(lg)	(7a)	(8a)	-	-
902	(lg)	(7a)	(8b),(8g)	-	-
903	(lg)	(7c)	(8a)	-	(8dd)
904	(lg)	(7c)	(8b),(8g)	-	(8dd)
905	(lg)	(7d)	-	(8r)	(8dd)
906	(lg)	(7d)	-	(8s),(8w)	(8dd)

Embodiment	Structural Formula	R ⁴	R ^{4a}	R ^{4b}	R ^{4c}
907	(la)	(7a)	(8d)	-	-
908	(la)	(7a)	(8e)	-	-
909	(la)	(7a)	(8j)	-	-
910	(la)	(7a)	(8o)	-	-
911	(la)	(7a)	(8p)	-	-
912	(la)	(7a)	(8q)	-	-
913	(la)	(7c)	(8j)	-	(8dd)
914	(la)	(7d)	-	(8t)	(8dd)
915	(la)	(7d)	-	(8w)	(8dd)
916	(lb)	(7a)	(8d)	-	-
917	(lb)	(7a)	(8e)	-	-
918	(lb)	(7a)	(8j)	-	-
919	(lb)	(7a)	(8o)	-	-
920	(lb)	(7a)	(8p)	-	-

Embodiment	Structural Formula	R ⁴	R ^{4a}	R ^{4b}	R ^{4c}
921	(lb)	(7a)	(8q)	-	-
922	(lb)	(7c)	(8j)	-	(8dd)
923	(lb)	(7d)	-	(8t)	(8dd)
924	(lb)	(7d)	-	(8w)	(8dd)
925	(lc)	(7a)	(8d)	-	-
926	(lc)	(7a)	(8e)	-	-
927	(lc)	(7a)	(8j)	-	-
928	(lc)	(7a)	(8o)	-	-
929	(lc)	(7a)	(8p)	-	-
930	(lc)	(7a)	(8q)	-	-
931	(lc)	(7c)	(8j)	-	(8dd)
932	(lc)	(7d)	-	(8t)	(8dd)
933	(lc)	(7d)	-	(8w)	(8dd)
934	(ld)	(7a)	(8d)	-	-
935	(ld)	(7a)	(8e)	-	-
936	(ld)	(7a)	(8j)	-	-
937	(ld)	(7a)	(8o)	-	-
938	(ld)	(7a)	(8p)	-	-
939	(ld)	(7a)	(8q)	-	-
940	(ld)	(7c)	(8j)	-	(8dd)
941	(ld)	(7d)	-	(8t)	(8dd)
942	(ld)	(7d)	-	(8w)	(8dd)
943	(le)	(7a)	(8d)	-	-
944	(le)	(7a)	(8e)	-	-
945	(le)	(7a)	(8j)	-	-
946	(le)	(7a)	(8o)	-	-
947	(le)	(7a)	(8p)	-	-
948	(le)	(7a)	(8q)	-	-
949	(le)	(7c)	(8j)	-	(8dd)
950	(le)	(7d)	-	(8t)	(8dd)
951	(le)	(7d)	-	(8w)	(8dd)
952	(lf)	(7a)	(8d)	-	-
953	(lf)	(7a)	(8e)	-	-
954	(lf)	(7a)	(8j)	-	-
955	(lf)	(7a)	(8o)	-	-
956	(lf)	(7a)	(8p)	-	-
957	(lf)	(7a)	(8q)	-	-
958	(lf)	(7c)	(8j)	-	(8dd)
959	(lf)	(7d)	-	(8t)	(8dd)
960	(lf)	(7d)	-	(8w)	(8dd)
961	(lg)	(7a)	(8d)	-	-
962	(lg)	(7a)	(8e)	-	-
963	(lg)	(7a)	(8j)	-	-
964	(lg)	(7a)	(8o)	-	-

Embodiment	Structural Formula	R ⁴	R ^{4a}	R ^{4b}	R ^{4c}
965	(lg)	(7a)	(8p)	-	-
966	(lg)	(7a)	(8q)	-	-
967	(lg)	(7c)	(8j)	-	(8dd)
968	(lg)	(7d)	-	(8t)	(8dd)
969	(lg)	(7d)	-	(8w)	(8dd)

[0031] In certain additional embodiments, including any of the embodiments described with reference to formulae (I) and (Ia)-(lg) and embodiments 1-969 above, each optionally substituted alkyl, alkenyl, and alkynyl recited in any one of preceding embodiments is unsubstituted. In alternative additional embodiments, including any of the embodiments described with reference to formulae (I) and (Ia)-(lg) and embodiments 1-969 above, each optionally substituted alkyl, alkenyl, and alkynyl recited in any one of preceding embodiments is independently substituted or unsubstituted. In further alternative additional embodiments, including any of the embodiments described with reference to formulae (I) and (Ia)-(lg) and embodiments 1-969 above, each optionally substituted alkyl, alkenyl, and alkynyl recited in any one of preceding embodiments is substituted.

[0032] In certain additional embodiments, including any of the embodiments described with reference to formulae (I) and (Ia)-(lg) and embodiments 1-969 above and the embodiment described in the paragraph immediately above, each cycloalkyl recited in any one of the preceding embodiments is a 3-7 membered monocyclic cycloalkyl. For example, in certain particular embodiments, including any of the embodiments described with reference to formulae (I) and (Ia)-(lg) and embodiments 1-969 above and the embodiment described in the paragraph immediately above, each cycloalkyl recited in any one of the preceding embodiments is a cyclopropyl, a cyclobutyl, a cyclopentyl, a cyclopentenyl, a cyclohexyl or a cyclohexenyl.

[0033] In certain additional embodiments, including any of the embodiments described with reference to formulae (I) and (Ia)-(lg) and embodiments 1-969 above and any embodiment described in the two paragraphs immediately above, each heterocycloalkyl recited in any one of the preceding embodiments is a 4-7 membered monocyclic heterocycloalkyl having 1-2 heteroatoms selected from O, S and N. For example, in certain particular embodiments, including any of the embodiments described with reference to formulae (I) and (Ia)-(lg) and embodiments 1-969 above and any embodiment described in the two paragraphs immediately above, each heterocycloalkyl recited in any one of the preceding embodiments is a pyrrolidinyl, a tetrahydrofuranyl, a tetrahydrothienyl, a piperidinyl, a piperazinyl, a morpholinyl, a

thiomorpholinyl, a tetrahydro-2H-pyranyl, or a tetrahydro-2H-thiopyranyl. In certain particular embodiments, including any of the embodiments described with reference to formulae (I) and (Ia)-(Ig) and embodiments 1-969 above and any embodiment described in the two paragraphs immediately above, each heterocycloalkyl recited in any one of the preceding embodiments is a pyrrolidine, a piperidine, a piperazine, a tetrahydrofuran, a (1H)dihydropyran, or a morpholine (e.g., each unsubstituted).

[0034] In certain additional embodiments, including any of the embodiments described with reference to formulae (I) and (Ia)-(Ig) and embodiments 1-969 above and any embodiment described in the three paragraphs immediately above, each aryl is phenyl.

[0035] In certain additional embodiments, including any of the embodiments described with reference to formulae (I) and (Ia)-(Ig) and embodiments 1-969 above and any embodiment described in the four paragraphs immediately above, each heteroaryl is a 5-6 membered monocyclic heteroaryl having 1-3 heteroatoms selected from O, S and N. For example, in certain particular embodiments, including any of the embodiments described with reference to formulae (I) and (Ia)-(Ig) and embodiments 1-969 above and any embodiment described in the four paragraphs immediately above, each heteroaryl is a monocyclic heteroaryl is substituted with 0-3 R^8 , e.g., is unsubstituted, substituted with one R^8 or substituted with two R^8 . In certain particular embodiments, including any of the embodiments described with reference to formulae (I) and (Ia)-(Ig) and embodiments 1-969 above and any embodiment described in the four paragraphs immediately above, each heteroaryl is a furanyl, a thienyl, a pyrrolyl, a pyrazolyl, an imidazolyl, an oxazolyl or a thiazolyl.

[0036] In certain additional embodiments, including any of the embodiments described with reference to formulae (I) and (Ia)-(Ig) and embodiments 1-969 above and any embodiment described in the paragraphs immediately above, each R^7 is independently oxo, C_1 - C_4 alkyl, Cl, F, Br, -CN, -SF₅, -N₃, nitro, -SR^A, -S(O)₁₋₂R^A, -OR^A, -NR^BR^A, -C(O)R^A, -C(O)NR^BR^A, -NR^BC(O)R^A, -C(S)NR^BR^A, -NR^BC(S)R^A, -CO₂R^A, -OC(O)R^A, -C(O)SR^A, -SC(O)R^A, -C(S)OR^A, -OC(S)R^A, -C(S)SR^A, -SC(S)R^A, -S(O)₁₋₂OR^A, -OS(O)₁₋₂R^A, -S(O)₁₋₂NR^BR^A, or -NR^BS(O)₁₋₂R^A. For example, in certain additional embodiments, including any of the embodiments described with reference to formulae (I) and (Ia)-(Ig) and embodiments 1-969 above and any embodiment described in the paragraphs immediately above, each R^7 is independently oxo, C_1 - C_4 alkyl, Cl, F, Br, -CN, -SF₅, -N₃, nitro, -SR^A, -S(O)₁₋₂R^A, -OR^A, -NR^BR^A, or -C(O)R^A.

[0037] In certain additional embodiments, including any of the embodiments described with reference to formulae (I) and (Ia)-(Ig) and embodiments 1-969 above and any embodiment

described in the paragraphs immediately above, each R^8 is independently C_1 - C_4 alkyl, Cl, F, Br, -CN, -SF₅, -N₃, nitro, -SR^A, -S(O)₁₋₂R^A, -OR^A, -NR^BR^A, -C(O)R^A, -C(O)NR^BR^A, -NR^BC(O)R^A, -C(S)NR^BR^A, -NR^BC(S)R^A, -CO₂R^A, -OC(O)R^A, -C(O)SR^A, -SC(O)R^A, -C(S)OR^A, -OC(S)R^A, -C(S)SR^A, -SC(S)R^A, -S(O)₁₋₂OR^A, -OS(O)₁₋₂R^A, -S(O)₁₋₂NR^BR^A, or -NR^BS(O)₁₋₂R^A. In certain additional embodiments, including any of the embodiments described with reference to formulae (I) and (Ia)-(Ig) and embodiments 1-969 above and any embodiment described in the paragraphs immediately above, each R^8 is independently C_1 - C_4 alkyl, Cl, F, Br, -CN, SF₅, -N₃, nitro, -SR^A, -S(O)₁₋₂R^A, -OR^A, -NR^BR^A, or -C(O)R^A.

[0038] In some embodiments, the present disclosure relates in particular to a compound selected from:

2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonic acid;
 sodium 2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonate;
 3'-methyl-3-(methylsulfonyl)-4-pentyl-[1,1'-biphenyl]-2,6-diol;
 3-(cyclopropylsulfonyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-2,6-diol;
 3-(tert-butylsulfonyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-2,6-diol;
 3-(benzylsulfonyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-2,6-diol;
 3'-methyl-4-pentyl-3-(phenylsulfonyl)-[1,1'-biphenyl]-2,6-diol;
 3'-methyl-3-((4-nitrophenyl)sulfonyl)-4-pentyl-[1,1'-biphenyl]-2,6-diol;
 3'-methyl-4-pentyl-3-(pyridin-3-ylsulfonyl)-[1,1'-biphenyl]-2,6-diol;
 3-(furan-3-ylsulfonyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-2,6-diol;
 3-((1H-imidazol-4-yl)sulfonyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-2,6-diol;
 3'-methyl-3-(oxetan-3-ylsulfonyl)-4-pentyl-[1,1'-biphenyl]-2,6-diol;
 3'-methyl-4-pentyl-3-((perfluorophenyl)sulfonyl)-[1,1'-biphenyl]-2,6-diol;
 4-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)cyclohexan-1-one;
 1-(2-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)ethyl)pyrrolidine-2,5-dione;

3-((2-(dimethylamino)ethyl)sulfonyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-2,6-diol;
 1-(3-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)piperidin-1-yl)ethan-
 1-one;
 3-((2-chloropyrimidin-5-yl)sulfonyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-2,6-diol;
 2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;
 2,6-dihydroxy-N,3'-dimethyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;
 2,6-dihydroxy-N,N,3'-trimethyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;
 N-cyclopropyl-2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;
 2,6-dihydroxy-N-isopropyl-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;
 2,6-dihydroxy-3'-methyl-4-pentyl-N-phenyl-[1,1'-biphenyl]-3-sulfonamide;
 N-benzyl-2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;
 3'-methyl-3-((4-methylpiperazin-1-yl)sulfonyl)-4-pentyl-[1,1'-biphenyl]-2,6-diol;
 3'-methyl-4-pentyl-3-(piperidin-1-ylsulfonyl)-[1,1'-biphenyl]-2,6-diol;
 3'-methyl-3-(morpholinosulfonyl)-4-pentyl-[1,1'-biphenyl]-2,6-diol;
 2,6-dihydroxy-3'-methyl-4-pentyl-N-(pyridin-3-yl)-[1,1'-biphenyl]-3-sulfonamide;
 2,6-dihydroxy-3'-methyl-4-pentyl-N-(pyrimidin-2-yl)-[1,1'-biphenyl]-3-sulfonamide;
 2,6-dihydroxy-3'-methyl-N-(2-oxopropyl)-4-pentyl-[1,1'-biphenyl]-3-sulfonamide; _
 1-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-
 yl)sulfonyl)azetidin-3-one;
 2,6-dihydroxy-3'-methyl-N-(oxetan-2-ylmethyl)-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;
 2,6-dihydroxy-3'-methyl-N-(oxetan-2-ylmethyl)-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;
 2,6-dihydroxy-3'-methyl-N-(oxetan-2-ylmethyl)-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;
 2,6-dihydroxy-3'-methyl-N-(oxetan-2-ylmethyl)-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;
 methyl ((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)alaninate;

N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-3-morpholinopropanamide;

4-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl])-3-sulfonamido)-4-oxobutanoic acid;

4-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl])-3-sulfonamido)-4-oxobutanoic acid;

2-amino-N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide;

N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(2-methoxyethoxy)acetamide;

2-amino-N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-3-hydroxypropanamide;

2-amino-N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)propanamide;

3-amino-N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-2-methylpropanamide;

N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide;

N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-3-oxobutanamide;

N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(3-methyl-1H-1,2,4-triazol-5-yl)acetamide;

N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-1H-1,2,4-triazole-5-carboxamide;

N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)oxetane-2-carboxamide;

N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)benzamide;

N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)nicotinamide;

N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-2-phenylacetamide;

N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(furan-2-yl)acetamide;

N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(oxazol-2-yl)acetamide;

N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(thiazol-2-yl)acetamide;

2-(1H-benzo[d]imidazol-2-yl)-N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide;

2,6-dihydroxy-3'-methyl-4-pentyl-N-(phenylsulfonyl)-[1,1'-biphenyl]-3-carboxamide;

N-(cyclohexylsulfonyl)-2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-carboxamide;

(E)-2,6-dihydroxy-3'-methyl-4-pentyl-N-(prop-1-en-1-ylsulfonyl)-[1,1'-biphenyl]-3-carboxamide;

N-((1H-benzo[d]imidazol-2-yl)sulfonyl)-2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-carboxamide;

N,N-diethyl-2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;

N-(2-bromoethyl)-2,6-dihydroxy-N-(2-hydroxyethyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;

2,2,2-trifluoroethyl 2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonate;

-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-4-(trifluoromethyl)benzamide;

N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)pivalamide;

2,6-dihydroxy-N,N,3'-trimethyl-4-propyl-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N-isopropyl-3'-methyl-4-propyl-[1,1'-biphenyl]-3-sulfonamide;

3-(ethylsulfonyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-2,6-diol;

tert-butyl 4-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)piperazine-1-carboxylate;

2,6-dihydroxy-3'-methyl-4-pentyl-N-(pyridin-3-ylsulfonyl)-[1,1'-biphenyl]-3-carboxamide;

2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonic acid;

sodium 2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonate;
5'-methyl-3-(methylsulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;
3-(cyclopropylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;
3-(tert-butylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;
3-(benzylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;
5'-methyl-4-pentyl-3-(phenylsulfonyl)-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;
5'-methyl-3-((4-nitrophenyl)sulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;
5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-3-(pyridin-3-ylsulfonyl)-[1,1'-biphenyl]-2,6-diol;
3-(furan-3-ylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;
3-((1H-imidazol-4-yl)sulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;
5'-methyl-3-(oxetan-3-ylsulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;
5'-methyl-4-pentyl-3-((perfluorophenyl)sulfonyl)-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;
4-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)cyclohexan-1-one;
1-(2-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)ethyl)pyrrolidine-2,5-dione;
3-((2-(dimethylamino)ethyl)sulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;
1-(3-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)piperidin-1-yl)ethan-1-one;
3-((2-chloropyrimidin-5-yl)sulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;
2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N,5'-dimethyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N,N,5'-trimethyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

N-cyclopropyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N-isopropyl-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-5'-methyl-4-pentyl-N-phenyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

N-benzyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

5'-methyl-3-((4-methylpiperazin-1-yl)sulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;

5'-methyl-4-pentyl-3-(piperidin-1-ylsulfonyl)-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;

5'-methyl-3-(morpholinosulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;

2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-N-(pyridin-3-yl)-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-N-(pyrimidin-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-N-(pyrimidin-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

1-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)azetidin-3-one;

2,6-dihydroxy-5'-methyl-N-(oxetan-2-ylmethyl)-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

3-((2-azaspiro[3.3]heptan-2-yl)sulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;

3-((2,6-diazaspiro[3.3]heptan-2-yl)sulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;

((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)alanine;

methyl ((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)alaninate;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-3-morpholinopropanamide;

4-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamido)-4-oxobutanoic acid;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-3-(4-methylpiperazin-1-yl)propanamide;

2-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(2-methoxyethoxy)acetamide;

2-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-3-hydroxypropanamide;

2-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)propanamide;

3-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-2-methylpropanamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-3-oxobutanamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-3-oxobutanamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-3-oxobutanamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-3-oxobutanamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-3-oxobutanamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)nicotinamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-2-phenylacetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(furan-2-yl)acetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(oxazol-2-yl)acetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(thiazol-2-yl)acetamide;

2-(1H-benzo[d]imidazol-2-yl)-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide;

2,6-dihydroxy-5'-methyl-4-pentyl-N-(phenylsulfonyl)-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-carboxamide;

N-(cyclohexylsulfonyl)-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-carboxamide;

(E)-2,6-dihydroxy-5'-methyl-4-pentyl-N-(prop-1-en-1-ylsulfonyl)-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-carboxamide;

N-((1H-benzo[d]imidazol-2-yl)sulfonyl)-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-carboxamide;

N,N-diethyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

N-(2-bromoethyl)-2,6-dihydroxy-N-(2-hydroxyethyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

2,2,2-trifluoroethyl 2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonate;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-4-(trifluoromethyl)benzamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)pivalamide;

2,6-dihydroxy-N,N,5'-trimethyl-2'-(prop-1-en-2-yl)-4-propyl-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N,N,5'-trimethyl-2'-(prop-1-en-2-yl)-4-propyl-[1,1'-biphenyl]-3-sulfonamide;

3-(ethylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;

tert-butyl 4-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)piperazine-1-carboxylate;

2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-N-(pyridin-3-ylsulfonyl)-[1,1'-biphenyl]-3-carboxamide;

2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonic acid;

sodium 2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonate;

5'-methyl-3-(methylsulfonyl)-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

3-(cyclopropylsulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

3-(tert-butylsulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

3-(benzylsulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

5'-methyl-4-pentyl-3-(phenylsulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

5'-methyl-3-((4-nitrophenyl)sulfonyl)-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

5'-methyl-4-pentyl-3-(pyridin-3-ylsulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

3-(furan-3-ylsulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

3-((1H-imidazol-4-yl)sulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

5'-methyl-3-(oxetan-3-ylsulfonyl)-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

5'-methyl-4-pentyl-3-((perfluorophenyl)sulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

4-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)cyclohexan-1-one;

1-(2-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)ethyl)pyrrolidine-2,5-dione;

3-((2-(dimethylamino)ethyl)sulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

1-(3-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)piperidin-1-yl)ethan-1-one;

3-((2-chloropyrimidin-5-yl)sulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N,N,5'-trimethyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

N-cyclopropyl-2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N-isopropyl-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-5'-methyl-4-pentyl-N-phenyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

N-benzyl-2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

5'-methyl-3-((4-methylpiperazin-1-yl)sulfonyl)-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

5'-methyl-4-pentyl-3-(piperidin-1-ylsulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

5'-methyl-3-(morpholinosulfonyl)-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

2,6-dihydroxy-5'-methyl-4-pentyl-N-(pyridin-3-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-5'-methyl-4-pentyl-N-(pyrimidin-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-5'-methyl-N-(2-oxopropyl)-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

1-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)azetidin-3-one;

2,6-dihydroxy-5'-methyl-N-(oxetan-2-ylmethyl)-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

3-((2-azaspiro[3.3]heptan-2-yl)sulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

3-((2,6-diazaspiro[3.3]heptan-2-yl)sulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

3-((2,6-diazaspiro[3.3]heptan-2-yl)sulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

methyl ((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)alaninate;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-3-morpholinopropanamide;

4-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl])-3-sulfonamido)-4-oxobutanoic acid;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-3-(4-methylpiperazin-1-yl)propanamide;

2-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(2-methoxyethoxy)acetamide;

2-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-3-hydroxypropanamide;

2-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)propanamide;

3-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-methylpropanamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-3-oxobutanamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(3-methyl-1H-1,2,4-triazol-5-yl)acetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-1H-1,2,4-triazole-5-carboxamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)oxetane-2-carboxamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)benzamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)nicotinamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-phenylacetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(furan-2-yl)acetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(oxazol-2-yl)acetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(thiazol-2-yl)acetamide;

2-(1H-benzo[d]imidazol-2-yl)-N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide;

2,6-dihydroxy-5'-methyl-4-pentyl-N-(phenylsulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide;

N-(cyclohexylsulfonyl)-2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide;

(E)-2,6-dihydroxy-5'-methyl-4-pentyl-N-(prop-1-en-1-ylsulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide;

N-((1H-benzo[d]imidazol-2-yl)sulfonyl)-2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide;

N,N-diethyl-2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

N-(2-bromoethyl)-2,6-dihydroxy-N-(2-hydroxyethyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,2,2-trifluoroethyl 2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonate;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-4-(trifluoromethyl)benzamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)pivalamide;

2,6-dihydroxy-N,N,5'-trimethyl-4-propyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N-isopropyl-5'-methyl-4-propyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

3-(ethylsulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

tert-butyl 4-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)piperazine-1-carboxylate;

2,6-dihydroxy-5'-methyl-4-pentyl-N-(pyridin-3-ylsulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide;

2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonic acid;

sodium 2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonate;

5'-methyl-3-(methylsulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

3-(cyclopropylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

3-(tert-butylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

3-(benzylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

5'-methyl-4-pentyl-3-(phenylsulfonyl)-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

5'-methyl-4-pentyl-3-(phenylsulfonyl)-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-3-(pyridin-3-ylsulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

3-(furan-3-ylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

3-((1H-imidazol-4-yl)sulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

5'-methyl-3-(oxetan-3-ylsulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

5'-methyl-3-(oxetan-3-ylsulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

4-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)cyclohexan-1-one;

1-(2-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)ethyl)pyrrolidine-2,5-dione;

3-((2-(dimethylamino)ethyl)sulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

1-(3-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)piperidin-1-yl)ethan-1-one;

3-((2-chloropyrimidin-5-yl)sulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N,5'-dimethyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N,N,5'-trimethyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

N-cyclopropyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N-isopropyl-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-5'-methyl-4-pentyl-N-phenyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

N-benzyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

5'-methyl-3-((4-methylpiperazin-1-yl)sulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

5'-methyl-4-pentyl-3-(piperidin-1-ylsulfonyl)-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

5'-methyl-3-(morpholinosulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-N-(pyrimidin-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-5'-methyl-N-(2-oxopropyl)-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

1-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)azetidin-3-one;

2,6-dihydroxy-5'-methyl-N-(oxetan-2-ylmethyl)-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

3-((2-azaspiro[3.3]heptan-2-yl)sulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

3-((2,6-diazaspiro[3.3]heptan-2-yl)sulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)alanine;

methyl ((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)alaninate;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-3-morpholinopropanamide;

4-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl])-3-sulfonamido)-4-oxobutanoic acid;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-3-(4-methylpiperazin-1-yl)propanamide;

2-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(2-methoxyethoxy)acetamide;

2-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-3-hydroxypropanamide;

2-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)propanamide;

3-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-methylpropanamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-3-oxobutanamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(3-methyl-1H-1,2,4-triazol-5-yl)acetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-1H-1,2,4-triazole-5-carboxamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)oxetane-2-carboxamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)oxetane-2-carboxamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)nicotinamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-phenylacetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(furan-2-yl)acetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(oxazol-2-yl)acetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(thiazol-2-yl)acetamide;

2-(1H-benzo[d]imidazol-2-yl)-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide;

2-(1H-benzo[d]imidazol-2-yl)-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide;

2-(1H-benzo[d]imidazol-2-yl)-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide;

(E)-2,6-dihydroxy-5'-methyl-4-pentyl-N-(prop-1-en-1-ylsulfonyl)-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide;

(E)-2,6-dihydroxy-5'-methyl-4-pentyl-N-(prop-1-en-1-ylsulfonyl)-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide;

N,N-diethyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

N-(2-bromoethyl)-2,6-dihydroxy-N-(2-hydroxyethyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,2,2-trifluoroethyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonate;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-4-(trifluoromethyl)benzamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)pivalamide;

2,6-dihydroxy-N,N,5'-trimethyl-2'-(prop-1-en-2-yl)-4-propyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N-isopropyl-5'-methyl-2'-(prop-1-en-2-yl)-4-propyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

3-(ethylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

tert-butyl 4-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)piperazine-1-carboxylate; and

2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-N-(pyridin-3-ylsulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide.

[0039] In some embodiments, the present disclosure relates in particular to a compound selected from:

3'-methyl-3-(methylsulfonyl)-4-pentyl-[1,1'-biphenyl]-2,6-diol;

2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N,N,3'-trimethyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;

N-cyclopropyl-2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N-isopropyl-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-3'-methyl-4-pentyl-N-phenyl-[1,1'-biphenyl]-3-sulfonamide;

N-benzyl-2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;

3'-methyl-3-(morpholinosulfonyl)-4-pentyl-[1,1'-biphenyl]-2,6-diol;

N,N-diethyl-2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;

N-(2-bromoethyl)-2,6-dihydroxy-N-(2-hydroxyethyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;

2,2,2-trifluoroethyl 2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonate;

-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-4-(trifluoromethyl)benzamide;

N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)pivalamide;

2,6-dihydroxy-N,N,3'-trimethyl-4-propyl-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N-isopropyl-3'-methyl-4-propyl-[1,1'-biphenyl]-3-sulfonamide;

3-(ethylsulfonyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-2,6-diol;

tert-butyl 4-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)piperazine-1-carboxylate;

2,6-dihydroxy-3'-methyl-4-pentyl-N-(pyridin-3-ylsulfonyl)-[1,1'-biphenyl]-3-carboxamide;

5'-methyl-3-(methylsulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;

2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N,N,5'-trimethyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

N-cyclopropyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N-isopropyl-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-5'-methyl-4-pentyl-N-phenyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

N-benzyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

5'-methyl-3-(morpholinosulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;

N,N-diethyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

N-(2-bromoethyl)-2,6-dihydroxy-N-(2-hydroxyethyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

2,2,2-trifluoroethyl 2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonate;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-4-(trifluoromethyl)benzamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)pivalamide;

2,6-dihydroxy-N,N,5'-trimethyl-2'-(prop-1-en-2-yl)-4-propyl-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N,N,5'-trimethyl-2'-(prop-1-en-2-yl)-4-propyl-[1,1'-biphenyl]-3-sulfonamide;

3-(ethylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;

tert-butyl 4-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)piperazine-1-carboxylate;

2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-N-(pyridin-3-ylsulfonyl)-[1,1'-biphenyl]-3-carboxamide;

5'-methyl-3-(methylsulfonyl)-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N,N,5'-trimethyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

N-cyclopropyl-2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N-isopropyl-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-5'-methyl-4-pentyl-N-phenyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

N-benzyl-2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

5'-methyl-4-pentyl-3-(piperidin-1-ylsulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

5'-methyl-3-(morpholinosulfonyl)-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

N,N-diethyl-2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

N-(2-bromoethyl)-2,6-dihydroxy-N-(2-hydroxyethyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,2,2-trifluoroethyl 2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonate;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-4-(trifluoromethyl)benzamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)pivalamide;

2,6-dihydroxy-N,N,5'-trimethyl-4-propyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N-isopropyl-5'-methyl-4-propyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

3-(ethylsulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

tert-butyl 4-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)piperazine-1-carboxylate;

2,6-dihydroxy-5'-methyl-4-pentyl-N-(pyridin-3-ylsulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide;

5'-methyl-3-(methylsulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N,N,5'-trimethyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

N-cyclopropyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N-isopropyl-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-5'-methyl-4-pentyl-N-phenyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

N-benzyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

5'-methyl-3-(morpholinosulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

N,N-diethyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

N-(2-bromoethyl)-2,6-dihydroxy-N-(2-hydroxyethyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,2,2-trifluoroethyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonate;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-4-(trifluoromethyl)benzamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)pivalamide;

2,6-dihydroxy-N,N,5'-trimethyl-2'-(prop-1-en-2-yl)-4-propyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N-isopropyl-5'-methyl-2'-(prop-1-en-2-yl)-4-propyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

3-(ethylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

tert-butyl 4-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)piperazine-1-carboxylate; and

2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-N-(pyridin-3-ylsulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide.

[0040] In some embodiments, the present disclosure relates in particular to a compound selected from:

2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

N-cyclopropyl-2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-5'-methyl-4-pentyl-N-phenyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

N-benzyl-2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

5'-methyl-3-(morpholinosulfonyl)-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol

N,N-diethyl-2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

tert-butyl 4-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)piperazine-1-carboxylate;

5'-methyl-3-(methylsulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

2,6-dihydroxy-N,N,5'-trimethyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

N-cyclopropyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N-isopropyl-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-5'-methyl-4-pentyl-N-phenyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

N-benzyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

5'-methyl-3-(morpholinosulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

N,N-diethyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

N-(2-bromoethyl)-2,6-dihydroxy-N-(2-hydroxyethyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,2,2-trifluoroethyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonate;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-4-(trifluoromethyl)benzamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)pivalamide;

2,6-dihydroxy-N,N,5'-trimethyl-2'-(prop-1-en-2-yl)-4-propyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N-isopropyl-5'-methyl-2'-(prop-1-en-2-yl)-4-propyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

3-(ethylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol; and

2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-N-(pyridin-3-ylsulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide.

[0041] In certain embodiments of the compounds as otherwise described herein, the compound is in the form of a pharmaceutically acceptable salt of the compound as described herein or an enantiomer, diastereomer, racemate, tautomer, or metabolite thereof. The person of ordinary skill in the art will appreciate that a variety of pharmaceutically acceptable salts may be provided, such as for example described in additional detail below.

[0042] In certain embodiments of the compounds as otherwise described herein, a compound is in the form of a solvate (e.g., a hydrate) of a compound as described herein or an enantiomer, diastereomer, racemate, tautomer, or metabolite thereof. The person of ordinary skill in the art will appreciate that a variety of solvates and/or hydrates may be formed.

[0043] The person of ordinary skill in the art will appreciate that the phrase “or an enantiomer, diastereomer, racemate, tautomer, or metabolite thereof, or a pharmaceutically acceptable salt,

solvate or hydrate of the compound, enantiomer, diastereomer, racemate, tautomer, or **metabolite**” includes compounds in the form of salts, solvates, hydrates of the base compounds (including its enantiomers, diastereomers, racemates, or tautomers) or a metabolite of the base compound. But in certain embodiments as described above, the compound is not in the form of a salt, solvate or hydrate.

Therapeutics Applications

[0044] In some embodiments, compounds of the present disclosure have an affinity for at least one cannabinoid receptor (e.g. CB1, CB2, 5HT1A, 5HT2A, GPR18, GPR55, GPR119, TRPV1, TRPV2, PPARs (such as PPAR γ), or a μ -opioid receptor). Thus, in another aspect, the present disclosure relates to the use of at least one of the compounds of the present disclosure to bind and/or interact with a cannabinoid receptor.

[0045] In some embodiments, compounds of the present disclosure may have an affinity for one or both of the CB1 receptor and CB2 receptor. In a particular embodiment, compounds of the present disclosure may have an affinity for the CB1 receptor, but not the CB2 receptor. In a particular embodiment, compounds of the present disclosure may have an affinity for the CB2 receptor, but not the CB1 receptor.

[0046] In some embodiments, compounds of the present disclosure may exhibit a selectivity for **one receptor over another**. As used herein, by “selectivity” it is meant that a compound binds, interacts with, or modulates preferentially one receptor over another. In an embodiment, a compound is selective for one receptor over another if its affinity for one receptor is at least 1.25-fold, at least 1.5-fold, at least 2-fold, at least 5-fold, at least 10-fold, at least 25-fold, at least 50-fold, or at least 100-fold greater for the one receptor than another receptor. In an embodiment, the affinity of a compound as disclosed herein for a receptor may be determined by a radioligand competitive binding assay, such as for example described in the examples herein.

[0047] In some embodiments, compounds of the present disclosure may have an affinity for the CB1 receptor, with selectivity for the CB1 receptor over the CB2 receptor.

[0048] In some embodiments, compounds of the present disclosure may have an affinity for the CB2 receptor, with selectivity for the CB2 receptor over the CB1 receptor.

[0049] In some embodiments, compounds of the present disclosure may function as an agonist, a partial agonist, an indirect agonist, an antagonist, an inverse agonist, a neutral agonist, or an

allosteric modulator to at least one cannabinoid receptor (e.g. CB1, CB2, 5HT1A, 5HT2A, GPR18, GPR55, GPR119, TRPV1, TPRV2, PPARs (such as PPAR γ), or a μ -opioid receptor). In some embodiments, compounds of the present disclosure may function as an agonist, a partial agonist, an indirect agonist, antagonist, inverse agonist, neutral agonist, or allosteric modulator to the CB1 and/or CB2 receptor. In some embodiments, compounds of the present disclosure may function as an agonist to the CB1 and/or CB2 receptor. In some embodiments, compounds of the present disclosure may function as an antagonist to the CB1 and/or CB2 receptor. In some embodiments, compounds of the present disclosure may function as an indirect agonist to the 5HT1A receptor.

[0050] In some embodiments, compounds of the present disclosure may act as a prodrug to a compound (e.g. a metabolite) that functions as an agonist, a partial agonist, an indirect agonist, an antagonist, an inverse agonist, or a neutral agonist to at least one of the cannabinoid receptors (e.g. CB1, CB2, 5HT1A, 5HT2A, GPR18, GPR55, GPR119, TRPV1, TPRV2, PPARs (e.g. PPAR γ), or a μ -opioid receptor).

[0051] The present disclosure further relates to use of a compound as disclosed herein as a therapeutically active substance or as a prodrug to a therapeutically active substance.

[0052] In an embodiment, the present disclosure relates to the use of a compound as disclosed herein for the treatment or prevention of a disease associated with a cannabinoid receptor (e.g. CB1, CB2, 5HT1A, 5HT2A, GPR18, GPR55, GPR119, TRPV1, TPRV2, PPARs (e.g. PPAR γ), or a μ -opioid receptor). In an embodiment, by “disease associated with a cannabinoid” it is meant to refer to a disease, disorder or condition that is treatable or preventable by acting on a cannabinoid receptor (e.g. CB1, CB2, 5HT1A, 5HT2A, GPR18, GPR55, GPR119, TRPV1, TPRV2, PPARs (e.g. PPAR γ), or a μ -opioid receptor). In an embodiment, compounds of the present disclosure may treat or prevent the condition by acting as an agonist, partial agonist, antagonist, inverse agonist, neutral agonist, or an allosteric modulator to the cannabinoid receptor or as a prodrug of a compound (e.g. metabolite) that acts as an agonist, partial agonist, antagonist, inverse agonist, neutral agonist, or allosteric modulator to the cannabinoid receptor. In select embodiments, the cannabinoid receptor is CB1 or CB2.

[0053] In an embodiment, the present disclosure relates to the use of a compound as disclosed herein for selectively modulating the activity of one receptor over another receptor. In an embodiment, at least one of the receptors is a cannabinoid receptor. In an embodiment, both receptors are a cannabinoid receptor. In an embodiment, the receptors are CB1 and CB2. In

select embodiments, the present disclosure relates to the use of a compound as disclosed herein for selectively modulating the activity of a CB1 or CB2 receptor.

[0054] As used herein, by “selectively modulating” it is intended to refer to the ability of the compounds of the present disclosure to cause any change in activity of the receptor. In an embodiment, “selectively modulating” means to stimulate or inhibit the activity of the receptor, either directly or indirectly.

[0055] The disclosure also relates to methods of treating or preventing a disease, such as a disease associated with a cannabinoid receptor (e.g. CB1 and/or CB2). These methods include administering to a subject in need of such treatment or prevention a therapeutically effective amount of one or more compounds of the disclosure as described herein (e.g., compounds of formula (I)) or a pharmaceutical composition of the disclosure as described herein.

[0056] In certain embodiments, the diseases of the disclosure include, but are not limited to ADHD/ADD, alcohol use disorder, **allergic asthma**, **ALS**, **Alzheimer's**, **anorexia** (e.g. HIV-related cachexia), anxiety disorders (e.g., social anxiety disorder, specific phobia, test anxiety, generalized anxiety disorder), arthritis, atherosclerosis, autism, bipolar disorder, burns, cancer, cancer pain, Charcot-Marie-Tooth disease, chronic inflammatory demyelinating polyneuropathies, chronic allograft nephropathy, cocaine use disorder, complex regional pain syndrome, congestive heart failure, depression, fibromyalgia, fragile X syndrome/FXTAS, frontotemporal dementias (behavioural variant), gingivitis pyrexia, glaucoma, glioblastoma, glomerulonephropathy, Huntington's disease, hypertrophic scars, IBD/IBS, inflammation, Inflammatory myopathies, ischemia, kidney fibrosis, keloids, leukodystrophies, liver fibrosis, liver cirrhosis, lung fibrosis, migraine, multiple sclerosis, myocardial infarction, nausea (e.g. CINV, motion sickness), neuropathic pain (e.g., postherpetic neuralgia, painful diabetic neuropathy), nightmare disorder, non-alcoholic fatty liver disease, obesity, obsessive-compulsive disorder, opioid sparing, opioid use disorder, osteoarthritis, osteoporosis, pain (e.g. acute or chronic pain), Parkinson's, post-concussion syndrome/traumatic brain injury, psychosis/schizophrenia, PTSD, regulation of bone mass, REM sleep behaviour disorder, reperfusion injury, Rett syndrome, rheumatoid arthritis, skin conditions (e.g. acne, psoriatic arthritis), sleep disorders (e.g., insomnia, RLS), spinocerebellar ataxias, systemic fibrosis, systemic sclerosis, thermal injury, tobacco use disorder/nicotine dependence, Tourette's, tumors, and trigeminal neuralgia.

[0057] The compounds and compositions of the disclosure as described herein may also be administered in combination with one or more secondary therapeutic agents. Thus, in certain embodiment, the method also includes administering to a subject in need of such treatment or

prevention a therapeutically effective amount of one or more compounds of the disclosure as described herein or a pharmaceutical composition of the disclosure as described herein and one or more secondary therapeutic agents. Examples of suitable secondary therapeutic agents include, but are not limited to, temozolomide, camptothecin, doxorubicin, daunorubicin, vincristine, paclitaxel, neocarzinostatin, calicheamicin, cisplatin, carboplatin, oxaliplatin, satraplatin, picoplatin, lurtotecan, annamycin, docetaxel, tamoxifen, epirubicin, methotrexate, vinblastin, vincristin, topotecan, prednisone, prednisolone, chloroquine, hydroxychloroquine, autophagy inhibitors, abt-737, leucovorin, psilocybin, psilocin, psiloacetin, netupitant, palonosetron, aprepitant, 3,4-methylenedioxymethamphetamine, nicotine, ketamine, lithium salts (e.g., lithium citrate), valproic acid, bevacizumab, bortezomib, fluorouracil, gemcitabine, irinotecan, oxaliplatin, adalimumab, azathioprine, infliximab, citalopram, mirtazapine, sertraline, esketamine, fluoxetine, paroxetine, venlafaxine, fenfluramine, vigabatrin, bupropion, atomoxetine, memantine, clobazam, stiripentol, cyclosporine, tacrolimus, methylprednisolone, megestrol acetate, biguanides (e.g., metformin), sulphonyl ureas (e.g., glipizide, tolbutamide), gabapentin, baclofen, clonazepam, dantrolene, diazepam, tizanidine, buprenorphine, naltrexone, opioids (e.g., codeine, oxycodone, morphine), amisulpride, aripiprazole, olanzapine, quetiapine, risperidone, clonidine, lomazenil, benzodiazepine, benzamide, dexamethasone, gemcitabine, and palmitoylethanolamide. When administered as a combination, the compounds and compositions of the disclosure as described herein and the secondary therapeutic agents can be formulated as separate compositions that are given simultaneously or sequentially, or the therapeutic agents can be given as a single composition. In certain embodiments, the secondary therapeutic agent may be administered in an amount below its established half maximal inhibitory concentration (IC_{50}). For example, the secondary therapeutic agent may be administered in an amount less than 1% of, e.g., less than 10%, or less than 25%, or less than 50%, or less than 75%, or even less than 90% of the inhibitory concentration (IC_{50}).

Prodrugs

[0058] In some embodiments, a compound as described herein may itself be a prodrug or may be further modified to provide a prodrug.

[0059] Prodrugs in accordance with the present disclosure may, for example, be produced by replacing appropriate functionalities present in the compounds disclosed herein, such as for example any of the embodiments described with reference to formulae (I) and (Ia)-(Ig) and embodiments 1-969 above, with certain moieties known to those skilled in the art as “pro-moieties” as described, for example, in *Design of Prodrugs* by H. Bundgaard (Elsevier,

1985) and Y.M. Choi-Sledeski and C.G. Wermuth, *Designing Prodrugs and Bioprecursors in Practice of Medicinal Chemistry*, (Fourth Edition), Chapter 28, 657-696 (Elsevier, 2015).

[0060] In exemplary embodiments, a prodrug in accordance with the present disclosure is (a) an ester or amide derivative of a carboxylic acid in a compound disclosed herein; (b) an ester, carbonate, carbamate, acetal, aminal, phosphate, or ether derivative of a hydroxyl group in a compound disclosed herein; (c) an amide, imine, carbamate or amine derivative of an amino group in a compound disclosed herein; (d) an oxime or imine derivative of a carbonyl group in a compound disclosed herein; or (e) a methyl, primary alcohol or aldehyde group that can be metabolically oxidized to a carboxylic acid in a compound disclosed herein.

[0061] Certain compounds of the present disclosure, such as for example any of the embodiments described with reference to formulae (I) and (Ia)-(Ig) and embodiments 1-969 above, may themselves act as prodrugs. In an embodiment, a compound of the present disclosure, such as for example any of the embodiments described with reference to formulae (I) and (Ia)-(Ig) and embodiments 1-969 above, may act as a prodrug of a cannabinoid, such as for example a natural cannabinoid (e.g., CBD or CBDA).

[0062] References to compounds disclosed herein are taken to include the compounds themselves and prodrugs thereof. The present disclosure includes such prodrug compounds as well as any pharmaceutically acceptable salts of such prodrug compounds, and/or any solvates, hydrates, enantiomers, diastereomers, racemates, tautomers, or metabolites of such prodrug compounds and their salts.

[0063] In some embodiments, a prodrug compound of the present disclosure may exhibit improved pharmacokinetics (PK), improved biodistribution, and/or improved formulation capabilities (e.g. stability in formulation). For example, in an embodiment, these characteristics may be improved over natural cannabinoids (e.g., CBD or CBDA).

[0064] In some embodiments, a prodrug compound of the present disclosure may exhibit unique or improved biological activity. For example, in an embodiment, these characteristics may be unique or improved over natural cannabinoids (e.g., CBD or CBDA).

Pharmaceutical Compositions and Dosage Forms

[0065] A compound as described herein can usefully be provided in the form of a pharmaceutical composition. Such compositions include the compound according to any one of the preceding aspects or embodiments described herein, together with a pharmaceutically acceptable excipient, diluent, or carrier.

[0066] The compounds may be formulated in the pharmaceutical composition per se, or in the form of a hydrate, solvate, or pharmaceutically acceptable salt, as previously described.

Typically, such salts are more soluble in aqueous solutions than the corresponding free acids and bases, but salts having lower solubility than the corresponding free acids and bases may also be formed.

[0067] The pharmaceutical composition can be, for example, in the form of a tablet, a capsule, or a parenteral formulation, but the person of ordinary skill in the art will appreciate that the compound can be provided in a wide variety of pharmaceutical compositions.

[0068] The compounds of the disclosure can be administered, for example, orally, topically, parenterally, by inhalation or spray or rectally in dosage unit formulations containing one or more pharmaceutically acceptable carriers, diluents or excipients. The term parenteral as used herein includes percutaneous, subcutaneous, intravascular (e.g., intravenous), intramuscular, or intrathecal injection or infusion techniques and the like. A medicament including a compound of the disclosure can be provided, for example, in any of the formulations and dosage forms as described herein.

[0069] Pharmaceutical compositions can be made using the presently disclosed compounds. For example, in one embodiment, a pharmaceutical composition includes a pharmaceutically acceptable carrier, diluent or excipient, and compound as described above with reference to any one of structural formulae.

[0070] In the pharmaceutical compositions disclosed herein, one or more compounds of the disclosure may be present in association with one or more pharmaceutically acceptable carriers, diluents or excipients, and, if desired, other active ingredients. The pharmaceutical compositions containing compounds of the disclosure may be in a form suitable for oral use, for example, as tablets, troches, lozenges, aqueous or oily suspensions, dispersible powders or granules, emulsion, hard or soft capsules, or syrups or elixirs.

[0071] Compositions intended for oral use can be prepared according to any suitable method for the manufacture of pharmaceutical compositions and such compositions may contain one or more agents selected from the group consisting of sweetening agents, flavoring agents, coloring agents and preservative agents in order to provide pharmaceutically elegant and palatable preparations. Tablets contain the active ingredient in admixture with non-toxic pharmaceutically acceptable excipients that are suitable for the manufacture of tablets. These excipients can be for example, inert diluents, such as calcium carbonate, sodium carbonate, lactose, calcium

phosphate or sodium phosphate; granulating and disintegrating agents, for example, corn starch, or alginic acid; binding agents, for example starch, gelatin or acacia, and lubricating agents, for example magnesium stearate, stearic acid or talc. The tablets can be uncoated or they can be coated by known techniques. In some cases such coatings can be prepared by suitable techniques to delay disintegration and absorption in the gastrointestinal tract and thereby provide a sustained action over a longer period. For example, a time delay material such as glyceryl monostearate or glyceryl distearate can be employed.

[0072] Formulations for oral use can also be presented as hard gelatin capsules, wherein the active ingredient is mixed with an inert solid diluent, for example, calcium carbonate, calcium phosphate or kaolin, or as soft gelatin capsules wherein the active ingredient is mixed with water or an oil medium, for example peanut oil, liquid paraffin or olive oil.

[0073] Formulations for oral use can also be presented as lozenges.

[0074] Formulations for oral use can also be presented as beverages or edibles. For example, in an embodiment, the compounds of the present disclosure may be presented in water-soluble formulations such as disclosed in PCT/CA2019/051698, comprising an emulsifier and a glycerin-based carrier surfactant. In other embodiments, the compounds of the present disclosure may be presented in compositions such as disclosed in PCT/CA2019/051704, comprising inulin and pectin.

[0075] Aqueous suspensions contain the active materials in admixture with excipients suitable for the manufacture of aqueous suspensions. Such excipients can be suspending agents, for example sodium carboxymethylcellulose, methylcellulose, hydropropylmethylcellulose, sodium alginate, polyvinylpyrrolidone, gum tragacanth and gum acacia; dispersing or wetting agents such as a naturally-occurring phosphatide, for example, lecithin, or condensation products of an alkylene oxide with fatty acids, for example polyoxyethylene stearate, or condensation products of ethylene oxide with long chain aliphatic alcohols, for example heptadecaethyleneoxycetanol, or condensation products of ethylene oxide with partial esters derived from fatty acids and a hexitol such as polyoxyethylene sorbitol monooleate, or condensation products of ethylene oxide with partial esters derived from fatty acids and hexitol anhydrides, for example polyethylene sorbitan monooleate. The aqueous suspensions may also contain one or more preservatives, for example ethyl, or n-propyl p-hydroxybenzoate, one or more coloring agents, one or more flavoring agents, and one or more sweetening agents, such as sucrose or saccharin.

[0076] Oily suspensions can be formulated by suspending the active ingredients in a vegetable oil, for example arachis oil, olive oil, sesame oil or coconut oil, or in a mineral oil such as liquid paraffin. The oily suspensions may contain a thickening agent, for example beeswax, hard paraffin or cetyl alcohol. Sweetening agents and flavoring agents may be added to provide palatable oral preparations. These compositions may be preserved by the addition of an anti-oxidant such as ascorbic acid.

[0077] Dispersible powders and granules suitable for preparation of an aqueous suspension by the addition of water provide the active ingredient in admixture with a dispersing or wetting agent, suspending agent and one or more preservatives. Suitable dispersing or wetting agents or suspending agents are exemplified by those already mentioned above. Additional excipients, for example sweetening, flavoring and coloring agents, can also be present.

[0078] Pharmaceutical compositions can also be in the form of oil-in-water emulsions. The oily phase can be a vegetable oil or a mineral oil or mixtures of these. Suitable emulsifying agents can be naturally-occurring gums, for example gum acacia or gum tragacanth, naturally-occurring phosphatides, for example soy bean, lecithin, and esters or partial esters derived from fatty acids and hexitol, anhydrides, for example sorbitan monooleate, and condensation products of the said partial esters with ethylene oxide, for example polyoxyethylene sorbitan monooleate. The emulsions can also contain sweetening and flavoring agents.

[0079] In some embodiments, the pharmaceutically acceptable carrier, diluent, or excipient is not water. In other embodiments, the water comprises less than 50% of the composition. In some embodiments, compositions comprising less than 50% water have at least 1%, 2%, 3%, 4% or 5% water. In other embodiments, the water content is present in the composition in a trace amount.

[0080] In some embodiments, the pharmaceutically acceptable carrier, diluent, or excipient is not alcohol. In other embodiments, the alcohol comprises less than 50% of the composition. In some embodiments, compositions comprising less than 50% alcohol have at least 1%, 2%, 3%, 4% or 5% alcohol. In other embodiments, the alcohol content is present in the composition in a trace amount.

[0081] Syrups and elixirs can be formulated with sweetening agents, for example glycerol, propylene glycol, sorbitol, glucose or sucrose. Such formulations can also contain a demulcent, a preservative, flavoring, and coloring agents. The pharmaceutical compositions can be in the form of a sterile injectable aqueous or oleaginous suspension. This suspension can be

formulated according to the known art using those suitable dispersing or wetting agents and suspending agents that have been mentioned above. The sterile injectable preparation can also be a sterile injectable solution or suspension in a non-toxic parentally acceptable diluent or solvent, for example as a solution in 1,3-butanediol. Among the acceptable vehicles and solvents that can be employed are water, Ringer's solution and isotonic sodium chloride solution. In addition, sterile, fixed oils can be employed as a solvent or suspending medium. For this purpose any bland fixed oil can be employed including synthetic mono- or diglycerides. In addition, fatty acids such as oleic acid find use in the preparation of injectables.

[0082] Compounds of the disclosure can also be administered in the form of suppositories, e.g., for rectal administration of the drug. These compositions can be prepared by mixing the compound with a suitable non-irritating excipient that is solid at ordinary temperatures but liquid at the rectal temperature and will therefore melt in the rectum to release the drug. Such materials include cocoa butter and polyethylene glycols.

[0083] Compounds of the disclosure can also be administered parenterally in a sterile medium. The drug, depending on the vehicle and concentration used, can either be suspended or dissolved in the vehicle. Advantageously, adjuvants such as local anesthetics, preservatives and buffering agents can be dissolved in the vehicle.

[0084] The compositions can be formulated in a unit dosage form of the active ingredient. The term "unit dosage forms" refers to physically discrete units suitable as unitary dosages for human subjects and other mammals, each unit containing a predetermined quantity of active material calculated to produce the desired therapeutic effect, in association with a suitable pharmaceutical excipient.

[0085] The compound can be effective over a wide dosage range and is generally administered in a therapeutically effective amount. It will be understood, however, that the amount of the compound actually administered will usually be determined by a physician, according to the relevant circumstances, including the condition to be treated or prevented, the chosen route of administration, the actual compound administered, the age, weight, and response of the individual patient, the severity of the patient's symptoms, and the like.

[0086] For preparing solid compositions such as tablets, the principal active ingredient is mixed with a pharmaceutical excipient to form a solid preformulation composition containing a homogeneous mixture of a compound described herein. When referring to these preformulation compositions as homogeneous, the active ingredient is typically dispersed evenly throughout

the composition so that the composition can be readily subdivided into equally effective unit dosage forms such as tablets, pills and capsules. This solid preformulation is then subdivided into unit dosage forms of the type described above containing from, for example, 0.1 to about 500 mg of the active ingredient of a compound described herein.

[0087] The tablets or pills can be coated or otherwise compounded to provide a dosage form affording the advantage of prolonged action. For example, the tablet or pill can comprise an inner dosage and an outer dosage component, the latter being in the form of an envelope over the former. The two components can be separated by an enteric layer which serves to resist disintegration in the stomach and permit the inner component to pass intact into the duodenum or to be delayed in release. A variety of materials can be used for such enteric layers or coatings, such materials including a number of polymeric acids and mixtures of polymeric acids with such materials as shellac, cetyl alcohol, and cellulose acetate.

[0088] The amount of compound or composition administered to a patient will vary depending upon what is being administered, the purpose of the administration, such as prophylaxis or therapy, the state of the patient, the manner of administration, and the like. In therapeutic applications, compositions can be administered to a patient already suffering from a disease in an amount sufficient to cure or at least partially arrest the symptoms of the disease and its complications. Effective doses will depend on the disease condition being treated or prevented as well as by the judgment of the attending clinician depending upon factors such as the severity of the disease, the age, weight and general condition of the patient, and the like.

[0089] The compositions administered to a patient can be in the form of pharmaceutical compositions described above. These compositions can be sterilized by conventional sterilization techniques, or may be sterile filtered. Aqueous solutions can be packaged for use as is, or lyophilized, the lyophilized preparation being combined with a sterile aqueous carrier prior to administration. The pH of the compound preparations typically will be between 3 and 11, more preferably from 5 to 9 and most preferably from 7 to 8. It will be understood that use of certain of the foregoing excipients, carriers, or stabilizers will result in the formation of pharmaceutical salts.

[0090] The therapeutic dosage of the compounds can vary according to, for example, the particular use for which the treatment is made, the manner of administration of the compound, the health and condition of the patient, and the judgment of the prescribing physician. The proportion or concentration of a compound described herein in a pharmaceutical composition can vary depending upon a number of factors including dosage, chemical characteristics (*e.g.*,

hydrophobicity), and the route of administration. For example, the compounds described herein can be provided in an aqueous physiological buffer solution containing about 0.1 to about 10% w/v of the compound for parenteral administration. Some typical dose ranges are from about 1 µg/kg to about 1 g/kg of body weight per day. In some embodiments, the dose range is from about 0.01 mg/kg to about 100 mg/kg of body weight per day. The dosage is likely to depend on such variables as the type and extent of progression of the disease or disorder, the overall health status of the particular patient, the relative biological efficacy of the compound selected, formulation of the excipient, and its route of administration. Effective doses can be extrapolated from dose-response curves derived from *in vitro* or animal model test systems.

[0091] The compounds described herein can also be formulated in combination with one or more additional active ingredients which can include any pharmaceutical agent such as anti-viral agents, vaccines, antibodies, immune enhancers, immune suppressants, anti-inflammatory agents and the like.

[0092] The person of ordinary skill in the art will formulate a compound as described into pharmaceutical formulations herein. For example, based on the physicochemical properties of the compound, the amount of the compound needed for a therapeutically effective amount, and the desired route of administration.

Definitions

[0093] Terms used herein may be preceded and/or followed by a single dash, "-", or a double dash, "=", to indicate the bond order of the bond between the named substituent and its parent moiety; a single dash indicates a single bond and a double dash indicates a double bond or a pair of single bonds in the case of a spiro-substituent. In the absence of a single or double dash it is understood that a single bond is formed between the substituent and its parent moiety; further, substituents are intended to be read "left to right" with reference to the chemical structure referred to unless a dash indicates otherwise. For example, arylalkyl, arylalkyl-, and -alkylaryl indicate the same functionality.

[0094] For simplicity, chemical moieties are defined and referred to throughout primarily as univalent chemical moieties (e.g., alkyl, aryl, etc.). Nevertheless, such terms are also used to convey corresponding multivalent moieties under the appropriate structural circumstances clear to those skilled in the art. For example, while an "alkyl" moiety can refer to a monovalent radical (e.g. CH₃-CH₂-), in some circumstances a bivalent linking moiety can be "alkyl," in which case those skilled in the art will understand the alkyl to be a divalent radical (e.g., -CH₂-CH₂-), which

is equivalent to the term "alkylene." (Similarly, in circumstances in which a divalent moiety is required and is stated as being "aryl," those skilled in the art will understand that the term "aryl" refers to the corresponding divalent moiety, arylene). All atoms are understood to have their normal number of valences for bond formation (i.e., 4 for carbon, 3 for N, 2 for O, and 2, 4, or 6 for S, depending on the oxidation state of the S). Nitrogens in the presently disclosed compounds can be hypervalent, e.g., an N-oxide or tetrasubstituted ammonium salt. On occasion a moiety may be defined, for example, as -B(A)_a, wherein a is 0 or 1. In such instances, when a is 0 the moiety is -B and when a is 1 the moiety is -B-A.

[0095] As used herein, the term "alkyl" includes a saturated hydrocarbon having a designated number of carbon atoms, such as 1 to 10 carbons (i.e., inclusive of 1 and 10), 1 to 8 carbons, 1 to 6 carbons, 1 to 3 carbons, or 1, 2, 3, 4, 5 or 6. Alkyl group may be straight or branched and depending on context, may be a monovalent radical or a divalent radical (i.e., an alkylene group). For example, the moiety "-(C₁-C₆alkyl)-O-" signifies connection of an oxygen through an alkylene bridge having from 1 to 6 carbons and C₁-C₃alkyl represents methyl, ethyl, and propyl moieties. Examples of "alkyl" include, for example, methyl, ethyl, propyl, isopropyl, butyl, iso-, sec- and tert-butyl, pentyl, and hexyl.

[0096] The term "alkoxy" represents an alkyl group of indicated number of carbon atoms attached to the parent molecular moiety through an oxygen bridge, such as alkyl-O- in which the term "alkyl" has the previously given definition. Examples of "alkoxy" include, for example, methoxy, ethoxy, propoxy, and isopropoxy.

[0097] The term "alkenyl", as used herein, represents an unsaturated hydrocarbon having a designated number of carbon atoms, such as 2 to 10 carbons (i.e., inclusive of 2 and 10), 2 to 8 carbons, 2 to 6 carbons, or 2, 3, 4, 5 or 6, unless otherwise specified, and containing at least one carbon-carbon double bond. Alkenyl group may be straight or branched and depending on context, may be a monovalent radical or a divalent radical (i.e., an alkenylene group). For example, the moiety "-(C₂-C₆ alkenyl)-O-" signifies connection of an oxygen through an alkenylene bridge having from 2 to 6 carbons. Representative examples of alkenyl include, but are not limited to, ethenyl, 2-propenyl, 2-methyl-2-propenyl, 3-butenyl, 4-pentenyl, 5-hexenyl, 2-heptenyl, 2-methyl-1-heptenyl, 3-decenyl, and 3,7-dimethylocta-2,6-dienyl.

[0098] The term "alkynyl", as used herein, represents an unsaturated hydrocarbon having a designated number of carbon atoms, such as 2 to 10 carbons (i.e., inclusive of 2 and 10), 2 to 8 carbons, 2 to 6 carbons, or 2, 3, 4, 5 or 6, unless otherwise specified, and containing at least one carbon-carbon triple bond. Alkynyl group may be straight or branched and depending on

context, may be a monovalent radical or a divalent radical (i.e., an alkynylene group). For example, the moiety “-(C₂-C₆ alkynyl)-O-” signifies connection of an oxygen through an alkynylene bridge having from 2 to 6 carbons. Representative examples of alkynyl include, but are not limited to, acetylenyl, 1-propynyl, 2-propynyl, 3-butynyl, 2-pentynyl, and 1-butynyl.

[0099] The term “aryl” represents an aromatic ring system having a single ring (e.g., phenyl) which is optionally fused to other aromatic hydrocarbon rings or non-aromatic hydrocarbon or heterocycle rings. “Aryl” includes ring systems having multiple condensed rings and in which at least one is carbocyclic and aromatic, (e.g., 1,2,3,4-tetrahydronaphthyl, naphthyl). Examples of aryl groups include phenyl, 1-naphthyl, 2-naphthyl, indanyl, indenyl, dihydronaphthyl, fluorenyl, tetralinyl, and 6,7,8,9-tetrahydro-5*H*-benzo[*a*]cycloheptenyl. “Aryl” also includes ring systems having a first carbocyclic, aromatic ring fused to a nonaromatic heterocycle, for example, 1*H*-2,3-dihydrobenzofuranyl and tetrahydroisoquinolinyl. The aryl groups herein are unsubstituted or, when specified as “optionally substituted”, can unless stated otherwise be substituted in one or more substitutable positions with various groups as indicated.

[0100] The terms “halogen” or “halo” indicate fluorine, chlorine, bromine, and iodine. In certain embodiments of each and every embodiment as otherwise described herein, the term “halogen” or “halo” refers to fluorine or chlorine. In certain embodiments of each and every embodiment described herein, the term “halogen” or “halo” refers to fluorine. The term “fluoroalkyl” indicates an alkyl group (i.e., as otherwise described herein) that is substituted with at least one fluorine. “Fluoroalkyl” includes alkyl groups substituted with multiple fluorines, such as perfluoroalkyl groups. Examples of fluoroalkyl groups include fluoromethyl, difluoromethyl, trifluoromethyl, pentafluoroethyl, 2,2,2-trifluoroethyl, 1,1,1,3,3,3-hexafluoroprop-2-yl and 2,2,3,3,3-pentafluoroprop-1-yl.

[0101] The term “heteroaryl” refers to an aromatic ring system containing at least one aromatic heteroatom selected from nitrogen, oxygen and sulfur in an aromatic ring. Most commonly, the heteroaryl groups will have 1, 2, 3, or 4 heteroatoms. The heteroaryl may be fused to one or more non-aromatic rings, for example, cycloalkyl or heterocycloalkyl rings, wherein the cycloalkyl and heterocycloalkyl rings are described herein. In one embodiment of the present compounds the heteroaryl group is bonded to the remainder of the structure through an atom in a heteroaryl group aromatic ring. In another embodiment, the heteroaryl group is bonded to the remainder of the structure through a non-aromatic ring atom. Examples of heteroaryl groups include, for example, pyridyl, pyrimidinyl, quinolinyl, benzothienyl, indolyl, indolinyl, pyridazinyl, pyrazinyl, isoindolyl, isoquinolyl, quinazolinyl, quinoxalinyl, phthalazinyl, imidazolyl, isoxazolyl,

pyrazolyl, oxazolyl, thiazolyl, indolizynyl, indazolyl, benzothiazolyl, benzimidazolyl, benzofuranyl, furanyl, thienyl, pyrrolyl, oxadiazolyl, thiadiazolyl, benzo[1,4]oxazinyl, triazolyl, tetrazolyl, isothiazolyl, naphthyridinyl, isochromanlyl, chromanlyl, isoindolinyl, isobenzothienyl, benzoxazolyl, pyridopyridinyl, purinyl, benzodioxolyl, triazinyl, pteridinyl, benzothiazolyl, imidazopyridinyl, imidazothiazolyl, benzisoxazinyl, benzoxazinyl, benzopyranyl, benzothiopyranyl, chromonyl, chromanonyl, pyridinyl-*N*-oxide, isoindolinonyl, benzodioxanyl, benzoxazolinonyl, pyrrolyl *N*-oxide, pyrimidinyl *N*-oxide, pyridazinyl *N*-oxide, pyrazinyl *N*-oxide, quinolinyl *N*-oxide, indolyl *N*-oxide, indolinyl *N*-oxide, isoquinolyl *N*-oxide, quinazolinyl *N*-oxide, quinoxalinyl *N*-oxide, phthalazinyl *N*-oxide, imidazolyl *N*-oxide, isoxazolyl *N*-oxide, oxazolyl *N*-oxide, thiazolyl *N*-oxide, indolizynyl *N*-oxide, indazolyl *N*-oxide, benzothiazolyl *N*-oxide, benzimidazolyl *N*-oxide, pyrrolyl *N*-oxide, oxadiazolyl *N*-oxide, thiadiazolyl *N*-oxide, triazolyl *N*-oxide, tetrazolyl *N*-oxide, benzothiopyranyl *S*-oxide, benzothiopyranyl *S,S*-dioxide. Preferred heteroaryl groups include pyridyl, pyrimidyl, quinolinyl, indolyl, pyrrolyl, furanyl, thienyl and imidazolyl, pyrazolyl, indazolyl, thiazolyl and benzothiazolyl. In certain embodiments, each heteroaryl is selected from pyridyl, pyrimidinyl, pyridazinyl, pyrazinyl, imidazolyl, isoxazolyl, pyrazolyl, oxazolyl, thiazolyl, furanyl, thienyl, pyrrolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, isothiazolyl, pyridinyl-*N*-oxide, pyrrolyl *N*-oxide, pyrimidinyl *N*-oxide, pyridazinyl *N*-oxide, pyrazinyl *N*-oxide, imidazolyl *N*-oxide, isoxazolyl *N*-oxide, oxazolyl *N*-oxide, thiazolyl *N*-oxide, pyrrolyl *N*-oxide, oxadiazolyl *N*-oxide, thiadiazolyl *N*-oxide, triazolyl *N*-oxide, and tetrazolyl *N*-oxide. Preferred heteroaryl groups include pyridyl, pyrimidyl, quinolinyl, indolyl, pyrrolyl, furanyl, thienyl, imidazolyl, pyrazolyl, indazolyl, thiazolyl and benzothiazolyl. The heteroaryl groups herein are unsubstituted or, when specified as “optionally substituted”, can unless stated otherwise be substituted in one or more substitutable positions with various groups, as indicated.

[0102] The term “heterocycloalkyl” refers to a non-aromatic ring or ring system containing at least one heteroatom that is preferably selected from nitrogen, oxygen and sulfur, wherein said heteroatom is in a non-aromatic ring. The heterocycloalkyl may have 1, 2, 3 or 4 heteroatoms. The heterocycloalkyl may be saturated (i.e., a heterocycloalkyl) or partially unsaturated (i.e., a heterocycloalkenyl). Heterocycloalkyl includes monocyclic groups of three to eight annular atoms as well as bicyclic and polycyclic ring systems, including bridged and fused systems, wherein each ring includes three to eight annular atoms. The heterocycloalkyl ring is optionally fused to other heterocycloalkyl rings and/or non-aromatic hydrocarbon rings. In certain embodiments, the heterocycloalkyl groups have from 3 to 7 members in a single ring. In other embodiments, heterocycloalkyl groups have 5 or 6 members in a single ring. In some

embodiments, the heterocycloalkyl groups have 3, 4, 5, 6 or 7 members in a single ring. Examples of heterocycloalkyl groups include, for example, azabicyclo[2.2.2]octyl (in each case also “quinuclidinyl” or a quinuclidine derivative), azabicyclo[3.2.1]octyl, 2,5-diazabicyclo[2.2.1]heptyl, morpholinyl, thiomorpholinyl, thiomorpholinyl S-oxide, thiomorpholinyl S,S-dioxide, 2-oxazolidonyl, piperazinyl, homopiperazinyl, piperazinonyl, pyrrolidinyl, azepanyl, azetidiny, pyrrolinyl, tetrahydropyranyl, piperidinyl, tetrahydrofuranyl, tetrahydrothienyl, 3,4-dihydroisoquinolin-2(1*H*)-yl, isoindolindionyl, homopiperidinyl, homomorpholinyl, homothiomorpholinyl, homothiomorpholinyl S,S-dioxide, oxazolidinonyl, dihydropyrazolyl, dihydropyrrolyl, dihydropyrazinyl, dihydropyridinyl, dihydropyrimidinyl, dihydrofuryl, dihydropyranyl, imidazolidonyl, tetrahydrothienyl S-oxide, tetrahydrothienyl S,S-dioxide and homothiomorpholinyl S-oxide. Especially desirable heterocycloalkyl groups include morpholinyl, 3,4-dihydroisoquinolin-2(1*H*)-yl, tetrahydropyranyl, piperidinyl, aza-bicyclo[2.2.2]octyl, γ -butyrolactonyl (i.e., an oxo-substituted tetrahydrofuranyl), γ -butyrolactamyl (i.e., an oxo-substituted pyrrolidine), pyrrolidinyl, piperazinyl, azepanyl, azetidiny, thiomorpholinyl, thiomorpholinyl S,S-dioxide, 2-oxazolidonyl, imidazolidonyl, isoindolindionyl, piperazinonyl. The heterocycloalkyl groups herein are unsubstituted or, when specified as “optionally substituted”, can unless stated otherwise be substituted in one or more substitutable positions with various groups, as indicated.

[0103] The term “cycloalkyl” refers to a non-aromatic carbocyclic ring or ring system, which may be saturated (i.e., a cycloalkyl) or partially unsaturated (i.e., a cycloalkenyl). The cycloalkyl ring may be optionally fused to or otherwise attached (e.g., bridged systems) to other cycloalkyl rings. Certain examples of cycloalkyl groups of the present disclosure have from 3 to 7 members in a single ring, such as having 5 or 6 members in a single ring. In some embodiments, the cycloalkyl groups have 3, 4, 5, 6 or 7 members in a single ring. Examples of cycloalkyl groups include, for example, cyclohexyl, cyclopentyl, cyclobutyl, cyclopropyl, tetrahydronaphthyl and bicyclo[2.2.1]heptane. The cycloalkyl groups herein are unsubstituted or, when specified as “optionally substituted”, may be substituted in one or more substitutable positions with various groups, as indicated.

[0104] The term “ring system” encompasses monocycles, as well as fused and/or bridged polycycles.

[0105] The term “amino” signifies the primary amino group, the secondary amino group, or the tertiary amino group, as context dictates.

[0106] The term “carbonyl” signifies the -C(O)- group.

[0107] The terms “hydroxy” and “hydroxyl” signify the -OH group.

[0108] The term “oxo” means a doubly bonded oxygen, sometimes designated as =O or for example in describing a carbonyl “C(O)” may be used to show an oxo substituted carbon.

[0109] The term “oxy” signifies the -O- group.

[0110] The term “sulfonyl” signifies the -SO₂- group.

[0111] The term “substituted,” when used to modify a specified group or radical, means that one or more hydrogen atoms of the specified group or radical are each, independently of one another, replaced with the same or different substituent groups as defined below, unless specified otherwise.

[0112] As used herein, the term “metabolite” means a compound that results from the metabolism of a compound of the present disclosure, including from any of the embodiments described with reference to formulae (I) and (Ia)-(Ig) and embodiments 1-969 above. In an embodiment, the metabolite is an active metabolite meaning that it is a physiologically active compound. In an embodiment, the metabolite is an active compound obtained from metabolism of a prodrug as described herein.

[0113] The term “pharmaceutically acceptable” is meant as reference to a compound, substance or composition that is generally safe, non-toxic and biologically acceptable.

[0114] As used herein, the phrase “pharmaceutically acceptable salt” refers to both pharmaceutically acceptable acid and base addition salts. Without limitation, such pharmaceutically acceptable salts include salts of acids such as hydrochloric, phosphoric, hydrobromic, sulfuric, sulfinic, formic, toluenesulfonic, methanesulfonic, nitric, benzoic, citric, tartaric, maleic, hydroiodic, alkanoic such as acetic, HOOC-(CH₂)_n-COOH where n is 0-4, and the like. Non-toxic pharmaceutical base addition salts include, without limitation, salts of bases such as sodium, potassium, calcium, ammonium, and the like. Those skilled in the art will recognize a wide variety of non-toxic pharmaceutically acceptable addition salts.

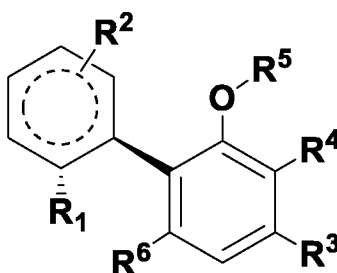
[0115] One of ordinary skill in the art of medicinal chemistry also will appreciate that the disclosed structures are intended to include isotopically enriched forms of the present compounds. As used herein “isotopes” includes those atoms having the same atomic number but different mass numbers. As is known to those of skill in the art, certain atoms, such as hydrogen occur in different isotopic forms. For example, hydrogen includes three isotopic forms, protium, deuterium and tritium. As will be apparent to those of skill in the art upon

consideration of the present compounds, certain compounds can be enriched at a given position with a particular isotope of the atom at that position. For example, compounds having a fluorine atom, may be synthesized in a form enriched in the radioactive fluorine isotope ^{18}F . Similarly, compounds may be enriched in the heavy isotopes of hydrogen: deuterium and tritium; and similarly can be enriched in a radioactive isotope of carbon, such as ^{13}C . Such isotopic variant compounds undergo different metabolic pathways and can be useful, for example, in studying the ubiquitination pathway and its role in disease. Of course, in certain embodiments, the compound has substantially the same isotopic character as naturally-occurring materials.

[0116] The compounds of the present disclosure may contain chiral centers, which may be either of the (R) or (S) configuration, or may comprise a mixture thereof. Accordingly, the present invention also includes stereoisomers of the compounds described herein, where applicable, either individually or admixed in any proportions. Stereoisomers may include, but are not limited to, enantiomers, diastereomers, racemic mixtures (racemates), and combinations thereof. Such stereoisomers can be prepared and separated using conventional techniques, either by reacting enantiomeric starting materials, or by separating isomers of compounds of the present invention.

[0117] Isomers may further include tautomers and geometric isomers. Examples of geometric isomers include, but are not limited to, cis isomers or trans isomers across a double bond. Other isomers are contemplated among the compounds of the present disclosure. The isomers may be used either in pure form or in admixture with other isomers of the compounds disclosed herein.

[0118] One of ordinary skill in the art of chemistry will also appreciate that the disclosed structures, unless otherwise indicated are intended to include all possible stereoisomers of the claimed molecule, including mixtures of certain or all stereoisomers. However, compounds drawn with certain stereochemistry at one or more stereocenters are indicative of the compounds in that particular embodiment having the indicated stereochemistry. Compounds and stereocenters drawn with ambiguous stereochemistry are meant to convey any stereoisomer or mixture thereof, e.g., a racemic mixture of compounds or a purified subset of stereoisomers. In some embodiments, compounds of the present disclosure may have a natural CBD-type stereochemistry as indicated below:



[0119] As used herein, the terms “individual,” “patient,” or “subject”, used interchangeably, refer to any animal, including mammals, and preferably humans.

[0120] As used herein, the phrase “therapeutically effective amount” or “effective amount” refers to the amount of active compound or pharmaceutical agent that elicits the biological or medicinal response that is being sought in a cell, tissue, system, animal, individual or human by a researcher, veterinarian, medical doctor or other clinician.

[0121] In certain embodiments, an effective amount can be an amount suitable for

- (i) inhibiting the progression the disease;
- (ii) prophylactic use for example, preventing or limiting development of a disease, condition or disorder in an individual who may be predisposed or otherwise at risk to the disease, condition or disorder but does not yet experience or display the pathology or symptomatology of the disease;
- (iii) inhibiting the disease; for example, inhibiting a disease, condition or disorder in an individual who is experiencing or displaying the pathology or symptomatology of the disease, condition or disorder;
- (iv) ameliorating the referenced disease state, for example, ameliorating a disease, condition or disorder in an individual who is experiencing or displaying the pathology or symptomatology of the disease, condition or disorder (i.e., reversing or improving the pathology and/or symptomatology) such as decreasing the severity of disease; or
- (v) eliciting the referenced biological effect.

[0122] As used herein, the terms “treatment” and “treating” means (i) ameliorating the referenced disease state, condition, or disorder (or a symptom thereof), such as, for example, ameliorating a disease, condition or disorder in an individual who is experiencing or displaying the pathology or symptomatology of the disease, condition or disorder (i.e., reversing or improving the pathology and/or symptomatology) such as decreasing the severity of disease or

symptom thereof, or inhibiting the progression of disease; or (ii) eliciting the referenced biological effect (e.g., inducing apoptosis, or inhibiting glutathione synthesis).

[0123] As used herein, the terms “preventing” or “prevent” means completely or partially preclude or delay the onset in a subject of a referenced disease state, condition, or disorder (or a symptom thereof).

Methods of Preparation

[0124] Many general references providing commonly known chemical synthetic schemes and conditions useful for synthesizing the disclosed compounds are available (see, e.g., Smith and March, *March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*, Fifth Edition, Wiley-Interscience, 2001; or Vogel, *A Textbook of Practical Organic Chemistry, Including Qualitative Organic Analysis*, Fourth Edition, New York: Longman, 1978).

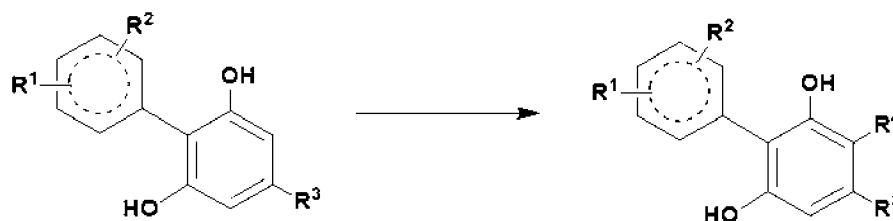
[0125] Compounds as described herein can be purified by any of the means known in the art, including chromatographic means, such as HPLC, preparative thin layer chromatography, flash column chromatography and ion exchange chromatography. Any suitable stationary phase can be used, including normal and reversed phases as well as ionic resins. Most typically the disclosed compounds are purified via silica gel and/or alumina chromatography. See, e.g., *Introduction to Modern Liquid Chromatography*, 2nd Edition, ed. L. R. Snyder and J. J. Kirkland, John Wiley and Sons, 1979; and *Thin Layer Chromatography*, ed E. Stahl, Springer-Verlag, New York, 1969. In further embodiments, compounds may be purified by preparative HPLC.

[0126] During any of the processes for preparation of the subject compounds, it may be necessary and/or desirable to protect sensitive or reactive groups on any of the molecules concerned. This may be achieved by means of conventional protecting groups as described in standard works, such as J. F. W. McOmie, *Protective Groups in Organic Chemistry*, Plenum Press, London and New York 1973, in T. W. Greene and P. G. M. Wuts, *Protective Groups in Organic Synthesis*, Third edition, Wiley, New York 1999, in *The Peptides*; Volume 3 (editors: E. Gross and J. Meienhofer), Academic Press, London and New York 1981, in *Methoden der organischen Chemie*, Houben-Weyl, 4.sup.th edition, Vol. 15/I, Georg Thieme Verlag, Stuttgart 1974, in H.-D. Jakubke and H. Jeschkeit, *Aminosäuren, Peptide, Proteine*, Verlag Chemie, Weinheim, Deerfield Beach, and Basel 1982, and/or in Jochen Lehmann, *Chemie der Kohlenhydrate: Monosaccharide and Derivate*, Georg Thieme Verlag, Stuttgart 1974. The protecting groups may be removed at a convenient subsequent stage using methods known from the art.

[0127] A “leaving group” as used herein (e.g. suitable as LG) refers to a moiety of a reactant (e.g., the alkylhalogenide of the disclosure) that is displaced from the first reactant in the chemical reaction. A comprehensive and non-limiting list of suitable leaving groups can be found in J. March, *Advanced Organic Chemistry*, John Wiley and Sons, N.Y. (2013). Examples of suitable leaving groups include, but are not limited to, halogen (such as Cl or Br), acetoxy, and sulfonyloxy groups (such as methyl sulfonyloxy, trifluoromethylsulfonyloxy (“triflate”), p-toluenesulfonyloxy (“tosylate”)).

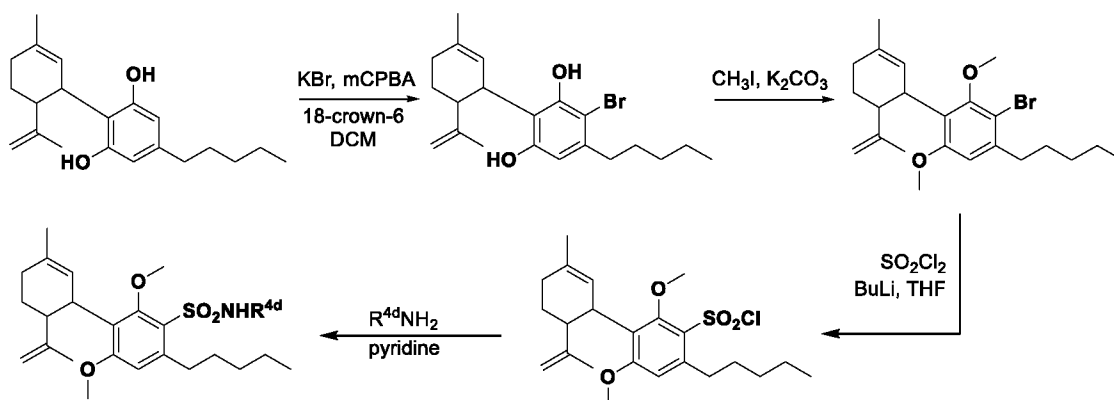
[0128] The compounds disclosed herein can be made using procedures familiar to the person of ordinary skill in the art and as described herein, for example in Schemes 1 – 7. One of skill in the art can adapt the reaction sequences of schemes and examples as provided herein to fit the desired target molecule. Of course, in certain situations one of skill in the art will use different reagents to affect one or more of the individual steps or to use protected versions of certain of the substituents. Additionally, one skilled in the art would recognize that compounds of the disclosure can be synthesized using different routes altogether. For example, the person of ordinary skill in the art may adapt the procedures described herein and/or other procedures familiar to the person of ordinary skill in the art to make the compounds described herein.

Scheme 1:



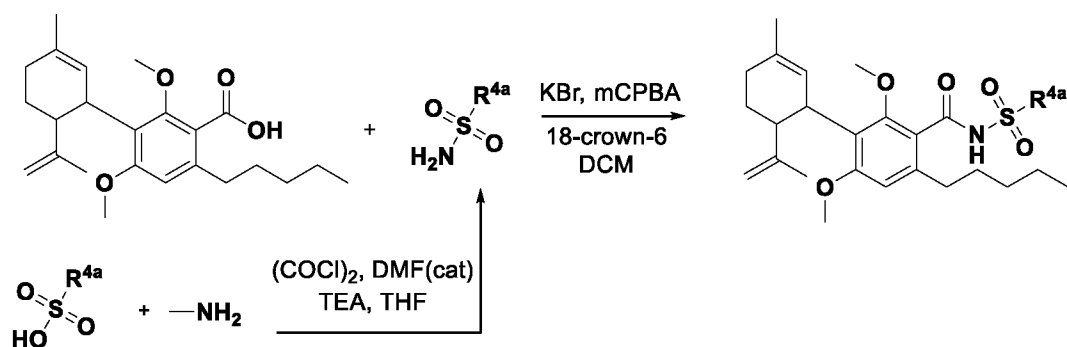
wherein R¹, R², R³, and R⁴ are as defined in formula(I).

Scheme 2:



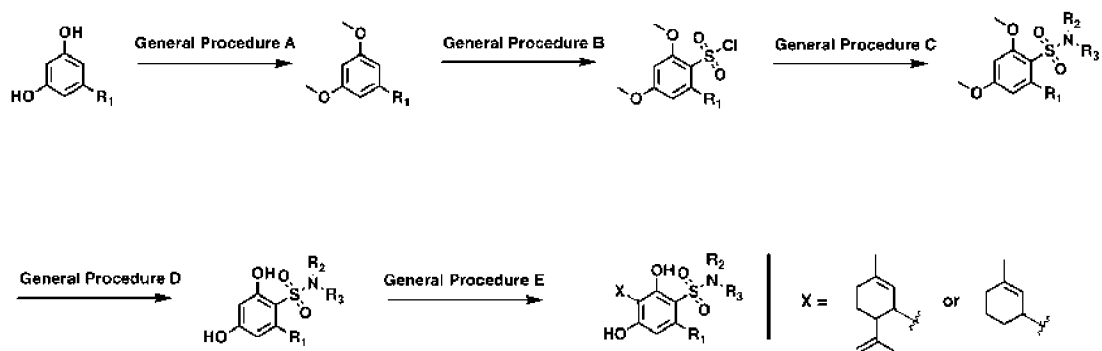
wherein R^{4d} is as defined in formula (I).

Scheme 3:

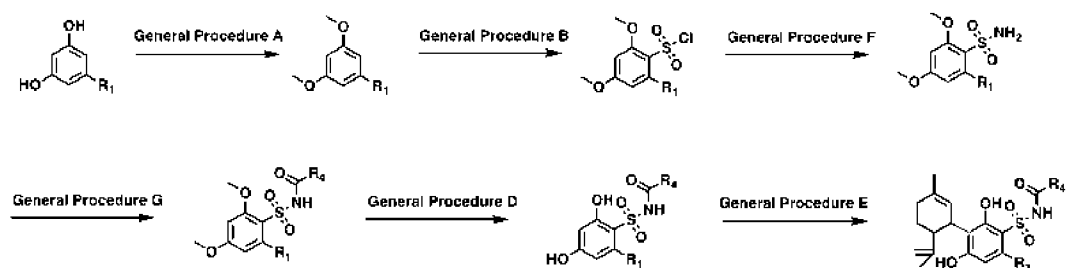


wherein R^{4a} is as defined in formula (I).

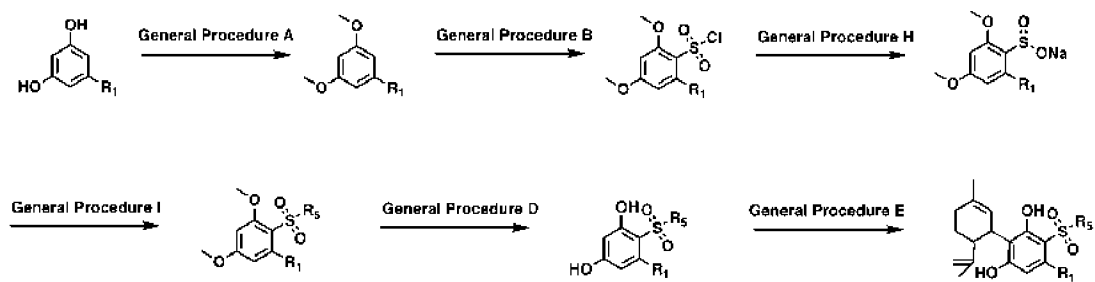
Scheme 4:



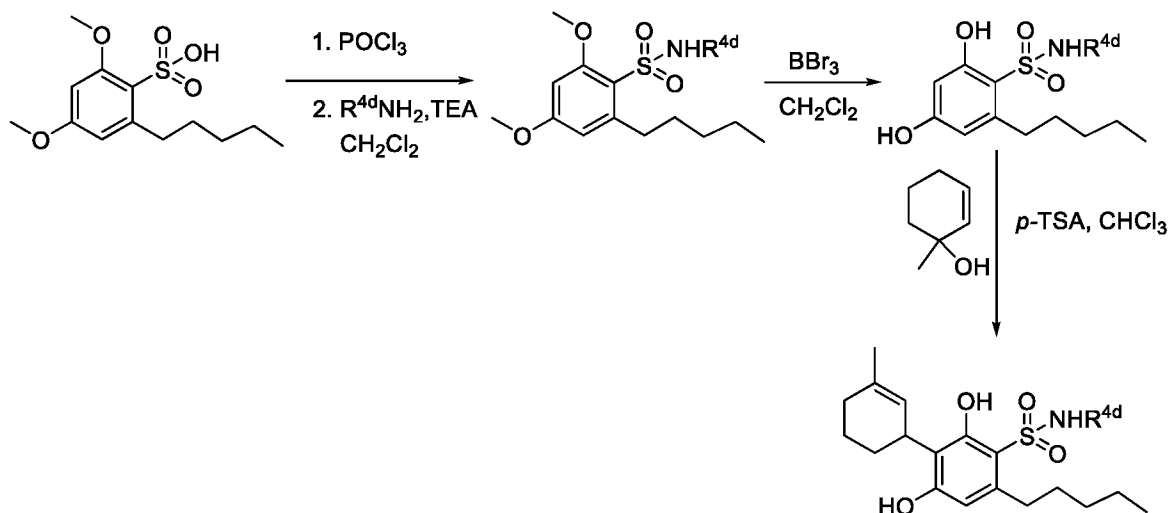
Scheme 5:



Scheme 6:



Scheme 7:



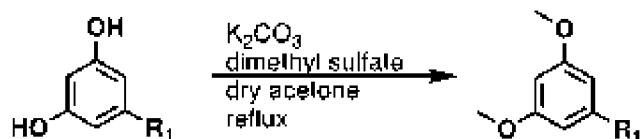
wherein R^{4d} is as defined in formula (I).

EXAMPLES

[0129] The preparation of the compounds of the disclosure is illustrated further by the following examples, which are not to be construed in any way as limiting the disclosure in scope or spirit to the specific procedures and compounds described in them. These examples are offered to illustrate the invention.

Compound Synthesis and Formulation

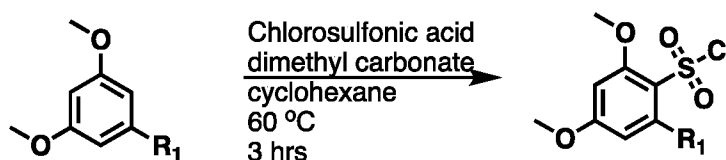
Example 1: General procedure A – Methylation of a benzene-1,3-diol



[0130] To a stirred solution of a respective benzene-1,3-diol (1 eq.) in dry acetone (0.6 M) was added potassium carbonate (3 eq.) at room temperature under nitrogen atmosphere. The resulting mixture was then added with dimethyl sulfate (3 eq.) and stirred at reflux for 14 h. The reaction mixture was cooled to room temperature and insoluble solid was filtered out. The

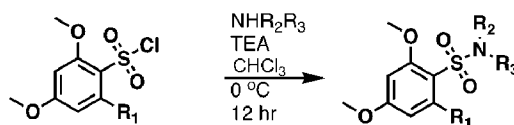
collected filtrate was concentrated under reduced pressure using rotatory evaporator. The crude mixture was diluted in ether and washed with 1M HCl. The collected organic layer was dried with sodium sulfate, filtered and evaporated under reduced pressure. The resulting residue was purified by flash chromatography eluting in gradient of ethyl acetate in hexanes to afford the desired product.

Example 2: General procedure B – Chlorosulfonylation of a 1,3-dimethoxybenzene

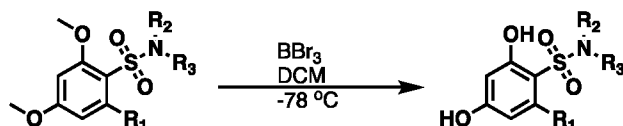


[0131] To a stirred solution of a respective 1,3-dimethoxybenzene (1 eq.) was added cyclohexane (1.9 M) and the resulting solution was cooled in the ice bath at 0 °C. The solution was then added with dimethyl carbonate (5 eq.), followed by slow addition of chlorosulfonic acid (5 eq.). The resulting mixture was then stirred in the oil bath pre-heated at 60 °C. After 3 h, the mixture was cooled to 0 °C and quenched with water. The mixture was then extracted with DCM three times, and the collected organic layers were dried with sodium sulfate, filtered and evaporated under reduced pressure. The resulting residue was purified by flash chromatography eluting in gradient of ethyl acetate in hexanes to afford the desired product.

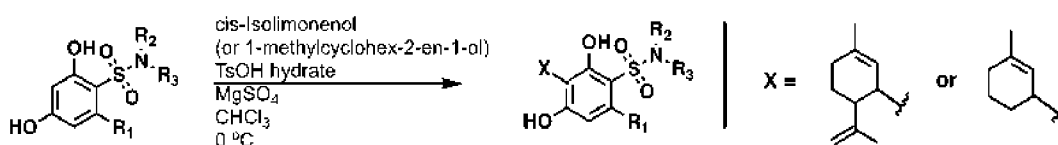
Example 3: General procedure C – Formation of a sulfonamide



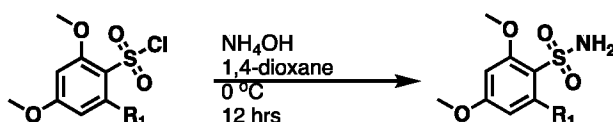
[0132] A respective sulfonyl chloride (1 eq.) was dissolved in anhydrous CHCl_3 (0.3 M – 0.45 M) and the reaction mixture was cooled in the ice bath at 0 °C. To this solution was added respective amines (1.1 eq.), followed by the dropwise addition of triethylamine (1.5 eq.). The reaction mixture was allowed to stir for 12 h while slowly warming up to 25 °C. The mixture was quenched with water and extracted with DCM three times. The collected organic layers were dried with sodium sulfate, filtered and evaporated under reduced pressure using rotatory evaporator. The resulting residue was purified by flash chromatography on silica gel eluting in gradient of ethyl acetate in hexanes to afford the desired product.

Example 4: General procedure D – Demethylation

[0133] A solution of a sulfonamide (1 eq.) in anhydrous DCM (0.23 M) was cooled to -78 °C. After 15 min, to the solution was added with BBr₃ in a slow dropwise manner. The resulting solution was stirred for 12 h while slowly warming up to room temperature. The reaction was quenched with 1M HCl and extracted with DCM three times. The collected organic layers were washed once with saturated sodium chloride solution, dried with sodium sulfate, filtered and evaporated under reduced pressure using rotatory evaporator. The resulting residue was purified by flash chromatography on silica gel eluting in gradient of ethyl acetate in hexanes to afford the desired product.

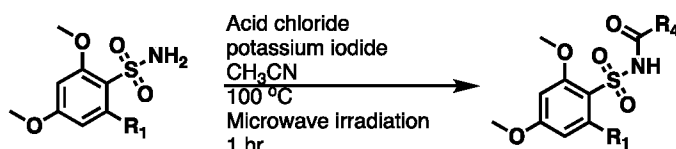
Example 5: General procedure E – Friedel-Crafts alkylation

[0134] A respective sulfonamide (1 eq.) was dissolved in anhydrous CHCl₃ (0.1 M) and cooled to 0 °C under a nitrogen atmosphere. To the solution was added *p*-toluenesulfonic acid hydrate (0.1 eq.) and magnesium sulfate (0.9 eq.). The reaction mixture was then added with a solution of cis-isolimonenol or 1-methylcyclohex-2-en-1-ol (1.1 eq.) in anhydrous CHCl₃ (0.1 M) at 0 °C in a dropwise manner. The reaction was then stirred for 12 h while gradually warming up to room temperature. The reaction mixture was quenched with saturated sodium bicarbonate solution and extracted three times with DCM. The collected organic layers were dried with sodium sulfate, filtered and evaporated under reduced pressure using rotatory evaporator. The resulting residue was purified by flash chromatography on silica gel eluting in gradient of ethyl acetate in hexanes to afford the desired product.

Example 6: General procedure F – Conversion of sulfonyl chloride to primary sulfonamide

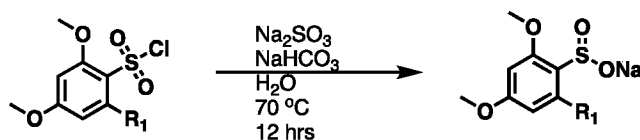
[0135] A respective sulfonyl chloride (1 eq.) was dissolved in 1,4-dioxane (0.48 M) and cooled to 0 °C in the ice bath. The resulting solution was then added with NH_4OH (16 eq.) and the reaction was stirred for 12 h while slowly warming up to room temperature. The reaction mixture was quenched with water and extracted three times with DCM. The collected organic layers were washed once with saturated sodium chloride solution, dried with sodium sulfate, filtered and evaporated under reduced pressure using rotatory evaporator to yield the desired product.

Example 7: General procedure G – Conversion of a sulfonamide to an acylsulfonamide



[0136] A respective sulfonamide (1 eq.) and potassium iodide (0.3 eq.) were suspended in CH_3CN (1 M). The reaction mixture was then added with acid chloride (1.2 eq.) and tightly sealed. The mixture was stirred at $100\text{ }^\circ\text{C}$ under microwave irradiation for 1 hour. Upon cooling to room temperature, the mixture was quenched with saturated sodium thiosulfate solution and extracted with DCM three times. The collected organic layers were dried with sodium sulfate, filtered and evaporated under reduced pressure using rotatory evaporator. The resulting residue was purified by flash chromatography on silica gel eluting in gradient of EtOAc in Hexanes to afford the desired product.

Example 8: General Procedure H – Conversion of a sulfonyl chloride to a sodium sulfonate



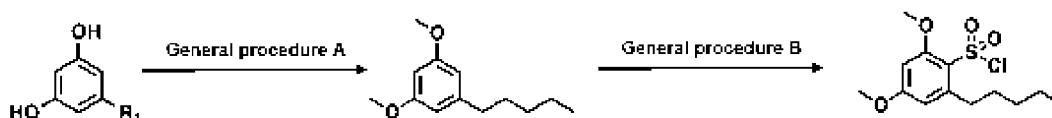
[0137] To a stirred solution of sodium sulfite (4 eq.) and sodium bicarbonate (4 eq.) in water (0.1 M) was added sulfonyl chloride (1 eq.) at room temperature. The reaction mixture was stirred at $70\text{ }^\circ\text{C}$ for 12 h. The reaction mixture was then evaporated under reduced pressure. The resulting residue was suspended in ethanol (0.05 M) and stirred for 20 min at room temperature. The suspension was filtered and the collected filtrate evaporated under the reduced pressure to yield the desired product.

Example 9: General Procedure I – Conversion of a sulfinate salt to a sulfone

[0138] To a stirred solution of sodium sulfinate (1 eq.) in anhydrous THF or 1,4-dioxane (0.15 M) was added alkyl halide (2 eq.) under an argon atmosphere. The reaction was sealed and

stirred at 70 °C for 12 h. The reaction mixture was quenched with water and extracted with DCM three times. The collected organic layers were dried with sodium sulfate, filtered and evaporated under reduced pressure. The resulting residue was purified by flash chromatography on silica gel eluting in gradient of ethyl acetate in hexanes to afford the desired product.

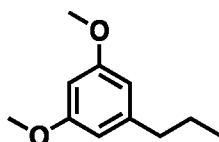
Example 10: Preparation of 2,4-dimethoxy-6-pentylbenzenesulfonyl chloride



[0139] General procedure A was followed using 5-pentylbenzene-1,3-diol (10 g, 55.48 mmol, 1 eq.), dimethyl sulfate (15.78 ml, 166.44 mmol, 3 eq.), K₂CO₃ (23 g, 166.44 mmol, 3 eq.) and dry acetone (92 mL) to give 1,3-dimethoxy-5-pentylbenzene (10 g, 48 mmol, 86% yield).

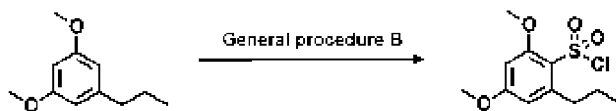
[0140] General procedure B was followed using 1,3-dimethoxy-5-pentylbenzene (14.5 g, 69.61 mmol, 1 eq.), chlorosulfonic acid (23.17 ml, 348.06 mmol, 5 eq.), dimethyl carbonate (32.11 g, 356.47 mmol, 5.12 eq.) and cyclohexane (39 mL) to give 2,4-dimethoxy-6-pentylbenzenesulfonyl chloride (9 g, 29.33 mmol, 42% yield).

Example 11: Preparation of 1,3-dimethoxy-5-pentylbenzene



[0141] To a stirred solution of 1-bromo-3,5-dimethoxy-benzene (10 g, 46.07 mmol, 1 eq.) in anhydrous toluene (200 mL, 0.23 M) under Argon atmosphere was added propylboronic acid (6.08 g, 69.11 mmol). The reaction mixture was then added with PdCl₂(dppf) (0.69 g, 943 μmol, 0.02 eq.) and K₃PO₄ (29.34 g, 138.21 mmol, 3 eq.) The reaction mixture was stirred under refluxing conditions at 110 °C for 12 hours. The reaction mixture was cooled to room temperature and diluted with Et₂O, filtered through Celite and the collected organic layers were dried with magnesium sulfate, filtered and concentrated under reduced pressure to yield 1,3-dimethoxy-5-pentylbenzene as a pale orange oil (8.18 g, 45.38 mmol, 98%).

Example 12: Preparation of 2,4-dimethoxy-6-pentylbenzenesulfonyl chloride



[0142] General procedure B was followed using 1,3-dimethoxy-5-pentylbenzene (3 g, 16.64 mmol, 1 eq.), chlorosulfonic acid (5.54 ml, 83.22 mmol, 5 eq.), dimethyl carbonate (7.68 g, 85.23 mmol, 5.12 eq.) and cyclohexane (8.8 mL) to give 2,4-dimethoxy-6-pentylbenzenesulfonyl chloride (1.88 g, 6.74 mmol, 40% yield).

Example 13: *N,N*-diethyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide (**62d**)



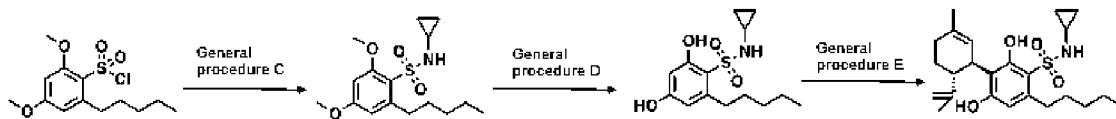
[0143] General procedure C was followed using 2,4-dimethoxy-6-pentylbenzenesulfonyl chloride (0.3 g, 0.977 mmol, 1 eq.), triethylamine (TEA; 0.14 ml, 0.98 mmol, 1 eq.), *N*-ethylethaneamine (0.11 mL, 1.08 mmol, 1.1 eq.) and CHCl_3 (3.3 mL) to give *N,N*-diethyl-2,4-dimethoxy-6-pentylbenzenesulfonamide (0.280 g, 0.815 mmol, 83% yield).

[0144] General procedure D was followed using *N,N*-diethyl-2,4-dimethoxy-6-pentylbenzenesulfonamide (0.280 g, 0.815 mmol, 1 eq.), BBr_3 (4.08 ml, 4.08 mmol, 5 eq.) and CH_2Cl_2 (3.54 mL) to give *N,N*-diethyl-2,4-dihydroxy-6-pentylbenzenesulfonamide (0.21 g, 0.666 mmol, 81% yield).

[0145] General procedure E was followed using *N,N*-diethyl-2,4-dihydroxy-6-pentylbenzenesulfonamide (0.2 g, 0.634 mmol, 1 eq.), *p*-toluenesulfonic acid hydrate (12.1 mg, 0.063 mmol, 0.1 eq.), magnesium sulfate (24 mg), *cis*-isolimonenol (0.11 mL, 0.697 mmol, 1.1 eq.), and anhydrous CH_3Cl (6.34 mL) to give (1'*R*,2'*R*)-*N,N*-diethyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide as a thick oil (44 mg, 0.097 mmol, 15% yield). ^1H NMR (400 MHz, CDCl_3) δ 10.58 (s, 1H), 6.56 (s, 1H), 6.33 (s, 1H), 5.59 (s, 1H), 4.50 – 4.45 (m, 1H), 4.35 – 4.29 (m, 1H), 4.15 – 4.06 (m, 1H), 3.35 – 3.14 (m, 4H), 2.82 (ddd, $J = 14.3, 10.7, 5.3$ Hz, 1H), 2.64 (ddd, $J = 14.3, 10.7, 5.5$ Hz, 1H), 2.43 – 2.32 (m, 1H), 2.31 – 2.19 (m, 1H), 2.17 – 2.08 (m, 1H), 1.86 – 1.77 (m, 5H), 1.72 (s, 3H), 1.70 – 1.52

(m, 2H), 1.44 – 1.32 (m, 4H), 1.09 (t, $J = 7.1$ Hz, 6H), 0.97 – 0.88 (m, 3H). LRMS (-) (m/z): $[M-H]^-$ calculated for $C_{25}H_{39}NO_4S$, 448.26; found, 448.30.

Example 14: *N*-cyclopropyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide (**22d**)

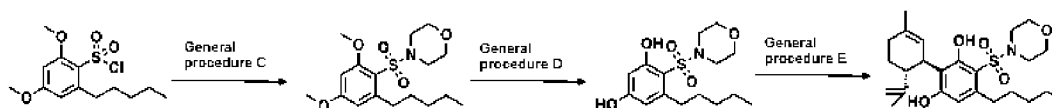


[0146] General procedure C was followed using 2,4-dimethoxy-6-pentylbenzenesulfonyl chloride (0.28 g, 0.916 mmol, 1 eq.), TEA (0.13 ml, 0.92 mmol, 1 eq.), cyclopropylamine (0.070 mL, 1.01 mmol, 1.1 eq.) and $CHCl_3$ (3.1 mL) to give *N*-cyclopropyl-2,4-dimethoxy-6-pentylbenzenesulfonamide (0.260 g, 0.794 mmol, 86% yield).

[0147] General procedure D was followed using *N*-cyclopropyl-2,4-dimethoxy-6-pentylbenzenesulfonamide (0.260 g, 0.794 mmol, 1 eq.), BBr_3 (3.97 mL, 3.97 mmol, 5 eq.) and CH_2Cl_2 (3.97 mL) to give *N*-cyclopropyl-2,4-dihydroxy-6-pentylbenzenesulfonamide (0.18 g, 0.601 mmol, 75% yield).

[0148] General procedure E was followed using *N*-cyclopropyl-2,4-dihydroxy-6-pentylbenzenesulfonamide (0.14 g, 0.467 mmol, 1 eq.), *p*-toluenesulfonic acid hydrate (8.9 mg, 0.047 mmol, 0.1 eq.), magnesium sulfate (18 mg), *cis*-isolimonenol (0.083 mL, 0.514 mmol, 1.1 eq.), and anhydrous CH_3Cl (4.7 mL) to give (1'*R*,2'*R*)-*N*-cyclopropyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide as a thick oil (55 mg, 0.126 mmol, 27% yield). ^1H NMR (400 MHz, $CDCl_3$) δ 10.25 (s, 1H), 6.55 (s, 1H), 6.36 (s, 1H), 5.57 (s, 1H), 5.03 (s, 1H), 4.45 (s, 1H), 4.37 (s, 1H), 4.19 – 4.07 (m, 1H), 2.85 (ddd, $J = 14.0, 10.3, 5.5$ Hz, 1H), 2.72 (ddd, $J = 14.1, 10.4, 5.7$ Hz, 1H), 2.46 – 2.36 (m, 1H), 2.32 – 2.20 (m, 2H), 2.18 – 2.08 (m, 1H), 1.87 – 1.77 (m, 5H), 1.72 (s, 3H), 1.70 – 1.55 (m, 0H), 1.43 – 1.30 (m, $J = 3.3$ Hz, 4H), 0.97 – 0.87 (m, 3H), 0.68 – 0.46 (m, 4H). LRMS (-) (m/z): $[M-H]^-$ calculated for $C_{24}H_{35}NO_4S$, 432.23; found, 432.20.

Example 15: 5'-methyl-3-(morpholinosulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol (**28d**)

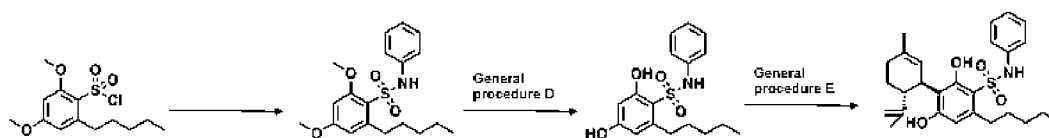


[0149] General procedure C was followed using 2,4-dimethoxy-6-pentylbenzenesulfonyl chloride (0.4 g, 1.30 mmol, 1 eq.), TEA (0.2 ml, 1.43 mmol, 1.1 eq.), morpholine (0.11 g, 1.3 mmol, 1 eq.) and CHCl_3 (4.3 mL) to give 4-((2,4-dimethoxy-6-pentylphenyl)sulfonyl)morpholine (0.420 g, 1.17 mmol, 90% yield).

[0150] General procedure D was followed using 4-(2,4-dimethoxy-6-pentylphenyl)sulfonylmorpholine (0.420 g, 1.17 mmol, 1 eq.), BBr_3 (4.7 ml, 4.7 mmol, 4 eq.) and CH_2Cl_2 (5.08 mL) to give 4-(morpholinosulfonyl)-5-pentylbenzene-1,3-diol (0.2 g, 0.607 mmol, 51% yield).

[0151] General procedure E was followed using 4-morpholinosulfonyl-5-pentyl-benzene-1,3-diol (0.2 g, 0.607 mmol, 1 eq.), p-toluenesulfonic acid hydrate (11.55 mg, 0.061 mmol, 0.1 eq.), magnesium sulfate (26 mg), cis-isolimonenol (0.108 mL, 0.668 mmol, 1.1 eq.), and anhydrous CHCl_3 (6.1 mL) to afford (1'R,2'R)-5'-methyl-3-(morpholinosulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol as a thick oil (39 mg, 0.084 mmol, 13% yield). ^1H NMR (400 MHz, CDCl_3) δ 10.17 (s, 1H), 6.63 (s, 1H), 6.37 (s, 1H), 5.59 (s, 1H), 4.46 (s, 1H), 4.34 (s, 1H), 4.09 (s, 1H), 3.71 (t, $J = 4.8$ Hz, 4H), 3.18 – 3.03 (m, 4H), 2.95 – 2.84 (m, 1H), 2.71 (ddd, $J = 14.6, 10.4, 5.7$ Hz, 1H), 2.44 – 2.33 (m, 1H), 2.33 – 2.21 (m, 1H), 2.19 – 2.08 (m, 1H), 1.88 – 1.77 (m, 5H), 1.72 (s, 3H), 1.68 – 1.61 (m, 2H), 1.41 – 1.32 (m, 4H), 0.98 – 0.89 (m, 3H). LRMS (+) (m/z): $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{25}\text{H}_{37}\text{NO}_5\text{S}$, 464.24; found, 464.10.

Example 16: 2,6-dihydroxy-5'-methyl-4-pentyl-N-phenyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide (**24d**)



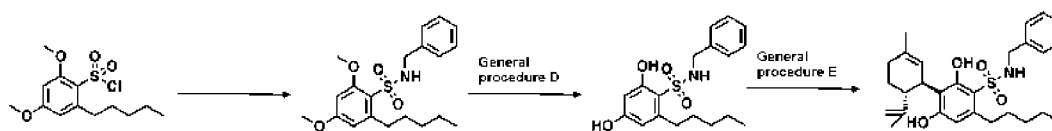
[0152] 2,4-dimethoxy-6-pentyl-benzenesulfonyl chloride (0.25 g, 0.81 mmol, 1 eq.) was dissolved in anhydrous CHCl_3 (2.7 mL) and the reaction mixture was cooled in the ice bath at 0 °C. To this solution was added aniline (0.15 ml, 1.63 mmol, 2 eq.). The reaction mixture was allowed to stir for 12 hrs while slowly warming up to 25 °C. The mixture was quenched with water and extracted with DCM three times. The collected organic layers were dried with sodium sulfate, filtered and evaporated under reduced pressure using rotatory evaporator. The resulting residue was then separated on a pad of silica gel using Biotage Isolera eluting in gradient of

ethyl acetate in hexanes to give 2,4-dimethoxy-6-pentyl-*N*-phenylbenzenesulfonamide (0.167 g, 0.46 mmol, 56% yield).

[0153] General procedure D was followed using 2,4-dimethoxy-6-pentyl-*N*-phenylbenzenesulfonamide (0.17 g, 0.36 mmol, 1 eq.), BBr₃ (1.87 ml, 1.87 mmol, 4 eq.) and CH₂Cl₂ (2.0 mL) to give 2,4-dihydroxy-6-pentyl-*N*-phenylbenzenesulfonamide (0.130 g, 0.388 mmol, 82% yield).

[0154] General procedure E was followed using 2,4-dihydroxy-6-pentyl-*N*-phenylbenzenesulfonamide (0.13 g, 0.388 mmol, 1 eq.), *p*-toluenesulfonic acid hydrate (7.37 mg, 0.039 mmol, 0.1 eq.), magnesium sulfate (17 mg), cis-isolimonenol (0.069 mL, 0.426 mmol, 1.1 eq.), and anhydrous CH₃Cl (3.9 mL) to afford (1'*R*,2'*R*)-2,6-dihydroxy-5'-methyl-4-pentyl-*N*-phenyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide as a thick oil (39 mg, 0.083 mmol, 21% yield). ¹H NMR (400 MHz, CDCl₃) δ 9.98 (s, 1H), 7.30 – 7.24 (m, 3H), 7.20 – 7.13 (m, 1H), 6.99 – 6.91 (m, 2H), 6.55 (s, 1H), 6.33 (s, 1H), 5.52 (s, 1H), 4.51 – 4.44 (m, 1H), 4.33 (d, *J* = 2.3 Hz, 1H), 4.08 (d, *J* = 9.7 Hz, 1H), 2.86 (ddd, *J* = 15.6, 10.3, 5.6 Hz, 1H), 2.74 (ddd, *J* = 14.5, 10.3, 5.6 Hz, 1H), 2.36 (q, *J* = 8.5 Hz, 1H), 2.30 – 2.18 (m, 1H), 2.18 – 2.07 (m, 1H), 1.87 – 1.76 (m, 5H), 1.68 (s, 3H), 1.66 – 1.50 (m, 2H), 1.44 – 1.30 (m, 4H), 0.98 – 0.86 (m, 3H). LRMS (+) (*m/z*): [M+H]⁺ calculated for C₂₇H₃₅NO₄S, 470.23; found, 470.20.

Example 17: Synthesis of *N*-benzyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide (**25d**)

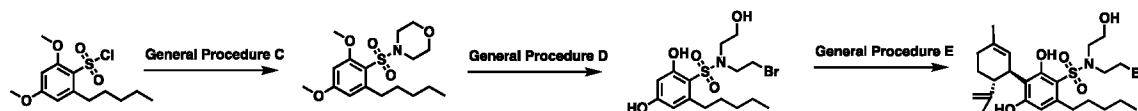


[0155] 2,4-dimethoxy-6-pentyl-benzenesulfonyl chloride (0.25 g, 0.81 mmol, 1 eq.) was dissolved in anhydrous CHCl₃ (2.7 mL) and the reaction mixture was cooled in the ice bath at 0 °C. To this solution was added benzylamine (0.18 ml, 1.63 mmol, 2 eq.). The reaction mixture was allowed to stir for 12 h while slowly warming up to 25 °C. The mixture was quenched with water and extracted with DCM three times. The collected organic layers were dried with sodium sulfate, filtered and evaporated under reduced pressure using rotatory evaporator. The resulting residue was then separated on a pad of silica gel using Biotage Isolera eluting in gradient of ethyl acetate in hexanes to give *N*-benzyl-2,4-dimethoxy-6-pentylbenzenesulfonamide (0.171 g, 0.45 mmol, 55% yield).

[0156] General procedure D was followed using *N*-benzyl-2,4-dimethoxy-6-pentyl-*N*-phenylbenzenesulfonamide (0.2 g, 0.529 mmol, 1 eq.), BBr₃ (2.12 ml, 2.12 mmol, 4 eq.) and CH₂Cl₂ (2.3 mL) to give *N*-benzyl-2,4-dihydroxy-6-pentylbenzenesulfonamide (0.120 g, 0.343 mmol, 64% yield).

[0157] General procedure E was followed using *N*-benzyl-2,4-dihydroxy-6-pentylbenzenesulfonamide (0.12 g, 0.343 mmol, 1 eq.), *p*-toluenesulfonic acid hydrate (6.53 mg, 0.034 mmol, 0.1 eq.), magnesium sulfate (15 mg), cis-isolimonenol (0.061 mL, 0.377 mmol, 1.1 eq.), and anhydrous CH₃Cl (3.4 mL) to afford (1'*R*,2'*R*)-*N*-benzyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide as a thick oil (39 mg, 0.081 mmol, 23% yield). ¹H NMR (400 MHz, CDCl₃) δ 10.26 (s, 1H), 7.36 – 7.30 (m, 3H), 7.23 – 7.15 (m, 2H), 6.63 (s, 1H), 6.38 (s, 1H), 5.60 (s, 1H), 4.65 (s, 1H), 4.46 (s, 1H), 4.35 (s, 1H), 4.19 – 3.90 (m, 3H), 2.86 (ddd, *J* = 15.2, 10.4, 5.5 Hz, 1H), 2.73 (ddd, *J* = 14.5, 10.3, 5.6 Hz, 1H), 2.40 (q, *J* = 8.4 Hz, 1H), 2.33 – 2.09 (m, 1H), 1.88 – 1.78 (m, 5H), 1.73 (s, 3H), 1.70 – 1.49 (m, 3H), 1.41 – 1.27 (m, 4H), 0.94 – 0.86 (m, 3H). LRMS (-) (*m/z*): [M-H]⁻ calculated for C₂₈H₃₇NO₄S, 484.24; found, 484.20.

Example 18: *N*-(2-bromoethyl)-2,6-dihydroxy-*N*-(2-hydroxyethyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide (**63d**)



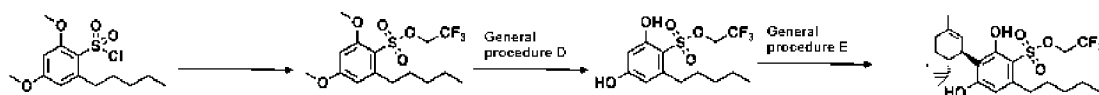
[0158] General procedure C was followed using 2,4-dimethoxy-6-pentylbenzenesulfonyl chloride (0.4 g, 1.30 mmol, 1 eq.), TEA (0.2 ml, 1.43 mmol, 1.1 eq.), morpholine (0.11 g, 1.3 mmol, 1 eq.) and CHCl₃ (4.3 mL) to give 4-((2,4-dimethoxy-6-pentylphenyl)sulfonyl)morpholine (0.420 g, 1.17 mmol, 90% yield).

[0159] General procedure D was followed using 4-((2,4-dimethoxy-6-pentylphenyl)sulfonyl)morpholine (0.230 g, 0.643 mmol, 1 eq.), BBr₃ (3.2 ml, 3.22 mmol, 5 eq.) and CH₂Cl₂ (2.8 mL) to give *N*-(2-bromoethyl)-2,4-dihydroxy-*N*-(2-hydroxyethyl)-6-pentylbenzenesulfonamide (0.14 g, 0.264 mmol, 52% yield).

[0160] General procedure E was followed using *N*-(2-bromoethyl)-2,4-dihydroxy-*N*-(2-hydroxyethyl)-6-pentylbenzenesulfonamide (0.14 g, 0.336 mmol, 1 eq.), *p*-toluenesulfonic acid hydrate (6.41 mg, 0.034 mmol, 0.1 eq.), magnesium sulfate (13 mg), cis-isolimonenol (0.059 mL, 0.371 mmol, 1.1 eq.), and anhydrous CH₃Cl (3.4 mL) to afford (1'*R*,2'*R*)-*N*-(2-bromoethyl)-

2,6-dihydroxy-N-(2-hydroxyethyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide as a thick oil (8 mg, 0.014 mmol, 4% yield). ¹H NMR (400 MHz, CDCl₃) δ 10.34 (s, 1H), 6.65 (s, 1H), 6.37 (s, 1H), 5.58 (s, 1H), 4.52 (dq, *J* = 2.9, 1.5 Hz, 1H), 4.34 (d, *J* = 2.5 Hz, 1H), 4.16 – 4.05 (m, 1H), 3.80 – 3.67 (m, 2H), 3.67 – 3.58 (m, 2H), 3.47 – 3.30 (m, 4H), 2.86 (ddd, *J* = 14.3, 10.6, 5.2 Hz, 1H), 2.66 (ddd, *J* = 14.3, 10.7, 5.4 Hz, 1H), 2.37 (dt, *J* = 10.0, 7.6 Hz, 1H), 2.33 – 2.19 (m, 1H), 2.19 – 2.09 (m, 1H), 1.88 – 1.78 (m, 5H), 1.73 (s, 3H), 1.70 – 1.52 (m, 1H), 1.44 – 1.32 (m, *J* = 3.3 Hz, 4H), 0.98 – 0.89 (m, 3H). LRMS (-) (*m/z*): [M-H]⁻ calculated for C₂₅H₃₈BrNO₅S, 544.16; found, 544.20.

Example 19: 2,2,2-trifluoroethyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonate (**64d**)



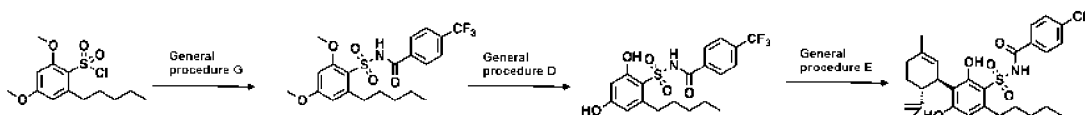
[0161] 2,4-dimethoxy-6-pentylbenzenesulfonyl chloride (0.2 g, 0.65 mmol, 1 eq.) was dissolved in anhydrous CH₂Cl₂ (2.6 mL). To this solution was added 2,2,2-trifluoroethanol (78.26 mg, 0.782 mmol, 1.2 eq.) followed by 1,4-diazabicyclo[2.2.2]octane (DABCO; 78.26 mg, 0.782 mmol, 1 eq.) in CH₂Cl₂ (1.3 mL). The reaction mixture was allowed to stir for 3 hrs at room temperature. The mixture was quenched with 0.1 M HCl and extracted with DCM three times. The collected organic layers were dried with sodium sulfate, filtered and evaporated under reduced pressure using rotatory evaporator. The resulting residue was then separated on a pad of silica gel using Biotage Isolera eluting in gradient of ethyl acetate in hexanes to afford 2,2,2-trifluoroethyl 2,4-dimethoxy-6-pentylbenzenesulfonate (0.18 g, 0.49 mmol, 74% yield).

[0162] General procedure D was followed using 2,2,2-trifluoroethyl 2,4-dimethoxy-6-pentylbenzenesulfonate (0.18 g, 0.486 mmol, 1 eq.), BBr₃ (1.94 mL, 1.94 mmol, 4 eq.) and CH₂Cl₂ (2.1 mL) to 2,2,2-trifluoroethyl 2,4-dihydroxy-6-pentylbenzenesulfonate (0.1 g, 0.292 mmol, 60% yield).

[0163] General procedure E was followed using 2,2,2-trifluoroethyl 2,4-dihydroxy-6-pentylbenzenesulfonate (0.1 g, 0.292 mmol, 1 eq.), *p*-toluenesulfonic acid hydrate (5.56 mg, 0.029 mmol, 0.1 eq.), magnesium sulfate (17 mg), cis-isolimonenol (0.052 mL, 0.321 mmol, 1.1 eq.), and anhydrous CH₃Cl (3 mL) to afford 2,2,2-trifluoroethyl (1'R,2'R)-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonate as a thick oil (11 mg, 0.023 mmol, 8% yield). ¹H NMR (400 MHz, CDCl₃) δ 9.52 (s, 1H), 6.82 (s, 1H), 6.43 (s, 1H),

5.59 (s, 1H), 4.50 (s, 1H), 4.39 – 4.23 (m, 2H), 4.18 – 4.06 (m, 2H), 2.89 (ddd, $J = 15.4, 10.3, 5.6$ Hz, 1H), 2.82 – 2.68 (m, 1H), 2.36 (q, $J = 10.0, 9.4$ Hz, 1H), 2.31 – 2.21 (m, 1H), 2.19 – 2.10 (m, 1H), 1.89 – 1.77 (m, 4H), 1.72 (s, 3H), 1.57 (s, 3H), 1.39 (p, $J = 3.9$ Hz, 3H), 0.98 – 0.89 (m, 3H). ^{19}F NMR (376 MHz, CDCl_3) δ -73.58 (t, $J = 7.9$ Hz). LRMS (-) (m/z): $[\text{M}-\text{H}]^-$ calculated for $\text{C}_{23}\text{H}_{31}\text{F}_3\text{NO}_5\text{S}$, 475.20; found, 475.18.

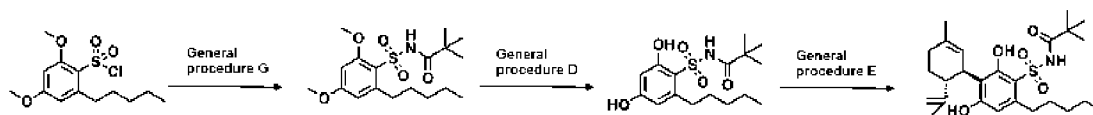
Example 20: N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-4-(trifluoromethyl)benzamide (**65d**)



[0164] General procedure G was followed using 2,4-dimethoxy-6-pentylbenzenesulfonamide (0.2 g, 0.695 mmol, 1 eq.), 4-(trifluoromethyl)benzoyl chloride (0.124 ml, 0.835 mmol, 1.2 eq.), potassium iodide (0.031 g, 0.187 mmol, 0.27 eq.) and CH_3CN (0.7 mL) to afford the desired product (0.085 g, 0.184 mmol, 26% yield).

[0165] The title compound was prepared according to Example 5 using N-(2,4-dihydroxy-6-pentyl-phenyl)sulfonyl-4-(trifluoromethyl)benzamide (0.09 g, 0.208 mmol, 1 eq.), *p*-toluenesulfonic acid hydrate (3.97 mg, 0.021 mmol, 0.1 eq.), magnesium sulfate (17 mg), *cis*-isolimonenol (0.037 mL, 0.229 mmol, 1.1 eq.), and anhydrous CH_3Cl (2 mL) to afford N-(((1'*R*,2'*R*)-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-4-(trifluoromethyl)benzamide as a thick oil (10 mg, 0.018 mmol, 8.4% yield). ^1H NMR (400 MHz, CDCl_3) δ 9.84 (s, 1H), 7.92 (d, $J = 8.2$ Hz, 3H), 7.77 (d, $J = 8.1$ Hz, 3H), 6.80 (s, 2H), 6.35 (s, 1H), 5.62 (s, 1H), 4.59 (t, $J = 1.9$ Hz, 2H), 4.38 (d, $J = 2.2$ Hz, 1H), 4.19 (s, 1H), 2.85 (t, $J = 7.9$ Hz, 3H), 2.45 – 2.33 (m, 2H), 2.31 – 2.21 (m, 2H), 2.19 – 2.09 (m, 1H), 1.90 – 1.80 (m, 7H), 1.77 (s, 4H), 1.43 – 1.21 (m, 7H), 0.85 (t, $J = 7.1$ Hz, 4H). ^{19}F NMR (376 MHz, CDCl_3) δ -63.26. LRMS (+) (m/z): $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{29}\text{H}_{34}\text{F}_3\text{NO}_5\text{S}$, 564.65; found, 563.8.

Example 21: N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)pivalamide (**66d**)

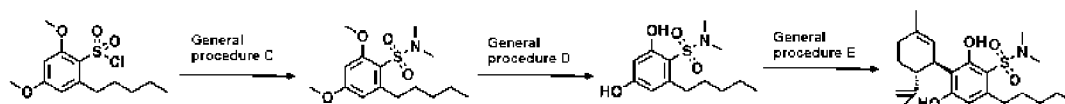


[0166] General procedure G was followed using 2,4-dimethoxy-6-pentylbenzenesulfonyl chloride (0.2 g, 0.695 mmol, 1 eq.), 2,2-dimethylpropanoyl chloride (0.1 ml, 0.835 mmol, 1.2 eq.), potassium iodide (0.031 g, 0.187 mmol, 0.27 eq.) and CH₃CN (1.4 mL) to give N-(2,4-dimethoxy-6-pentyl-phenyl)sulfonyl-2,2-dimethyl-propanamide (0.17 g, 0.457 mmol, 65% yield).

[0167] General procedure D was followed using N-((2,4-dimethoxy-6-pentylphenyl)sulfonyl)pivalamide (0.169 g, 0.455 mmol, 1 eq.), BBr₃ (2.27 ml, 2.27 mmol, 5 eq.) and CH₂Cl₂ (2 mL) to give N-(2,4-dihydroxy-6-pentyl-phenyl)sulfonyl-2,2-dimethyl-propanamide (0.126 g, 0.367 mmol, 80% yield).

[0168] General procedure E was followed using N-(2,4-dihydroxy-6-pentyl-phenyl)sulfonyl-2,2-dimethyl-propanamide (0.126 g, 0.367 mmol, 1 eq.), *p*-toluenesulfonic acid hydrate (6.98 mg, 0.037 mmol, 0.1 eq.), magnesium sulfate (17 mg), cis-isolimonenol (0.065 mL, 0.403 mmol, 1.1 eq.), and anhydrous CH₃Cl (3.66 mL) to afford N-(((1'R,2'R)-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)pivalamide as a thick oil (20 mg, 0.042 mmol, 11% yield). ¹H NMR (400 MHz, CDCl₃) δ 9.83 (s, 1H), 8.13 (s, 1H), 6.75 (s, 1H), 6.34 (s, 1H), 5.62 (s, 1H), 4.58 (t, *J* = 1.9 Hz, 1H), 4.36 (s, 1H), 4.21 – 4.14 (m, 1H), 2.84 – 2.76 (m, 2H), 2.42 – 2.32 (m, 1H), 2.30 – 2.18 (m, 1H), 2.18 – 2.09 (m, 1H), 1.86 – 1.78 (m, 4H), 1.75 (s, 3H), 1.45 – 1.32 (m, 4H), 1.33 – 1.26 (m, 3H), 1.20 (s, 9H), 0.95 (t, 3H). LRMS (-) (*m/z*): [M-H]⁻ calculated for C₂₆H₃₉NO₅S, 476.25; found, 475.9.

Example 22: 2,6-dihydroxy-N,N,5'-trimethyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide (**21d**)



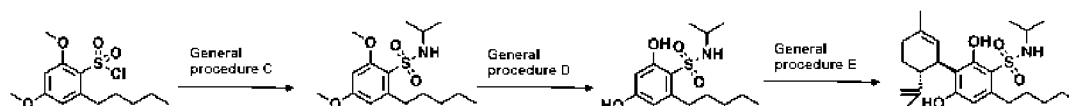
[0169] General procedure C was followed using 2,4-dimethoxy-6-pentyl-benzenesulfonyl chloride (0.4 g, 1.30 mmol, 1 eq.), TEA (0.2 ml, 1.47 mmol, 1.5 eq.), dimethylamine (0.053 g, 1.2 mmol, 1 eq.) and CH₂Cl₂ (2 mL) to afford 2,4-dimethoxy-N,N-dimethyl-6-pentylbenzenesulfonamide (0.196 g, 0.621 mmol, 63% yield). ¹H NMR (400 MHz, CDCl₃) δ

10.14 (s, 1H), 6.37 (d, $J = 2.6$ Hz, 1H), 6.30 (d, $J = 2.6$ Hz, 1H), 5.41 (s, 1H), 2.86 – 2.77 (m, 2H), 2.80 (s, 6H), 1.38 (m, $J = 2.9$ Hz, 4H), 1.29 (t, $J = 7.1$ Hz, 2H), 0.99 – 0.89 (m, 3H).

[0170] General procedure D was followed using 2,4-dimethoxy-*N,N*-dimethyl-6-pentylbenzenesulfonamide (0.196 g, 0.621 mmol, 1 eq.), BBr_3 (3.11 ml, 3.11 mmol, 5 eq.) and CH_2Cl_2 (2 mL) to afford 2,4-dihydroxy-*N,N*-dimethyl-6-pentylbenzenesulfonamide (0.13 g, 0.435 mmol, 70% yield).

[0171] General procedure E was followed using 2,4-dihydroxy-*N,N*-dimethyl-6-pentylbenzenesulfonamide (0.125 g, 0.434 mmol, 1 eq.), *p*-toluenesulfonic acid hydrate (8.27 mg, 0.044 mmol, 0.1 eq.), magnesium sulfate (52 mg), *cis*-isolimonenol (0.079 g, 0.522 mmol, 1.2 eq.), and anhydrous CH_3Cl (3 mL) to afford (1'*S*,2'*R*)-2,6-dihydroxy-*N,N*,5'-trimethyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide as a thick oil (40 mg, 0.098 mmol, 21% yield). ^1H NMR (CDCl_3 , 400 MHz): δ 10.33 (s, 1H), 6.60 (s, 1H), 6.35 (s, 1H), 5.59 (s, 1H), 4.48 (t, $J = 2.0$ Hz, 1H), 4.34 (s, 1H), 4.11 (d, $J = 10.1$ Hz, 1H), 2.87 (m, $J = 5.3$ Hz, 1H), 2.74 (s, 6H), 2.68 (dd, $J = 5.4$ Hz, 1H), 2.38 (q, $J = 8.5$ Hz, 1H), 2.31 – 2.20 (m, 1H), 2.13 (d, $J = 17.7$ Hz, 1H), 1.85 – 1.77 (m, 5H), 1.72 (s, 3H), 1.37 (dt, $J = 7.4, 3.8$ Hz, 4H), 0.95 – 0.89 (m, 3H). LRMS (+) (m/z): $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{23}\text{H}_{35}\text{NO}_4\text{S}$, 421.23; found, 421.90

Example 23: 2,6-dihydroxy-*N*-isopropyl-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide (**23d**)



[0172] General procedure C was followed using 2,4-dimethoxy-6-pentylbenzenesulfonyl chloride (0.3 g, 0.98 mmol, 1 eq.), TEA (0.2 ml, 1.47 mmol, 1.5 eq.), isopropylamine (0.1 ml, 1.2 mmol, 1 eq.) and CH_2Cl_2 (2 mL) to give *N*-isopropyl-2,4-dimethoxy-6-pentylbenzenesulfonamide (0.21 g, 0.634 mmol, 65% yield). ^1H NMR (400 MHz, CDCl_3) δ 6.44 – 6.40 (m, 2H), 5.08 (d, $J = 6.8$ Hz, 1H), 3.96 (s, 3H), 3.87 (s, 3H), 3.44 (m, $J = 6.5$ Hz, 1H), 3.12 – 3.03 (m, 2H), 1.67 (m, $J = 7.5$ Hz, 2H), 1.40 (m, $J = 7.7$ Hz, 4H), 1.09 (d, $J = 6.5$ Hz, 6H), 0.96 – 0.86 (m, 3H).

[0173] General procedure D was followed using *N*-isopropyl-2,4-dimethoxy-6-pentylbenzenesulfonamide (0.212 g, 0.643 mmol, 1 eq.), BBr_3 (3.22 ml, 3.22 mmol, 5 eq.) and CH_2Cl_2 (2 mL) to give 2,4-dihydroxy-*N*-isopropyl-6-pentylbenzenesulfonamide (0.12 g, 0.404 mmol, 62% yield).

[0174] General procedure E was followed using 2,4-dihydroxy-*N*-isopropyl-6-pentylbenzenesulfonamide (0.122 g, 0.405 mmol, 1 eq.), *p*-toluenesulfonic acid hydrate (7.70 mg, 0.040 mmol, 0.1 eq.), magnesium sulfate (49 mg), *cis*-isolimonenol (0.074 g, 0.486 mmol, 1.2 eq.), and anhydrous CH₃Cl (3 mL) to afford (1'*S*,2'*R*)-2,6-dihydroxy-*N*-isopropyl-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide as a thick oil (75 mg, 0.172 mmol, 42% yield): ¹H NMR (400 MHz, CDCl₃) δ 10.31 (s, 1H), 6.57 (s, 1H), 6.36 (s, 1H), 5.59 (s, 1H), 4.47 (s, 1H), 4.34 (s, 1H), 4.30 (d, *J* = 7.6 Hz, 1H), 4.11 (d, *J* = 10.1 Hz, 1H), 3.33 (m, *J* = 6.7 Hz, 1H), 2.87 (m, *J* = 5.5 Hz, 1H), 2.72 (m, *J* = 5.7 Hz, 1H), 2.39 (q, *J* = 8.5 Hz, 1H), 2.24 (s, 1H), 2.13 (d, *J* = 17.8 Hz, 1H), 1.87 – 1.77 (m, 5H), 1.73 (s, 3H), 1.45 – 1.35 (m, 5H), 1.15 (d, *J* = 6.5 Hz, 3H), 1.04 – 0.93 (m, 3H), 0.92 (t, *J* = 4.4 Hz, 3H). LRMS (+) (*m/z*): [M+H]⁺ calculated for C₂₄H₃₇NO₄S, 436.24; found, 435.90.

Example 24: 2,6-dihydroxy-*N,N*,5'-trimethyl-2'-(prop-1-en-2-yl)-4-propyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide (**67d**)



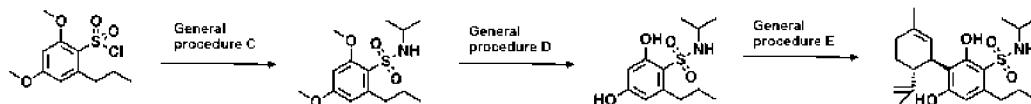
[0175] General procedure C was followed using 2,4-dimethoxy-6-propylbenzenesulfonyl chloride (0.3 g, 1.08 mmol, 1 eq.), TEA (0.23 mL, 1.61 mmol, 1.5 eq.), dimethylamine (0.075 mL, 1.3 mmol, 1.2 eq.) and CH₂Cl₂ (2 mL) to give 2,4-dimethoxy-*N,N*-dimethyl-6-propylbenzenesulfonamide (0.22 g).

[0176] General procedure D was followed using 2,4-dimethoxy-*N,N*-dimethyl-6-propylbenzenesulfonamide (0.221 g, 0.769 mmol, 1 eq.), BBr₃ (3.8 mL, 3.8 mmol, 5 eq.) and CH₂Cl₂ (4 mL) to give 2,4-dihydroxy-*N,N*-dimethyl-6-propylbenzenesulfonamide (0.134 g, 0.517 mmol, 67% yield).

[0177] General procedure E was followed using 2,4-dihydroxy-*N,N*-dimethyl-6-propylbenzenesulfonamide (0.134 g, 0.516 mmol, 1 eq.), *p*-toluenesulfonic acid hydrate (8.07 mg, 0.052 mmol, 0.1 eq.), magnesium sulfate (40 mg), *cis*-isolimonenol (0.087 g, 0.568 mmol, 1.1 eq.), and anhydrous CH₃Cl (4 mL) to afford (1'*R*,2'*R*)-2,6-dihydroxy-*N,N*,5'-trimethyl-2'-(prop-1-en-2-yl)-4-propyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide as a colorless oil (13 mg, 0.033 mmol, 6.3% yield): ¹H NMR (400 MHz, CDCl₃-*d*) δ 10.28 (s, 1H), 6.55 (s, 1H), 6.29 (s, 1H), 5.55 (s, 1H), 4.41 (s, 1H), 4.27 (s, 1H), 4.04 (d, 1H, ³*J* = 8.4 Hz), 2.82-2.73 (m, 1H), 2.67 (s, 6H), 2.65-2.57 (m, 1H), 2.31 (m, 1H), 2.17 (s, 1H), 2.06 (d, ³*J* = 6.4 Hz), 1.76 (s, 5H), 1.65 (s,

3H), 1.62-1.48 (m, 2H), 0.92 (t, 3H, $^3J = 7.33$ Hz). HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{21}H_{31}O_4SN$ 393.54, found 391.900.

Example 25: 2,6-dihydroxy-*N*-isopropyl-5'-methyl-2'-(prop-1-en-2-yl)-4-propyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide (**68d**)

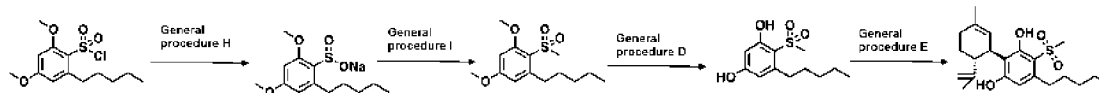


[0178] General procedure C was followed using 2,4-dimethoxy-6-propylbenzenesulfonyl chloride (0.3 g, 1.08 mmol, 1 eq.), TEA (0.23 ml, 1.61 mmol, 1.5 eq.), isopropylamine (0.11 ml, 1.3 mmol, 1.2 eq.) and CH_2Cl_2 (3 mL) to give *N*-isopropyl-2,4-dimethoxy-6-propylbenzenesulfonamide (0.22 g).

[0179] General procedure D was followed using *N*-isopropyl-2,4-dimethoxy-6-propylbenzenesulfonamide (0.220 g, 0.730 mmol, 1 eq.), BBr_3 (3.4 ml, 3.4 mmol, 5 eq.) and CH_2Cl_2 (3.4 mL) to give 2,4-dihydroxy-*N*-isopropyl-6-propylbenzenesulfonamide (0.07 g, 0.256 mmol, 35% yield).

[0180] General procedure E was followed using 2,4-dihydroxy-*N*-isopropyl-6-propylbenzenesulfonamide (0.052 g, 0.190 mmol, 1 eq.), *p*-toluenesulfonic acid hydrate (2.97 mg, 0.019 mmol, 0.1 eq.), magnesium sulfate (15 mg), *cis*-isolimonenol (0.032 g, 0.209 mmol, 1.1 eq.), and anhydrous CH_3Cl (1.5 mL) to afford (1'*R*,2'*R*)-2,6-dihydroxy-*N*-isopropyl-5'-methyl-2'-(prop-1-en-2-yl)-4-propyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide as colorless oil (6.1 mg, 0.015 mmol, 7.8% yield). ^1H NMR (400 MHz, $CDCl_3-d$) δ 10.31 (s, 1H), 6.55 (s, 1H), 6.35 (s, 1H), 5.58 (s, 1H), 4.47 (s, 1H), 4.33 (s, 1H), 4.11 (d, 1H, $^3J = 8.2$ Hz), 3.37-3.28 (m, 1H), 2.89-2.82 (m, 1H), 2.71-2.66 (m, 1H), 2.38 (dd, 1H, $^3J = 8.3$ Hz), 2.24 (m, 1H), 2.15 (s, 1H), 1.82 (s, 5H), 1.72 (s, 3H), 1.58 (s, 2H), 1.15 (d, 2H, $^3J = 6.5$ Hz), 1.01 (t, 3H, $^3J = 14.49$ Hz). HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{22}H_{33}O_4SN$ 407.57, found 405.90.

Example 26: 5'-methyl-3-(methylsulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol (**3d**)



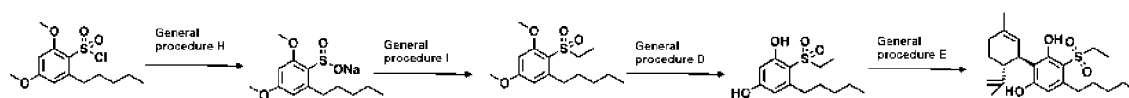
[0181] General procedure H was followed using 2,4-dimethoxy-6-pentyl-benzenesulfonyl chloride (0.153 g, 0.5 mmol, 1 eq.), sodium sulfite (0.25 g, 1.98 mmol, 3.97 eq.), sodium bicarbonate (0.167 g, 1.99 mmol, 3.98 eq.) and H₂O (5 mL) to give sodium 2,4-dimethoxy-6-pentylbenzenesulfinate (0.069 g, 0.234 mmol, 46% yield).

[0182] General procedure I was followed using sodium 2,4-dimethoxy-6-pentylbenzenesulfinate (0.500 g, 1.7 mmol, 1 eq.), iodomethane (0.362 g, 2.55 mmol, 1.5 eq.) and 1,4-dioxane (6 mL) to give 1,5-dimethoxy-2-(methylsulfonyl)-3-pentylbenzene (0.024 g, 0.084 mmol, 4.9% yield).

[0183] General procedure D was followed using 1,5-dimethoxy-2-(methylsulfonyl)-3-pentylbenzene (0.094 g, 0.327 mmol, 1 eq.), BBr₃ (1.63 mL, 1.63 mmol, 5 eq.) and CH₂Cl₂ (2 mL) to give 4-(methylsulfonyl)-5-pentylbenzene-1,3-diol (0.076 g, 0.294 mmol, 90% yield).

[0184] General procedure E was followed using 4-(methylsulfonyl)-5-pentylbenzene-1,3-diol (0.076 g, 0.294 mmol, 1 eq.), *p*-toluenesulfonic acid hydrate (4.6 mg, 0.029 mmol, 0.1 eq.), magnesium sulfate (22 mg), cis-isolimonenol (0.049 g, 0.324 mmol, 1.1 eq.), and anhydrous CH₃Cl (2.1 mL) to afford (1'R,2'R)-5'-methyl-3-(methylsulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol as colorless oil (5 mg, 0.013 mmol, 4.3% yield). ¹H NMR (400 MHz, CDCl₃-d) δ 10.15 (s, 1H), 6.66 (s, 1H), 6.34 (s, 1H), 5.57 (s, 1H), 4.53 (s, 1H), 4.32 (s, 1H), 4.08 (d, 1H, ³J = 9.1 Hz), 3.09 (s, 3H), 2.90-2.73 (m, 2H), 2.71-2.66 (m, 1H), 2.02 (s, 2H), 0.92 (t, 2H, ³J = 7.01 Hz). HRMS (ESI-TOF) *m/z* [M + H]⁺ calcd for C₂₂H₃₃O₄SN 407.57, found 405.90.

Example 27: 3-(ethylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol (**69d**)



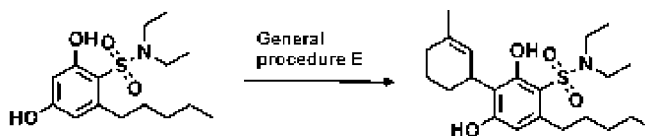
[0185] General procedure H was followed using 2,4-dimethoxy-6-pentyl-benzenesulfonyl chloride (0.153 g, 0.5 mmol, 1 eq.), sodium sulfite (0.25 g, 1.98 mmol, 3.97 eq.), sodium bicarbonate (0.167 g, 1.99 mmol, 3.98 eq.) and H₂O (5 mL) to give sodium 2,4-dimethoxy-6-pentylbenzenesulfinate (0.069 g, 0.234 mmol, 46% yield).

[0186] General procedure I was followed using sodium 2,4-dimethoxy-6-pentylbenzenesulfinate (0.250 g, 0.85 mmol, 1 eq.), bromoethane (0.185 g, 1.7 mmol, 2 eq.) and THF (3 mL) to give 2-(ethylsulfonyl)-1,5-dimethoxy-3-pentylbenzene (0.026 g).

[0187] General procedure D was followed using 2-(ethylsulfonyl)-1,5-dimethoxy-3-pentylbenzene (0.026 g, 0.088 mmol, 1 eq.), BBr₃ (0.5 mL, 0.5 mmol, 5 eq.) and CH₂Cl₂ (0.5 mL) to give 4-(ethylsulfonyl)-5-pentylbenzene-1,3-diol.

[0188] General procedure E was followed using 4-(ethylsulfonyl)-5-pentylbenzene-1,3-diol (0.046 g, 0.169 mmol, 1 eq.), *p*-toluenesulfonic acid hydrate (2.6 mg, 0.017 mmol, 0.1 eq.), magnesium sulfate (14 mg), cis-isolimonenol (0.028 g, 0.186 mmol, 1.1 eq.), and anhydrous CH₃Cl (1.4 mL) to afford (1'R,2'R)-3-(ethylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol as colorless oil (8.4 mg, 0.021 mmol, 12% yield). ¹H NMR (400 MHz, CDCl₃-d) δ 10.35 (s, 1H), 6.76 (s, 1H), 6.35 (s, 1H), 5.58 (s, 1H), 4.50 (s, 1H), 4.34 (s, 1H), 4.09 (d, 1H, ³J = 8.7 Hz), 3.15 (q, 2H, ³J = 7.3 Hz, ⁴J = 7.4 Hz), 2.92-2.85 (m, 1H), 2.74-2.67 (m, 1H), 2.37 (dd, 1H, ³J = 8.3 Hz, ⁴J = 6.4 Hz), 2.28-2.24 (m, 1H), 1.83 (s, 6H), 1.72 (s, 3H), 1.40-1.36 (m, 5H), 1.26 (t, 6H, ³J = 7.4 Hz), 0.92 (t, 3H, ³J = 2.28 Hz). HRMS (LCMS) *m/z* [M + H]⁺ calcd for C₂₃H₃₄O₄S 406.58, found 404.900.

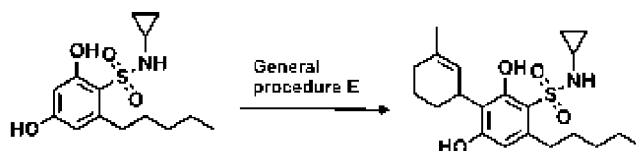
Example 28: N,N-diethyl-2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide (**62c**)



[0189] The procedures of Example 13 were followed to provide N,N-diethyl-2,4-dihydroxy-6-pentylbenzenesulfonamide.

[0190] General procedure E was followed using N,N-diethyl-2,4-dihydroxy-6-pentylbenzenesulfonamide (0.066 g, 0.209 mmol, 1 eq.), *p*-toluenesulfonic acid (7.2 mg, 0.042 mmol, 0.2 eq.), 1-methylcyclohex-2-en-1-ol (0.066 g, 0.209 mmol, 1 eq.), and anhydrous CH₃Cl (5 mL) to give N,N-diethyl-2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide (28 mg, 0.068 mmol, 32% yield): ¹H NMR (400 MHz, Chloroform-d) δ 10.69 (s, 1H), 6.84 (s, 1H), 6.34 (s, 1H), 5.65 (s, 1H), 4.04 (s, 1H), 3.29 (qd, *J* = 7.2, 2.8 Hz, 5H), 2.79 – 2.70 (m, 2H), 2.18 – 1.84 (m, 4H), 1.83 (s, 3H), 1.77 – 1.59 (m, 4H), 1.43 – 1.33 (m, 4H), 1.14 (t, *J* = 7.1 Hz, 6H), 0.96 – 0.90 (m, 3H).

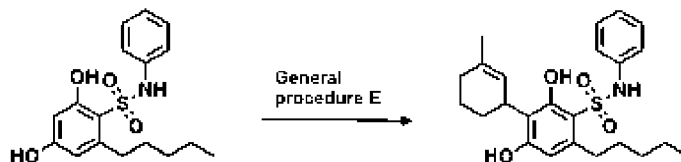
Example 29: N-cyclopropyl-2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide (**22c**)



[0191] The procedures of Example 14 were followed to provide N-cyclopropyl-2,4-dihydroxy-6-pentyl-benzenesulfonamide.

[0192] General procedure E was followed using N-cyclopropyl-2,4-dihydroxy-6-pentyl-benzenesulfonamide (0.035 g, 0.117 mmol, 1 eq.), *p*-toluenesulfonic acid (4.03 mg, 0.023 mmol, 0.2 eq.), 1-methylcyclohex-2-en-1-ol (0.035 g, 0.117 mmol, 1 eq.), and anhydrous CHCl_3 (5 mL) to give N-cyclopropyl-2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide (15 mg, 0.038 mmol, 32% yield): ^1H NMR (400 MHz, Chloroform-*d*) δ 10.37 (s, 1H), 6.88 (s, 1H), 6.36 (s, 1H), 5.66 (s, 1H), 4.94 (s, 1H), 4.07 (td, $J = 7.0, 6.5, 3.6$ Hz, 1H), 2.80 (tt, $J = 9.4, 4.8$ Hz, 2H), 2.37 – 2.28 (m, 1H), 2.10 (t, $J = 19.7$ Hz, 2H), 2.02 – 1.93 (m, 1H), 1.87 (s, 1H), 1.85 – 1.81 (s, 3H), 1.70 – 1.51 (m, 3H), 1.39 (tq, $J = 6.0, 2.8, 2.4$ Hz, 4H), 0.99 – 0.88 (m, 3H), 0.59 (ddd, $J = 10.9, 6.0, 3.4$ Hz, 4H).

Example 30: 2,6-dihydroxy-5'-methyl-4-pentyl-N-phenyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide (**24c**)

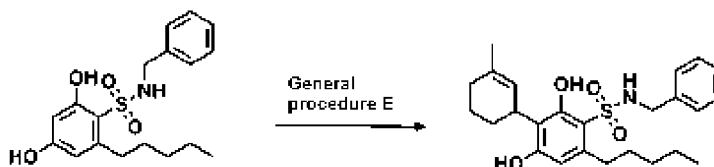


[0193] The procedures of Example 16 were followed to provide 2,4-dihydroxy-6-pentyl-N-phenyl-benzenesulfonamide.

[0194] General procedure E was followed using 2,4-dihydroxy-6-pentyl-N-phenyl-benzenesulfonamide (0.109 g, 0.325 mmol, 1 eq.), *p*-toluenesulfonic acid (12.35 mg, 0.065 mmol, 0.2 eq.), 1-methylcyclohex-2-en-1-ol (0.036 g, 0.325 mmol, 1 eq.), and anhydrous CHCl_3 (10 mL) to afford the desired product (45 mg, 0.105 mmol, 32% yield): ^1H NMR (400 MHz, Chloroform-*d*) δ 10.05 (s, 1H), 7.29 – 7.23 (m, 1H), 7.20 – 7.14 (m, 1H), 7.00 – 6.94 (m, 2H), 6.88 – 6.84 (m, 1H), 6.52 (s, 1H), 6.32 (s, 1H), 5.60 (s, 1H), 3.97 (d, $J = 3.2$ Hz, 1H), 2.91 – 2.74

(m, 2H), 2.20 – 2.00 (m, 2H), 1.87 (t, $J = 5.4$ Hz, 2H), 1.82 (s, 3H), 1.74 – 1.60 (m, 4H), 1.49 – 1.28 (m, 5H), 0.98 – 0.88 (m, 3H).

Example 31: N-benzyl-2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide (**25c**)



[0195] The procedures of Example 17 were followed to provide N-benzyl-2,4-dihydroxy-6-pentylbenzenesulfonamide.

[0196] General procedure E was followed using N-benzyl-2,4-dihydroxy-6-pentylbenzenesulfonamide (0.035 g, 0.1 mmol, 1 eq.), *p*-toluenesulfonic acid (1.9 mg, 0.01 mmol, 0.1 eq.), 1-methylcyclohex-2-en-1-ol (0.011 g, 0.1 mmol, 1 eq.), and anhydrous CHCl_3 (10 mL) to afford the desired product (14 mg, 0.032 mmol, 31% yield): ^1H NMR (400 MHz, Chloroform-*d*) δ 10.33 (s, 1H), 7.31 (dd, $J = 5.6, 1.7$ Hz, 3H), 7.21 (dd, $J = 7.2, 2.3$ Hz, 2H), 6.87 (s, 1H), 6.34 (s, 1H), 5.65 (s, 1H), 4.74 (t, $J = 6.1$ Hz, 1H), 4.13 (dd, $J = 6.1, 2.9$ Hz, 2H), 4.04 (tt, $J = 6.5, 3.2$ Hz, 1H), 2.85 – 2.76 (m, 2H), 2.12 (d, $J = 21.3$ Hz, 2H), 2.01 – 1.86 (m, 2H), 1.84 (s, 3H), 1.68 – 1.59 (m, 2H), 1.59 – 1.46 (m, 2H), 1.41 – 1.30 (m, 4H), 0.91 (t, 3H).

Example 32: 2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide (**19c**)

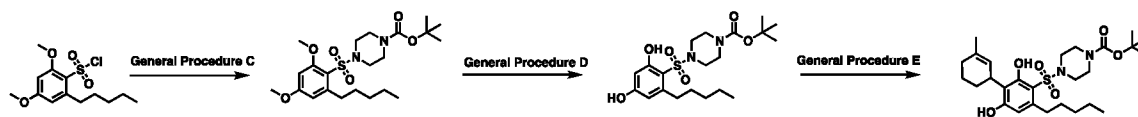


[0197] General procedure F was followed using 1,3-dimethoxy-5-pentylbenzene to provide 2,4-dimethoxy-6-pentylbenzenesulfonamide.

[0198] General procedure D was followed using 2,4-dimethoxy-6-pentylbenzenesulfonamide and 5 eq. BBr_3 to provide 2,4-dihydroxy-6-pentylbenzenesulfonamide.

[0199] General procedure E was followed using 2,4-dihydroxy-6-pentyl-benzenesulfonamide (0.060 g, 0.231 mmol, 1 eq.), *p*-toluenesulfonic acid (8.8 mg, 0.046 mmol, 0.2 eq.), 1-methylcyclohex-2-en-1-ol (0.026 g, 0.231 mmol, 1 eq.), and anhydrous CH₃Cl (3 mL) to afford the desired product (7.5 mg, 0.020 mmol, 8.8% yield): ¹H NMR (400 MHz, CDCl₃) δ 10.11 (s, 1H), 6.84 (s, 1H), 6.37 (s, 1H), 5.62 (s, 1H), 4.88 (s, 2H), 4.04 (s, 1H), 2.91 – 2.82 (m, 2H), 2.24 – 1.85 (m, 5H), 1.83 (s, 3H), 1.70 (q, *J* = 7.6 Hz, 3H), 1.45 – 1.35 (m, 4H), 0.93 (t, *J* = 7.0 Hz, 3H).

Example 33: tert-butyl 4-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)piperazine-1-carboxylate (**70c**)

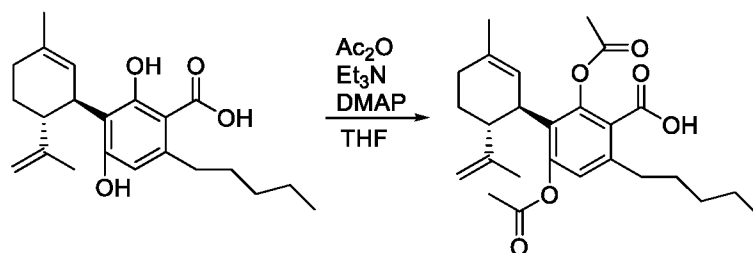


[0200] General procedure C was followed using tert-butyl piperazine-1-carboxylate to give tert-butyl 4-((2,4-dimethoxy-6-pentylphenyl)sulfonyl)piperazine-1-carboxylate (0.3 g).

[0201] General procedure D was followed using tert-butyl 4-((2,4-dimethoxy-6-pentylphenyl)sulfonyl)piperazine-1-carboxylate (0.3 g, 0.657 mmol, 1 eq.), BBr₃ (5.3 mL, 5.3 mmol, 8 eq.) and CH₂Cl₂ (3 mL) to give tert-butyl 4-((2,4-dihydroxy-6-pentylphenyl)sulfonyl)piperazine-1-carboxylate (0.035 g).

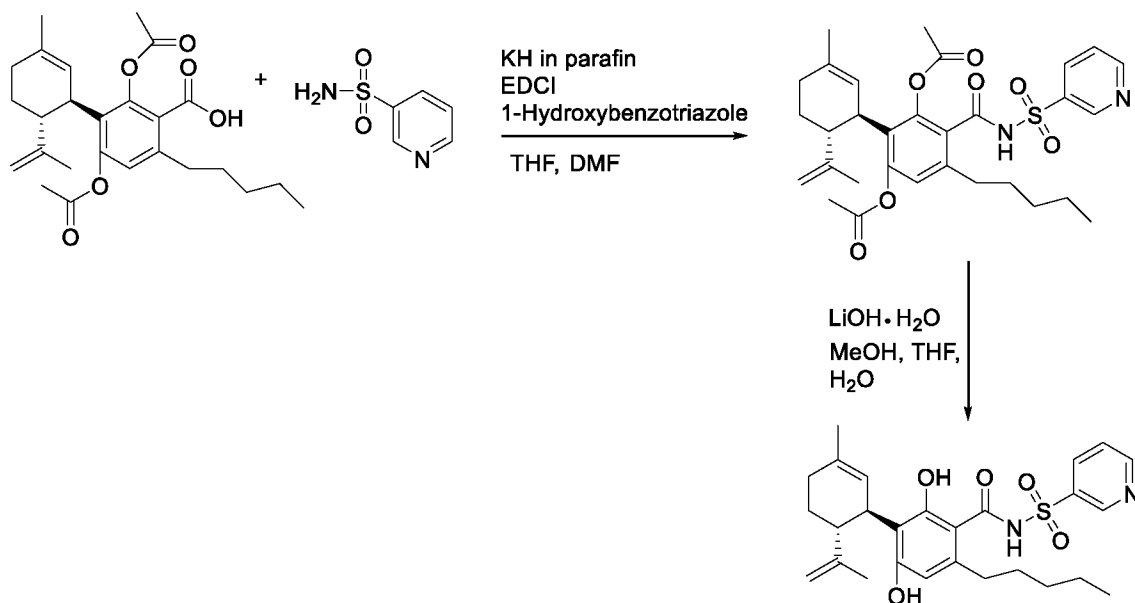
[0202] General procedure E was followed using tert-butyl 4-((2,4-dihydroxy-6-pentylphenyl)sulfonyl)piperazine-1-carboxylate (0.035 g, 0.082 mmol, 1 eq.), *p*-toluenesulfonic acid (1.6 mg, 0.008 mmol, 0.1 eq.), 1-methylcyclohex-2-en-1-ol (0.009 g, 0.082 mmol, 1 eq.), and anhydrous CH₃Cl (5 mL) to give tert-butyl 4-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)piperazine-1-carboxylate (15 mg, 0.028 mmol, 35% yield): ¹H NMR (400 MHz, Chloroform-*d*) δ 10.32 (1H), 6.92 (1H), 6.36 (1H), 5.65 (1H), 4.03 (1H), 3.51 – 3.49 (4H), 3.16 – 3.14 (4H), 2.81 – 2.76 (2H), 2.14 – 1.84 (5H), 1.83 (3H), 1.72 – 1.50 (4H), 1.47 (9H), 1.40 – 1.36 (4H), 0.95 – 0.91 (3H).

Example 34: Preparation of 2,6-diacetoxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxylic acid.



[0203] To a stirred solution of 2,4-dihydroxy-3-[(1R,6R)-6-isopropenyl-3-methyl-cyclohex-2-en-1-yl]-6-pentyl-benzoic acid (1.02 g, 2.85 mmol) and DMAP (17.41 mg, 142.50 μ mol) in THF (10 mL) and triethylamine (1.44 g, 14.25 mmol, 1.99 mL) under argon cooled to 0 °C was added acetic anhydride (640.09 mg, 6.27 mmol, 592.68 μ L) dropwise. The mixture (solution) was warmed to room temperature and stirred for 1 h. The pale yellow solution was then quenched with water (1 mL), stirred for a further 5 min then partitioned between ethyl acetate and water/brine/HCl. The organic phase was separated and washed with more water/brine/HCl (2x) brine (1x). Dried, filtered and concentrated in vacuo then chromatographed in 0-100% ethyl acetate in hexanes. Product containing fractions were concentrated in vacuo giving a white solid (1.10 g, 87% yield).

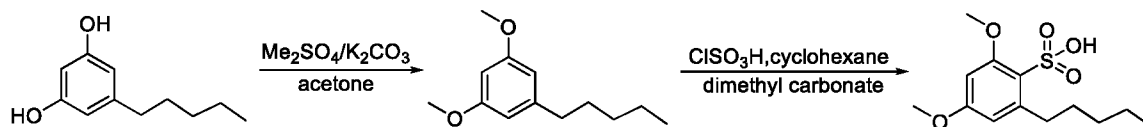
Example 35: 2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-N-(pyridin-3-ylsulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide (**71d**)



[0204] Preparation of 5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-3-((pyridin-3-ylsulfonyl)carbamoyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diyl diacetate: To a stirred solution of pyridine-3-sulfonamide (357.43 mg, 2.26 mmol) in dimethylformamide (DMF; 5 mL) under argon was added potassium hydride in paraffin (181.27 mg, 2.26 mmol, 50% purity); mixture was stirred for 1 h. Tetrahydrofuran (THF; 3 mL) was added to aid dissolution of paraffin; mild heating applied, stirred at room temperature. Meanwhile, a solution of 2,4-diacetoxy-3-[(1R,6R)-6-isopropenyl-3-methyl-cyclohex-2-en-1-yl]-6-pentyl-benzoic acid (200 mg, 451.93 μ mol) in DMF (2 mL) under argon was treated with 1-hydroxybenzotriazole (91.60 mg, 677.90 μ mol) and 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDCI; 129.95 mg, 677.90 μ mol). The mixture was stirred for 2 h. The mixture was then transferred via syringe to the above sulfonamide anion solution, dropwise and stirred for 45 min. The mixture was diluted with ethyl acetate and washed with brine/water/HCl (2x) and brine (2x). The organic phase was dried, filtered and concentrated in vacuo then chromatographed in 0-100% ethyl acetate in DCM. Product containing fractions were concentrated in vacuo giving a foamy solid, [3-acetoxy-2-[(1R,6R)-6-isopropenyl-3-methyl-cyclohex-2-en-1-yl]-5-pentyl-4-(3-pyridylsulfonylcarbamoyl)phenyl] acetate (138 mg, 52% yield).

[0205] 2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-N-(pyridin-3-ylsulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide (**71d**): To a stirred solution of [3-acetoxy-2-[(1R,6R)-6-isopropenyl-3-methyl-cyclohex-2-en-1-yl]-5-pentyl-4-(3-pyridylsulfonylcarbamoyl)phenyl] acetate (138.23 mg, 237.23 μ mol) in methanol (1 mL) was added lithium hydroxide monohydrate (49.77 mg, 1.19 mmol, 32.96 μ L) as a solution in water (999.95 μ L); THF (1 mL) was added to aid solubility. The resulting solution was stirred at room temperature for 3 h. Stirring continued overnight. The mixture was diluted with water, neutralized with HCl and extracted with DCM. The organic phase was dried, filtered and concentrated in vacuo then chromatographed in 0-50% ethyl acetate in hexanes to elute non-polar impurities (monodeprotected product) then 50-75% ethyl acetate in hexanes to elute the desired product. Further purified by reverse phase isolera (50-100 acetonitrile in water, 0.1% FA). Lyophilized to give (1'S,2'R)-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-N-(pyridin-3-ylsulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide (32.3 mg, 27% yield). ^1H NMR (400 MHz, DMSO) δ 9.21 (s, 1H), 9.05 (s, 1H), 8.81 (s, 1H), 8.30 (dt, J = 8.2, 1.9 Hz, 1H), 7.65 (dd, J = 8.1, 4.8 Hz, 1H), 6.04 (s, 1H), 5.10 (s, 1H), 4.50 – 4.39 (m, 2H), 3.82 (d, J = 10.1 Hz, 1H), 2.96 (s, 1H), 2.08 (s, 1H), 1.99 – 1.87 (m, 1H), 1.60 (d, J = 20.0 Hz, 8H), 1.23 (p, J = 7.7 Hz, 2H), 1.13 (q, J = 7.4 Hz, 2H), 1.04 (q, J = 7.6 Hz, 2H), 0.80 (t, J = 7.2 Hz, 3H). LRMS (ES $^-$): m/z calcd. for $\text{C}_{27}\text{H}_{34}\text{N}_2\text{O}_5\text{S}$: 498.64; Found: 496.80.

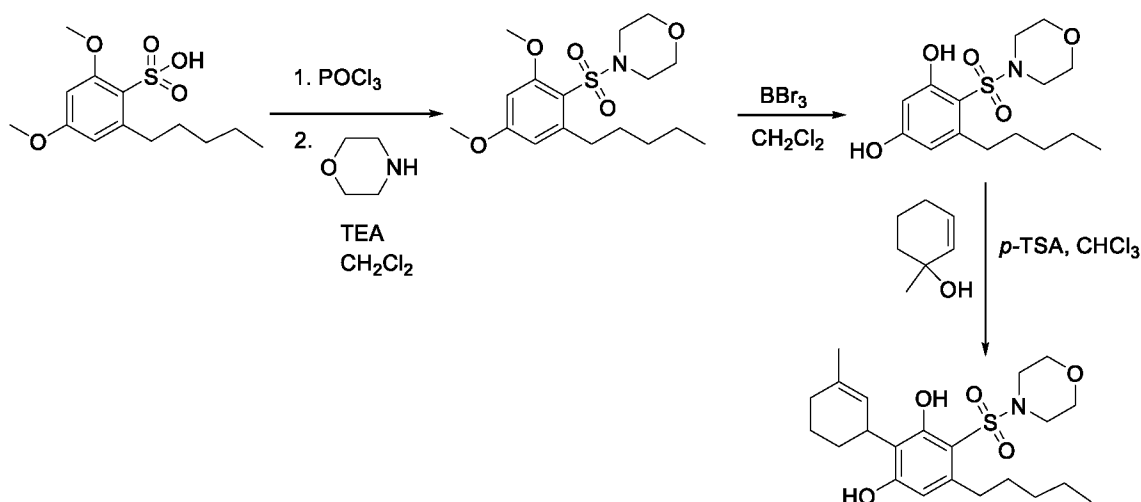
Example 36: Preparation of 2,4-dimethoxy-6-pentylbenzenesulfonic acid



[0206] Step 1: To a stirred solution of 5-pentylbenzene-1,3-diol (1.0 g, 5.55 mmol) in acetone (15 mL) was added potassium carbonate (2.3 g, 16.64 mmol) and dimethyl sulfate (2.1 g, 16.64 mmol). The resulting mixture was heated to reflux for 6 h and filtered through Celite® after cooling the reaction mixture to ambient temperature. The Celite® bed was washed with ether and the filtrate was concentrated. The resulting residue was purified by flash chromatography to afford 1,3-dimethoxy-5-pentylbenzene as a colorless oil (0.73 g, 63%). ^1H NMR (CDCl_3): δ 6.38 (d, 2H, $J = 2.3$ Hz); 6.33 (t, 1H, $J = 2.3$ Hz); 3.81 (s, 6H); 2.59-2.56 (m, 2H); 1.68-1.62 (m, 2H); 1.38-1.33 (m, 4H); 0.93 (t, 3H, $J = 7.1$ Hz).

[0207] Step 2: To a solution containing 1,3-dimethoxy-5-pentylbenzene (2.5 g, 12.0 mmol) in cyclohexane (40 mL) was added dimethyl carbonate (9.08 g, 1.0 mol) and heated to 65°C . Chlorosulfonic acid (6.99 g, 60.01 mmol) was added dropwise over a period of 15-20 min and the temperature was raised to 70°C . The reaction was stirred at that temperature for 1 h and cooled to room temperature. The reaction mixture was poured into ice-cooled water and extracted with ether, dried with anhydrous sodium sulfate, and concentrated. The resulting residue was purified by flash chromatography to afford 2,4-dimethoxy-6-pentylbenzenesulfonic acid as a colorless oil (2.5 g, 72%). ^1H NMR (CDCl_3): δ 6.44 (d, 1H, $J = 2.5$ Hz); 6.40 (d, 1H, $J = 2.5$ Hz); 4.02 (s, 3H); 3.90 (s, 3H); 3.06-3.02 (m, 2H); 1.70-1.62 (m, 2H); 1.41-1.34 (m, 4H); 0.92 (t, 3H, $J = 6.9$ Hz).

Example 37: 5'-methyl-3-(morpholinosulfonyl)-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol (**28c**)



[0208] Step 1: Into a microwave vial, 2,4-dimethoxy-6-pentylbenzenesulfonic acid (1.0 mmol), phosphorus oxy chloride (15.0 mmol) was added and heated to 110°C for 2 h. The reaction was cooled to room temperature and excess phosphoryl chloride was distilled off under vacuum and co-distilled with dichloromethane several times. The resulting residue was dissolved in dichloromethane (2 mL) which was added to an ice-cooled mixture of trimethylamine (TEA) and morpholine in dichloromethane (4 mL). The reaction was stirred for 18 h under nitrogen atmosphere and diluted with dichloromethane. After washing with water and concentrating, the resulting residue was purified by flash chromatography to afford 4-((2,4-dimethoxy-6-pentylphenyl)sulfonyl)morpholine (213 mg, 0.60 mmol, 91%). ¹H NMR (CDCl₃): δ 6.38 (d, 1H, *J* = 2.5 Hz), 6.36 (d, 1H, *J* = 2.5 Hz), 3.87 (s, 3H), 3.84 (s, 3H), 3.71 (t, 4H, *J* = 5.0 Hz), 3.25 (t, 4H, *J* = 5.0 Hz), 3.01-2.98 (m, 2H), 1.67-1.60 (m, 2H), 1.39-1.34 (m, 4H), 0.91-0.88 (m, 3H).

[0209] Step 2: Into a cryogenic cooled (-78°C) solution of 4-((2,4-dimethoxy-6-pentylphenyl)sulfonyl)morpholine (0.5 mmol) in dichloromethane (5 mL) was added 1.0 M solution of boron tribromide in dichloromethane. The reaction was allowed to attain ambient temperature and stirred for 18 h. The reaction was quenched by pouring it into an ice-cooled 1.0 M HCl solution and extracted with dichloromethane. The organic layer was concentrated and purified by flash chromatography to give 4-(morpholinosulfonyl)-5-pentylbenzene-1,3-diol (63 mg, 0.19 mmol, 31%). ¹H NMR (CDCl₃): δ 10.10 (s, 1H), 6.36 (d, 1H, *J* = 2.7 Hz), 6.29 (d, 1H, *J* = 2.7 Hz), 5.22 (s, 1H), 3.75 (t, 2H, *J* = 5.0 Hz), 3.66 (t, 2H, *J* = 7.0 Hz), 3.46-3.39 (m, 4H), 2.81-2.77 (m, 2H), 1.66-1.60 (m, 2H), 1.40-1.35 (m, 4H), 0.94-0.90 (m, 3H).

[0210] Step 3: 1-methylcyclohex-2-en-1-ol in chloroform was added dropwise to a mixture of a 4-(morpholinosulfonyl)-5-pentylbenzene-1,3-diol and pTSA in chloroform at 0°C. After the

addition, the ice bath was removed and the reaction stirred at ambient temperature for 18 h. The reaction mixture washed with saturated bicarbonate solution and water. The organic layer was concentrated, purified by preparative HPLC, and lyophilized to afford 5'-methyl-3-(morpholinosulfonyl)-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol (1.6 mg, 0.04 mmol, 9%). ¹H NMR (CDCl₃): δ 10.40 (s, 1H), 6.93 (s, 1H), 6.34 (s, 1H), 5.62 (s, 1H), 4.03-4.00 (m, 1H), 3.75 (t, 2H, J = 5.0 Hz), 3.64 (t, 2H, J = 7.0 Hz), 3.43-3.38 (m, 4H), 2.76-2.72 (m, 2H), 2.17-1.62 (m, 8H), 1.81 (s, 3H), 1.39-1.34 (m, 4H), 0.93-0.90 (m, 3H).

Example 38:

[0211] The following compounds may be prepared according to the procedures known to those of skill in the art in view of Schemes 1 – 7 and Examples 1-37:

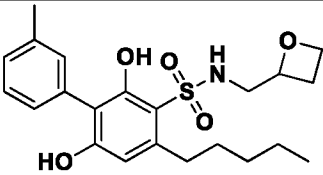
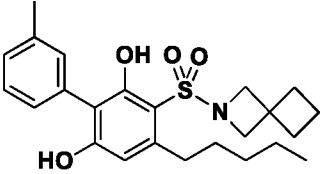
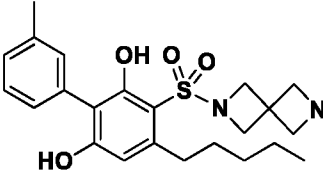
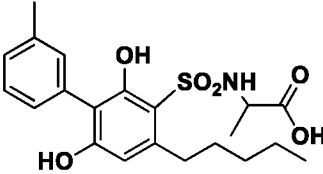
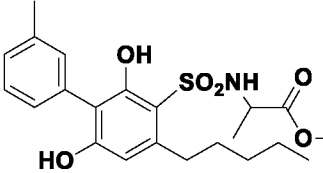
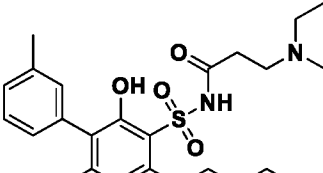
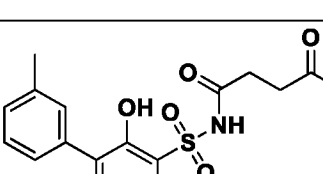
Comp. No.	Name	Structure
1a	2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonic acid	
2a	sodium 2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonate	
3a	3'-methyl-3-(methylsulfonyl)-4-pentyl-[1,1'-biphenyl]-2,6-diol	
4a	3-(cyclopropylsulfonyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-2,6-diol	

Comp. No.	Name	Structure
5a	3-(tert-butylsulfonyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-2,6-diol	
6a	3-(benzylsulfonyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-2,6-diol	
7a	3'-methyl-4-pentyl-3-(phenylsulfonyl)-[1,1'-biphenyl]-2,6-diol	
8a	3'-methyl-3-((4-nitrophenyl)sulfonyl)-4-pentyl-[1,1'-biphenyl]-2,6-diol	
9a	3'-methyl-4-pentyl-3-(pyridin-3-ylsulfonyl)-[1,1'-biphenyl]-2,6-diol	
10a	3-(furan-3-ylsulfonyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-2,6-diol	
11a	3-((1H-imidazol-4-yl)sulfonyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-2,6-diol	

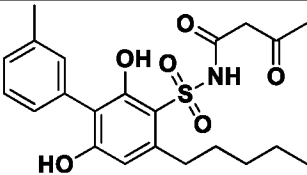
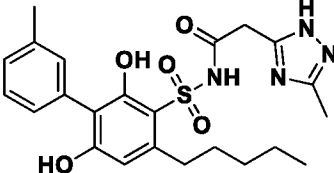
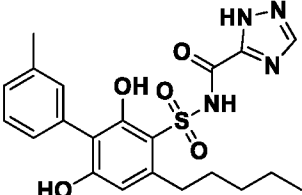
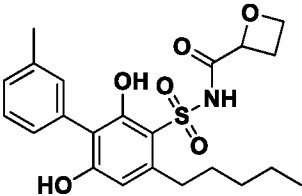
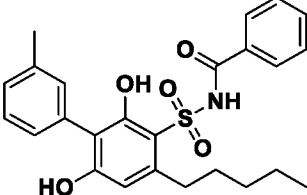
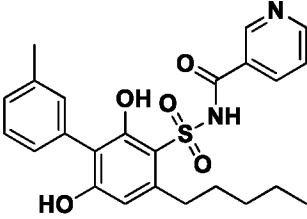
Comp. No.	Name	Structure
12a	3'-methyl-3-(oxetan-3-ylsulfonyl)-4-pentyl-[1,1'-biphenyl]-2,6-diol	
13a	3'-methyl-4-pentyl-3-((perfluorophenyl)sulfonyl)-[1,1'-biphenyl]-2,6-diol	
14a	4-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)cyclohexan-1-one	
15a	1-(2-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)ethyl)pyrrolidine-2,5-dione	
16a	3-((2-(dimethylamino)ethyl)sulfonyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-2,6-diol	
17a	1-(3-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)piperidin-1-yl)ethan-1-one	
18a	3-((2-chloropyrimidin-5-yl)sulfonyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-2,6-diol	

Comp. No.	Name	Structure
19a	2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide	
20a	2,6-dihydroxy-N,3'-dimethyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide	
21a	2,6-dihydroxy-N,N,3'-trimethyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide	
22a	N-cyclopropyl-2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide	
23a	2,6-dihydroxy-N-isopropyl-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide	
24a	2,6-dihydroxy-3'-methyl-4-pentyl-N-phenyl-[1,1'-biphenyl]-3-sulfonamide	
25a	N-benzyl-2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide	

Comp. No.	Name	Structure
26a	3'-methyl-3-((4-methylpiperazin-1-yl)sulfonyl)-4-pentyl-[1,1'-biphenyl]-2,6-diol	
27a	3'-methyl-4-pentyl-3-(piperidin-1-ylsulfonyl)-[1,1'-biphenyl]-2,6-diol	
28a	3'-methyl-3-(morpholinosulfonyl)-4-pentyl-[1,1'-biphenyl]-2,6-diol	
29a	2,6-dihydroxy-3'-methyl-4-pentyl-N-(pyridin-3-yl)-[1,1'-biphenyl]-3-sulfonamide	
30a	2,6-dihydroxy-3'-methyl-4-pentyl-N-(pyrimidin-2-yl)-[1,1'-biphenyl]-3-sulfonamide	
31a	2,6-dihydroxy-3'-methyl-N-(2-oxopropyl)-4-pentyl-[1,1'-biphenyl]-3-sulfonamide	
32a	1-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)azetidin-3-one	

Comp. No.	Name	Structure
33a	2,6-dihydroxy-3'-methyl-N-(oxetan-2-ylmethyl)-4-pentyl-[1,1'-biphenyl]-3-sulfonamide	
34a	3-((2-azaspiro[3.3]heptan-2-yl)sulfonyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-2,6-diol	
35a	3-((2,6-diazaspiro[3.3]heptan-2-yl)sulfonyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-2,6-diol	
36a	((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)alanine	
37a	methyl ((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)alaninate	
38a	N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-3-morpholinopropanamide	
39a	4-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamido)-4-oxobutanoic acid	

Comp. No.	Name	Structure
40a	N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-3-(4-methylpiperazin-1-yl)propanamide	
41a	2-amino-N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide	
42a	N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(2-methoxyethoxy)acetamide	
43a	2-amino-N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-3-hydroxypropanamide	
44a	2-amino-N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)propanamide	
45a	3-amino-N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-2-methylpropanamide	
46a	N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide	

Comp. No.	Name	Structure
47a	N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-3-oxobutanamide	
48a	N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(3-methyl-1H-1,2,4-triazol-5-yl)acetamide	
49a	N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-1H-1,2,4-triazole-5-carboxamide	
50a	N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)oxetane-2-carboxamide	
51a	N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)benzamide	
52a	N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)nicotinamide	

Comp. No.	Name	Structure
53a	N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-2-phenylacetamide	
54a	N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(furan-2-yl)acetamide	
55a	N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(oxazol-2-yl)acetamide	
56a	N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(thiazol-2-yl)acetamide	
57a	2-(1H-benzo[d]imidazol-2-yl)-N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide	
58a	2,6-dihydroxy-3'-methyl-4-pentyl-N-(phenylsulfonyl)-[1,1'-biphenyl]-3-carboxamide	
59a	N-(cyclohexylsulfonyl)-2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-carboxamide	

Comp. No.	Name	Structure
60a	(E)-2,6-dihydroxy-3'-methyl-4-pentyl-N-(prop-1-en-1-ylsulfonyl)-[1,1'-biphenyl]-3-carboxamide	
61a	N-((1H-benzo[d]imidazol-2-yl)sulfonyl)-2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-carboxamide	
62a	N,N-diethyl-2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide	
63a	N-(2-bromoethyl)-2,6-dihydroxy-N-(2-hydroxyethyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide	
64a	2,2,2-trifluoroethyl 2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonate	
65a	N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-4-(trifluoromethyl)benzamide	
66a	N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)pivalamide	

Comp. No.	Name	Structure
67a	2,6-dihydroxy-N,N,3'-trimethyl-4-propyl-[1,1'-biphenyl]-3-sulfonamide	
68a	2,6-dihydroxy-N-isopropyl-3'-methyl-4-propyl-[1,1'-biphenyl]-3-sulfonamide	
69a	3-(ethylsulfonyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-2,6-diol	
70a	tert-butyl 4-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)piperazine-1-carboxylate	
71a	2,6-dihydroxy-3'-methyl-4-pentyl-N-(pyridin-3-ylsulfonyl)-[1,1'-biphenyl]-3-carboxamide	
1b	2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonic acid	
2b	sodium 2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonate	

Comp. No.	Name	Structure
3b	5'-methyl-3-(methylsulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol	
4b	3-(cyclopropylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol	
5b	3-(tert-butylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol	
6b	3-(benzylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol	
7b	5'-methyl-4-pentyl-3-(phenylsulfonyl)-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol	
8b	5'-methyl-3-((4-nitrophenyl)sulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol	

Comp. No.	Name	Structure
9b	5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-3-(pyridin-3-ylsulfonyl)-[1,1'-biphenyl]-2,6-diol	
10b	3-(furan-3-ylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol	
11b	3-((1H-imidazol-4-yl)sulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol	
12b	5'-methyl-3-(oxetan-3-ylsulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol	
13b	5'-methyl-4-pentyl-3-((perfluorophenyl)sulfonyl)-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol	
14b	4-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)cyclohexan-1-one	

Comp. No.	Name	Structure
15b	1-(2-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)ethyl)pyrrolidine-2,5-dione	
16b	3-((2-(dimethylamino)ethyl)sulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol	
17b	1-(3-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)piperidin-1-yl)ethan-1-one	
18b	3-((2-chloropyrimidin-5-yl)sulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol	
19b	2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide	
20b	2,6-dihydroxy-N,5'-dimethyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide	

Comp. No.	Name	Structure
21b	2,6-dihydroxy-N,N,5'-trimethyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide	
22b	N-cyclopropyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide	
23b	2,6-dihydroxy-N-isopropyl-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide	
24b	2,6-dihydroxy-5'-methyl-4-pentyl-N-phenyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide	
25b	N-benzyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide	
26b	5'-methyl-3-((4-methylpiperazin-1-yl)sulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol	

Comp. No.	Name	Structure
27b	5'-methyl-4-pentyl-3-(piperidin-1-ylsulfonyl)-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol	
28b	5'-methyl-3-(morpholinosulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol	
29b	2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-N-(pyridin-3-yl)-[1,1'-biphenyl]-3-sulfonamide	
30b	2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-N-(pyrimidin-2-yl)-[1,1'-biphenyl]-3-sulfonamide	
31b	2,6-dihydroxy-5'-methyl-N-(2-oxopropyl)-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide	
32b	1-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)azetidin-3-one	

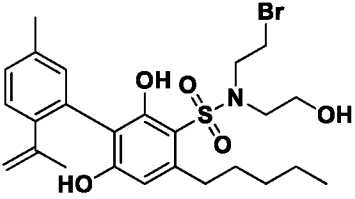
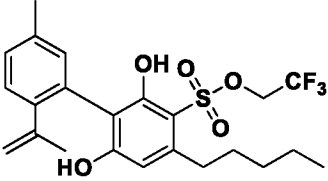
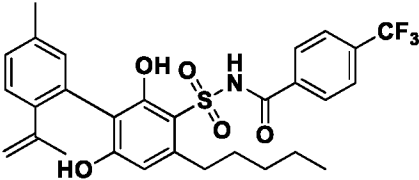
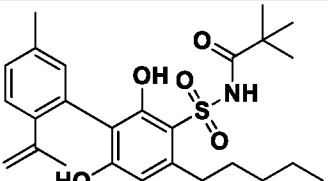
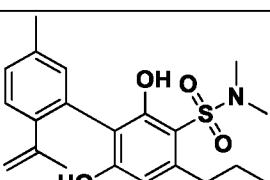
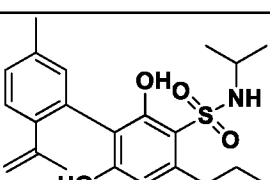
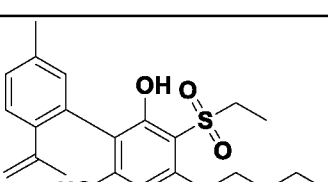
Comp. No.	Name	Structure
33b	2,6-dihydroxy-5'-methyl-N-(oxetan-2-ylmethyl)-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide	
34b	3-((2-azaspiro[3.3]heptan-2-yl)sulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol	
35b	3-((2,6-diazaspiro[3.3]heptan-2-yl)sulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol	
36b	((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)alanine	
37b	methyl ((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)alaninate	
38b	N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-3-morpholinopropanamide	

Comp. No.	Name	Structure
39b	4-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamido)-4-oxobutanoic acid	
40b	N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-3-(4-methylpiperazin-1-yl)propanamide	
41b	2-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide	
42b	N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(2-methoxyethoxy)acetamide	
43b	2-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-3-hydroxypropanamide	
44b	2-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)propanamide	

Comp. No.	Name	Structure
45b	3-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-2-methylpropanamide	
46b	N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide	
47b	N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-3-oxobutanamide	
48b	N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(3-methyl-1H-1,2,4-triazol-5-yl)acetamide	
49b	N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-1H-1,2,4-triazole-5-carboxamide	
50b	N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)oxetane-2-carboxamide	

Comp. No.	Name	Structure
51b	N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)benzamide	
52b	N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)nicotinamide	
53b	N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-2-phenylacetamide	
54b	N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(furan-2-yl)acetamide	
55b	N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(oxazol-2-yl)acetamide	
56b	N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(thiazol-2-yl)acetamide	

Comp. No.	Name	Structure
57b	2-((1H-benzo[d]imidazol-2-yl)-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide	
58b	2,6-dihydroxy-5'-methyl-4-pentyl-N-(phenylsulfonyl)-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-carboxamide	
59b	N-(cyclohexylsulfonyl)-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-carboxamide	
60b	(E)-2,6-dihydroxy-5'-methyl-4-pentyl-N-(prop-1-en-1-ylsulfonyl)-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-carboxamide	
61b	N-((1H-benzo[d]imidazol-2-yl)sulfonyl)-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-carboxamide	
62b	N,N-diethyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide	

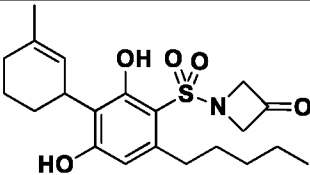
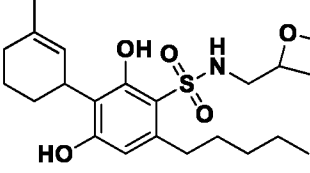
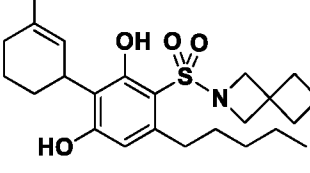
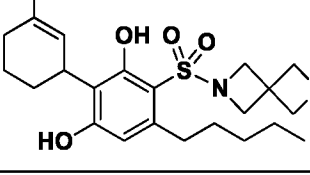
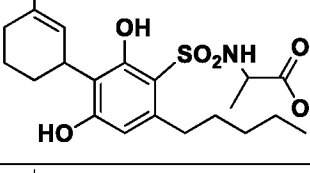
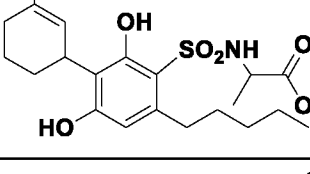
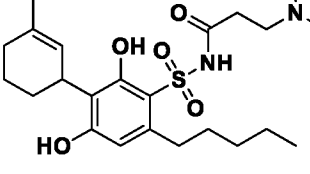
Comp. No.	Name	Structure
63b	N-(2-bromoethyl)-2,6-dihydroxy-N-(2-hydroxyethyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide	
64b	2,2,2-trifluoroethyl 2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonate	
65b	N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-4-(trifluoromethyl)benzamide	
66b	N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)pivalamide	
67b	2,6-dihydroxy-N,N,5'-trimethyl-2'-(prop-1-en-2-yl)-4-propyl-[1,1'-biphenyl]-3-sulfonamide	
68b	2,6-dihydroxy-N-isopropyl-5'-methyl-2'-(prop-1-en-2-yl)-4-propyl-[1,1'-biphenyl]-3-sulfonamide	
69b	3-(ethylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol	

Comp. No.	Name	Structure
70b	tert-butyl 4-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)piperazine-1-carboxylate	
71b	2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-N-(pyridin-3-ylsulfonyl)-[1,1'-biphenyl]-3-carboxamide	
1c	2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonic acid	
2c	sodium 2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonate	
3c	5'-methyl-3-(methylsulfonyl)-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	
4c	3-(cyclopropylsulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	
5c	3-(tert-butylsulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	

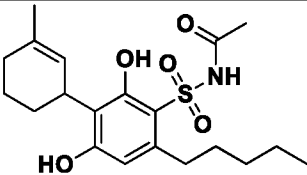
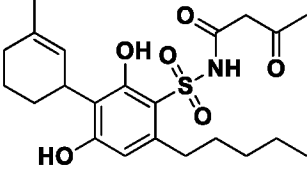
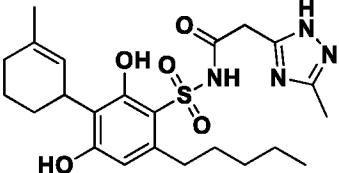
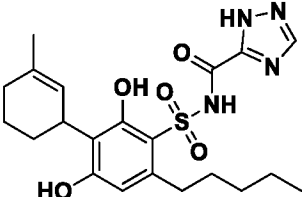
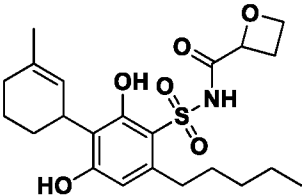
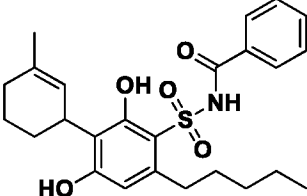
Comp. No.	Name	Structure
6c	3-(benzylsulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	
7c	5'-methyl-4-pentyl-3-(phenylsulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	
8c	5'-methyl-3-((4-nitrophenyl)sulfonyl)-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	
9c	5'-methyl-4-pentyl-3-(pyridin-3-ylsulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	
10c	3-(furan-3-ylsulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	
11c	3-((1H-imidazol-4-yl)sulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	
12c	5'-methyl-3-(oxetan-3-ylsulfonyl)-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	

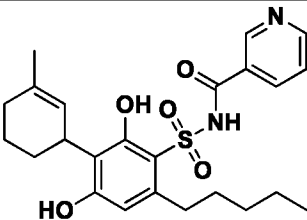
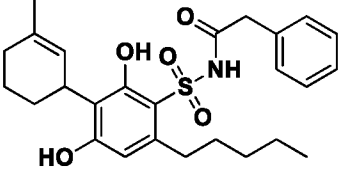
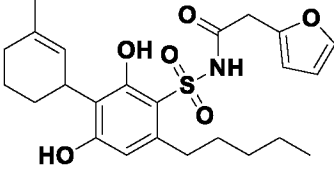
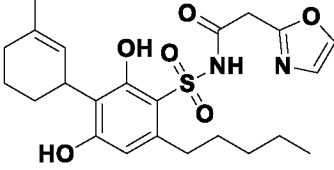
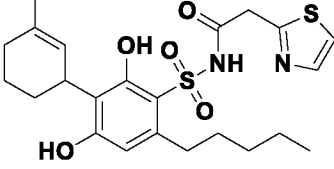
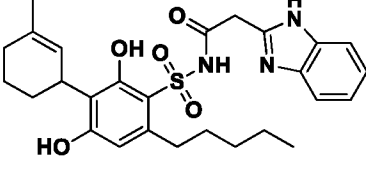
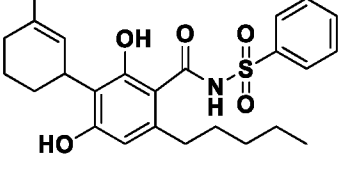
Comp. No.	Name	Structure
13c	5'-methyl-4-pentyl-3-((perfluorophenyl)sulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	
14c	4-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)cyclohexan-1-one	
15c	1-(2-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)ethyl)pyrrolidine-2,5-dione	
16c	3-((2-(dimethylamino)ethyl)sulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	
17c	1-(3-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)piperidin-1-yl)ethan-1-one	
18c	3-((2-chloropyrimidin-5-yl)sulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	
20c	2,6-dihydroxy-N,5'-dimethyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide	

Comp. No.	Name	Structure
21c	2,6-dihydroxy-N,N,5'-trimethyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide	
23c	2,6-dihydroxy-N-isopropyl-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide	
26c	5'-methyl-3-((4-methylpiperazin-1-yl)sulfonyl)-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	
27c	5'-methyl-4-pentyl-3-(piperidin-1-ylsulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	
29c	2,6-dihydroxy-5'-methyl-4-pentyl-N-(pyridin-3-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide	
30c	2,6-dihydroxy-5'-methyl-4-pentyl-N-(pyrimidin-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide	
31c	2,6-dihydroxy-5'-methyl-N-(2-oxopropyl)-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide	

Comp. No.	Name	Structure
32c	1-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)azetidin-3-one	
33c	2,6-dihydroxy-5'-methyl-N-(oxetan-2-ylmethyl)-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide	
34c	3-((2-azaspiro[3.3]heptan-2-yl)sulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	
35c	3-((2,6-diazaspiro[3.3]heptan-2-yl)sulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	
36c	((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)alanine	
37c	methyl ((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)alaninate	
38c	N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-3-morpholinopropanamide	

Comp. No.	Name	Structure
39c	4-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl])-3-sulfonamido)-4-oxobutanoic acid	
40c	N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl])-3-yl)sulfonyl)-3-(4-methylpiperazin-1-yl)propanamide	
41c	2-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl])-3-yl)sulfonyl)acetamide	
42c	N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl])-3-yl)sulfonyl)-2-(2-methoxyethoxy)acetamide	
43c	2-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl])-3-yl)sulfonyl)-3-hydroxypropanamide	
44c	2-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl])-3-yl)sulfonyl)propanamide	
45c	3-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl])-3-yl)sulfonyl)-2-methylpropanamide	

Comp. No.	Name	Structure
46c	N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide	
47c	N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-3-oxobutanamide	
48c	N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(3-methyl-1H-1,2,4-triazol-5-yl)acetamide	
49c	N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-1H-1,2,4-triazole-5-carboxamide	
50c	N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)oxetane-2-carboxamide	
51c	N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)benzamide	

Comp. No.	Name	Structure
52c	N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)nicotinamide	
53c	N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-phenylacetamide	
54c	N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(furan-2-yl)acetamide	
55c	N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(oxazol-2-yl)acetamide	
56c	N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(thiazol-2-yl)acetamide	
57c	2-(1H-benzo[d]imidazol-2-yl)-N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide	
58c	2,6-dihydroxy-5'-methyl-4-pentyl-N-(phenylsulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide	

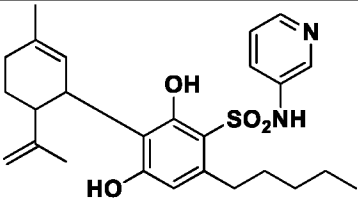
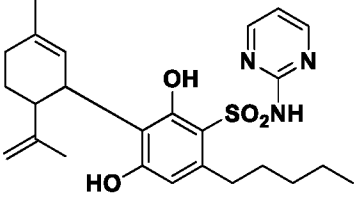
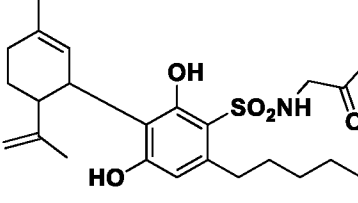
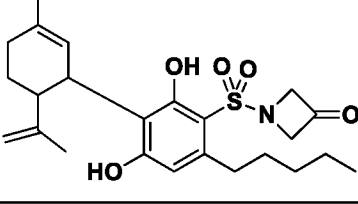
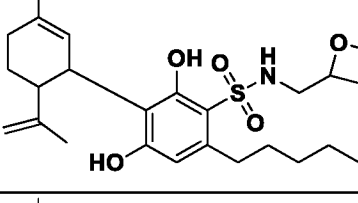
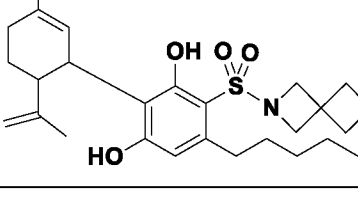
Comp. No.	Name	Structure
59c	N-(cyclohexylsulfonyl)-2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide	
60c	(E)-2,6-dihydroxy-5'-methyl-4-pentyl-N-(prop-1-en-1-ylsulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide	
61c	N-((1H-benzo[d]imidazol-2-yl)sulfonyl)-2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide	
63c	N-(2-bromoethyl)-2,6-dihydroxy-N-(2-hydroxyethyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide	
64c	2,2,2-trifluoroethyl 2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonate	
65c	N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-4-(trifluoromethyl)benzamide	
66c	N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)pivalamide	

Comp. No.	Name	Structure
67c	2,6-dihydroxy-N,N,5'-trimethyl-4-propyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide	
68c	2,6-dihydroxy-N-isopropyl-5'-methyl-4-propyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide	
69c	3-(ethylsulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	
71c	2,6-dihydroxy-5'-methyl-4-pentyl-N-(pyridin-3-ylsulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide	
1d	2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonic acid	
2d	sodium 2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonate	
4d	3-(cyclopropylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	

Comp. No.	Name	Structure
5d	3-(tert-butylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	
6d	3-(benzylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	
7d	5'-methyl-4-pentyl-3-(phenylsulfonyl)-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	
8d	5'-methyl-4-pentyl-3-(4-nitrophenylsulfonyl)-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	
9d	5'-methyl-4-pentyl-2'-(3-pyridylsulfonyl)-3-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	
10d	3-(furan-3-ylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	

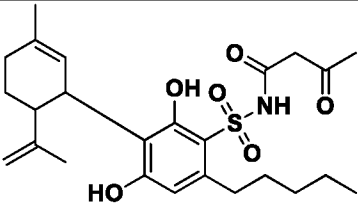
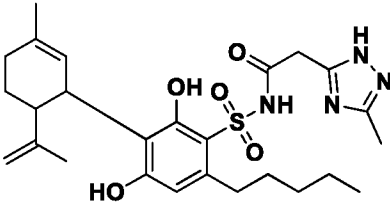
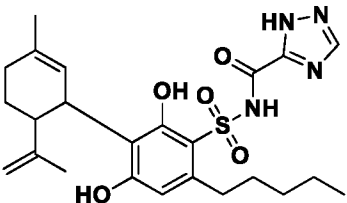
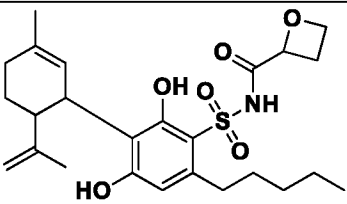
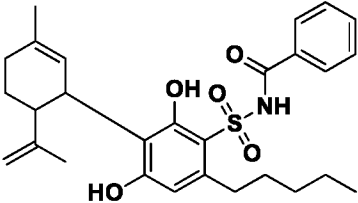
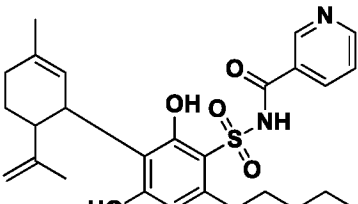
Comp. No.	Name	Structure
11d	3-((1H-imidazol-4-yl)sulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	
12d	5'-methyl-3-(oxetan-3-ylsulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	
13d	5'-methyl-4-pentyl-3-((perfluorophenyl)sulfonyl)-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	
14d	4-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)cyclohexan-1-one	
15d	1-(2-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)ethyl)pyrrolidine-2,5-dione	
16d	3-((2-(dimethylamino)ethyl)sulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	

Comp. No.	Name	Structure
17d	1-(3-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)piperidin-1-yl)ethan-1-one	
18d	3-((2-chloropyrimidin-5-yl)sulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	
19d	2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide	
20d	2,6-dihydroxy-N,5'-dimethyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide	
26d	5'-methyl-3-((4-methylpiperazin-1-yl)sulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	
27d	5'-methyl-4-pentyl-3-(piperidin-1-ylsulfonyl)-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	

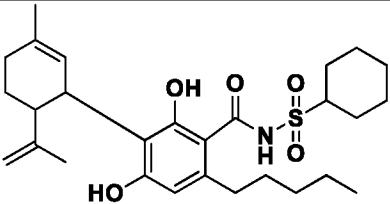
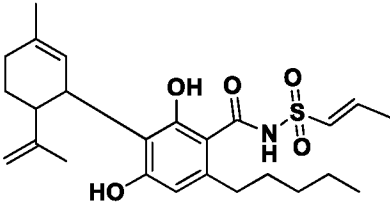
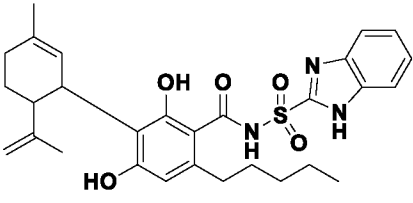
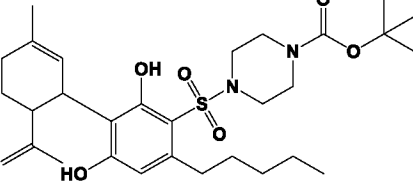
Comp. No.	Name	Structure
29d	2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-N-(pyridin-3-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide	
30d	2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-N-(pyrimidin-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide	
31d	2,6-dihydroxy-5'-methyl-N-(2-oxopropyl)-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide	
32d	1-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)azetidin-3-one	
33d	2,6-dihydroxy-5'-methyl-N-(oxetan-2-ylmethyl)-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide	
34d	3-((2-azaspiro[3.3]heptan-2-yl)sulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	

Comp. No.	Name	Structure
35d	3-((2,6-diazaspiro[3.3]heptan-2-yl)sulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol	
36d	((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)alanine	
37d	methyl ((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)alaninate	
38d	N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-3-morpholinopropanamide	
39d	4-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamido)-4-oxobutanoic acid	
40d	N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-3-(4-methylpiperazin-1-yl)propanamide	

Comp. No.	Name	Structure
41d	2-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide	
42d	N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(2-methoxyethoxy)acetamide	
43d	2-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-3-hydroxypropanamide	
44d	2-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)propanamide	
45d	3-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-methylpropanamide	
46d	N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide	

Comp. No.	Name	Structure
47d	N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-3-oxobutanamide	
48d	N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(3-methyl-1H-1,2,4-triazol-5-yl)acetamide	
49d	N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-1H-1,2,4-triazole-5-carboxamide	
50d	N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)oxetane-2-carboxamide	
51d	N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)benzamide	
52d	N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)nicotinamide	

Comp. No.	Name	Structure
53d	N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-phenylacetamide	
54d	N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(furan-2-yl)acetamide	
55d	N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(oxazol-2-yl)acetamide	
56d	N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(thiazol-2-yl)acetamide	
57d	2-(1H-benzo[d]imidazol-2-yl)-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide	
58d	2,6-dihydroxy-5'-methyl-4-pentyl-N-(phenylsulfonyl)-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide	

Comp. No.	Name	Structure
59d	N-(cyclohexylsulfonyl)-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide	
60d	(E)-2,6-dihydroxy-5'-methyl-4-pentyl-N-(prop-1-en-1-ylsulfonyl)-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide	
61d	N-((1H-benzo[d]imidazol-2-yl)sulfonyl)-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide	
70d	tert-butyl 4-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)piperazine-1-carboxylate	

[0212] The disclosure also provides analogs of compounds 19a, 20a, 22a-25a, 29a-31a, 33a, 36a-61a, 65a, 66a, 68a, 71a, 19b, 20b, 22b-25b, 29b-31b, 33b, 36b-61b, 65b, 66b, 68b, 71b, 19c, 20c, 22c-25c, 29c-31c, 33c, 36c-61c, 65c, 66c, 68c, 71c, 19d, 20d, 22d-25d, 29d-31d, 33d, and 36d-61d in which the amino moiety in sulfonamide is methylated. For example, such an analog of compound 61a is N-((1H-benzo[d]imidazol-2-yl)sulfonyl)-2,6-dihydroxy-N,3'-dimethyl-4-pentyl-[1,1'-biphenyl]-3-carboxamide; such analogs of all other compounds of the Table are specifically contemplated where chemically reasonable.

Radioligand Competitive Binding Assays – CB1 and CB2

Example 37:

[0213] Compounds of the present disclosure were tested for CB1 receptor binding affinity and for CB2 receptor binding affinity. As used herein, “binding affinity” is represented by the IC_{50}

value, which was experimentally determined as described herein. The lower the IC_{50} value the higher the binding affinity. A compound of the present disclosure may be said to have "binding selectivity" if it has a higher binding affinity for one receptor compared to the other. For example, a compound that has an IC_{50} of 1 μM for CB1 and 0.1 μM for CB2 is 10 times more selective for the CB2 receptor.

CB1 Membrane Preparation

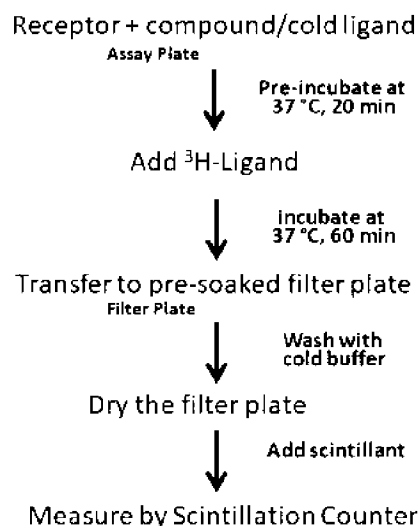
[0214] The membranes were prepared from CHO-K1 (Chinese hamster ovary) cells stably transfected with the human CB1 receptor (Cat.# ES-110-C; Perkin Elmer, Boston, MA). The cells were grown adherently and maintained in Ham's F12 medium containing 10% fetal bovine serum (FBS), penicillin, streptomycin and geneticin (G418) at 37°C in a humid atmosphere of 5% CO₂ following the manufacturer's instructions.

[0215] For membrane preparation the cells were washed with PBS and scraped off the plates in cold homogenization buffer (25 mM HEPES (pH 7.4), 2 mM EDTA) containing protease inhibitor cocktail (Sigma Cat.# P8340). The cell suspension was homogenized with a Pro-PK-01200D Polytron Homogenizer (Pro Scientific) and then centrifuged for 30 min at 120,000 × g. The supernatant was discarded and the pellet was re-suspended in the homogenization buffer and stored at -80°C until the time of use.

CB1 Radioligand Binding Assay:

[0216] CP 55,940 is a synthetic cannabinoid that mimics the effects of naturally occurring THC. It acts as a full agonist at both cannabinoid CB1 and CB2 receptors. Radiolabeled ligands represent one of the most sensitive methods for probing receptor binding biology. In this experiment, 3H radiolabeled CP 55,940, i.e. [3H]CP 55,940 (Perkin Elmer, Boston, MA), was used as a radioligand for the CB1 receptor.

[0217] [3H]CP 55,940 displacement assays were used for the determination of the binding affinity of compounds for the CB1 receptor (Scheme 8; below).

Scheme 8 Schematic representation of the radioligand binding assay for CB1 and CB2

[0218] The competition binding experiments (single dose and dose-response) were performed by incubating 0.8 nM of [³H]CP 55,940 (specific activity 101 Ci/mmol, Perkin Elmer) and different concentrations of compounds disclosed herein with membranes prepared as above from CHO-K1 cells expressing human CB1 receptor (6 µg of protein/well), 50 mM Tris–HCl (pH 7.4), 5 mM MgCl₂, 1 mM CaCl₂, and 2 mg/mL BSA.

[0219] For the single dose experiments, the compound stocks (usually 10 mM in DMSO) were diluted to working stocks in the binding buffer to give the final compound concentrations of 10 µM and 1 µM. For the dose-response experiments, the test compounds were sequentially diluted to provide the desired concentration range for the IC₅₀ determination. In each case the compounds were pre-incubated with the membrane for 20 min, before adding the radioligand.

[0220] After incubation with the radioligand for 60 min at 37°C, the incubation was terminated by rapid filtration of the assay mixture through MultiScreen®_{HTS}⁺ 96-well filter plates (Millipore, Cat.# MSFCNXB), pre-soaked for 60 min with 50 mM Tris–HCl (pH 7.4) containing 0.33% polyethylenimine (PEI). The nonspecific binding (NSB) was determined in the presence of 10 µM unlabelled CP 55,940. After drying the filter plate at 50°C for at least 60 min, the filter-bound radioactivity was determined by scintillation spectrometry using the 1450 MicroBeta Plate Counter (Perkin Elmer, Boston, MA). From the dose-response experiments, the IC₅₀ values were determined (see **Table 1**, CB1 IC₅₀).

[0221] Some compounds of the present disclosure exhibited selectivity for the CB1 receptor over the CB2 receptor (see e.g. **Table 1**). In **Table 1** below, the fold difference in selectivity between CB1 and CB2 binding is indicated, with the fold difference presented in the column of the receptor that exhibited the higher binding affinity (i.e. CB1 or CB2). Where the test compound had about the same affinity for both receptors, this is represented by a value of 1.00 in the column for both receptors.

CB2 Membrane Preparation

[0222] The membranes were prepared from CHO-K1 (Chinese hamster ovary) cells stably transfected with the human CB2 receptor (Cat.# ES-111-C; Perkin Elmer, Boston, MA). The cells were grown adherently and maintained in Ham's F12 medium containing 10% fetal bovine serum (FBS), penicillin, streptomycin and geneticin (G418) at 37°C in a humid atmosphere of 5% CO₂ following the manufacturer's instructions.

[0223] For membrane preparation the cells were washed with PBS and scraped off the plates in cold homogenization buffer (25 mM HEPES (pH 7.4), 2 mM EDTA) containing protease inhibitor cocktail (Sigma Cat.# P8340). The cell suspension was homogenized with a Pro-PK-01200D Polytron Homogenizer (Pro Scientific) and then centrifuged for 30 min at 120,000 × g. The supernatant was discarded and the pellet was re-suspended in the homogenization buffer and stored at -80°C until the time of use.

CB2 Radioligand Binding Assay

[0224] In this experiment, 3H radiolabeled CP 55,940, i.e. [3H]CP 55,940 (Perkin Elmer, Boston, MA), was used as a radioligand for the CB2 receptor to determine the binding affinity of compounds for the CB2 receptor (Scheme 8; above).

[0225] The competition binding experiments (single dose and dose-response) were performed by incubating 0.6 nM of [3H]CP55,940 (specific activity 101 Ci/mmol, Perkin Elmer) and different concentrations of compounds disclosed herein with membranes prepared as above from CHO-K1 cells expressing human CB2 receptor (1 µg of protein/well), 50 mM Tris-HCl (pH 7.4), 5 mM MgCl₂, 1 mM CaCl₂, and 2 mg/mL BSA.

[0226] For the single dose experiments, the compound stocks (usually 10 mM in DMSO) were diluted to working stocks in the binding buffer to give the final compound concentrations of 10 µM and 1 µM. For the dose-response experiments the test compounds were sequentially diluted to provide the desired concentration range for the IC₅₀ determination. In each case the compounds were pre-incubated with the membrane for 20 min, before adding the radioligand.

[0227] After incubation with the radioligand for 60 min at 37°C, the incubation was terminated by rapid filtration of assay mixture through MultiScreen®_{HTS}⁺ 96-well filter plates (Millipore, Cat.# MSFCNXB), pre-soaked for 60 min with 50 mM Tris-HCl (pH 7.4) containing 0.33 % polyethylenimine (PEI). The nonspecific binding (NSB) was determined in the presence of 10 µM unlabelled CP55,940. After drying the filter plate at 50°C for at least 60 min, the filter-bound radioactivity was determined by scintillation spectrometry using the 1450 MicroBeta Plate Counter (Perkin Elmer, Boston, MA). From the dose-response experiments, the IC₅₀ values were determined (see **Table 1**, CB2 IC₅₀).

[0228] Some compounds of the present disclosure exhibited selectivity for the CB2 receptor over the CB1 receptor (see e.g. **Table 1**). Again, in **Table 1** below, the fold difference in selectivity between CB1 and CB2 binding is indicated, with the fold difference presented in the column of the receptor that exhibited the higher binding affinity (i.e. CB1 or CB2). Where the test compound had about the same affinity for both receptors, this is represented by a value of 1.00 in the column for both receptors.

Table 1: Data from Radioligand Competitive Binding Assays

Compound			Selectivity	
	CB1 IC ₅₀	CB2 IC ₅₀	CB1	CB2
22c	C	B	—	11.59
71c	B	B	1.14	—
24c	C	B	—	3.60
25c	B	B	—	1.50
62c	B	A	—	31.82
19c	C	C	1.00	1.00
28c	—	B	—	—
62d	B	B	—	6.29
22d	C	C	—	1.52
28d	B	A	—	8.20
24d	C	C	—	1.67
25d	C	C	—	2.00
63d	C	C	1.00	1.00
64d	B	B	2.00	—

21d	B	B	—	1.41
67d	C	C	—	3.08
23d	C	B	—	2.56
68d	C	C	—	1.74
3d	C	C	—	2.00

A = <0.1 μ MB = 0.1 μ M to 0.99 μ MC = 1.00 μ M to 5.00 μ M

PathHunter® β -Arrestin Functional Assay

Example 38:

[0229] In the PathHunter® β -Arrestin system from DiscoverRx (Eurofins, Fremont, CA), a small peptide, the ProLink™ (PK), is fused to the intracellular sequence of a GPCR target, and a complementing peptide, the enzyme acceptor (EA) fragment, is fused to β -arrestin. After binding to its specific ligand, the GPCR target recruits β -arrestin, forcing the complementation of the two β -galactosidase enzyme fragments (EA and PK) to produce a functional β -galactosidase enzyme. The enzyme activity, and thus the amount of ligand bound to the GPCR, is detected with a single addition of a reagent cocktail to lyse the cells and produce a chemiluminescent signal before being analyzed using a traditional plate reader.

CB1 Receptor Response to Ligand using DiscoverRx Cells

[0230] PathHunter® CHO-K1 CNR1 β -Arrestin cells (DiscoverRx, cat. Number 93-0959C2) stably expressing CB1 receptor (CB1R) were grown in Ham's F12 medium containing 10% fetal bovine serum (FBS), 1% penicillin/streptomycin, 300 μ g/mL Hygromycin B and 800 μ g/mL geneticin (G418) and maintained in 37°C incubators at 5% CO₂.

[0231] For CB1R dose-response assays, cells were plated in 96-well white flat bottom plates at a density of 40,000 cells/well and incubated overnight at 37°C in 5 % CO₂. The following day, the compound stocks (10 mM in DMSO) were sequentially diluted (11 point 3-fold dilutions) in DMSO to provide the desired concentration range for the EC₅₀ (agonist mode) or IC₅₀ (antagonist mode) determination. In agonist mode, CP 55,940 (CAS number 83002-04-4) was used, whereas in antagonist mode the synthetic cannabinoid rimonabant (CAS number 158681-13-1) was used as a reference compound.

[0232] Media was aspirated from the plate wells and cells washed with PBS, followed by adding 49.5 μ L (agonist mode) or 49 μ L (antagonist mode) of PBS to each well and 0.5 μ L of test

compound or CP55,940. Cells were then incubated for 90 minutes at 37°C in the agonist mode. Alternatively, in the antagonist mode cells were incubated with test compound or rimonabant for 30 minutes (37°C), followed by an additional incubation with 0.5 µL of 2-AG (CAS number 53847-30-6) at an EC₈₀ concentration (determined as 4 µM final concentration) for 90 min (37°C).

[0233] The incubation was terminated by adding the detection reagent (19 parts of 1% CHAPS, 5 parts Emerald-II and 1 part Galacton-Star), equivalent to 50% of the assay volume to each wells. Plates were incubated for 1 hour in the dark at room temperature, followed by chemiluminescence detection using a microplate reader.

[0234] Data were analysed by generating nonlinear regression curves. The response of agonists was normalized to the effect of CP55,940 reference agonist and the response of antagonists was normalized to the effect of rimonabant.

[0235] Compounds of the present disclosure were tested in agonist and antagonist mode. In agonist mode, for example, compound 62c was found to exhibit an EC₅₀ towards the human CB1 receptor of about 0.499 µM with a relative efficacy in comparison to CP55,940 of about 56%. In antagonist mode, for example, compounds 22c, 28c, 71c, 22d and 62d were found to exhibit an IC₅₀ towards human CB1 receptor between about 0.775 µM and about 3.0 µM, with a relative inhibition in comparison to rimonabant of between about 11% and about 79%.

AequoScreen Functional Assay

Example 39:

[0236] Aequorin is a photoprotein originating from the jellyfish *Aequorea Victoria*. The apo-enzyme (apoequorin) requires a hydrophobic prosthetic group, coelenterazine, to be converted to aequorin, the active form of the enzyme. This enzyme possesses 3 calcium binding sites which control its activity. Upon calcium binding, aequorin oxidizes coelenterazine into coelenteramide with the production of CO₂ and emission of light. The consumption of aequorin is proportional to the calcium concentration. Therefore, measurement of the light emitted upon oxidation of coelenterazine is a reliable tool for measurement of intracellular calcium flux. In the AequoScreen, cells co-expressing apoequorin and the target GPCR are incubated with the co-factor Coelenterazine h in order to reconstitute the active aequorin enzyme.

CB1 Receptor AequoScreen

[0237] Chinese hamster ovary (CHO) cells stably expressing the cytoplasmic luminescent reporter aequorin and the human G-protein $G\alpha_{16}$ ((CHO-K1 aeq/G16) Perkin Elmer, Waltham, MA, USA, Product No.: ES-000-A24) were grown in Ham's F-12 medium supplemented with 10% fetal bovine serum (FBS), 1% penicillin and streptomycin (pen/strep) and 0.25 mg/ml Zeocin. Cells were maintained in incubators at 37°C in 5% CO₂.

[0238] FuGene from Promega (Catalog number selected: E2691) was used to transiently transfect CHO-K1 aeq/G16 cells with an expression vector containing the open reading frame (ORF) expression clone for CNR1 (NM_016083.4; bacterial stock; Gencopeia Inc.) at a ratio of 15 ng of plasmid DNA to 480,000 cells. Cells were incubated for 24 h after transfection in incubators at 37°C in 5% CO₂.

[0239] The following day, cells were dislodged using 5 mM EDTA and resuspended in assay medium [DMEM/Ham's F12 with HEPES, without phenol red + 0.1% protease-free BSA]. Before the functional assay was performed, Coelenterazine h was added to the cell suspension at a final concentration of 5 μ M, and incubated at room temperature overnight, with constant gentle agitation in the dark.

[0240] After incubation, the mixture was diluted 3-fold in assay media and kept under constant gentle agitation at room temperature. Test compounds and CP55,940 were sequentially diluted (11 point 3-fold dilutions) in DMSO to provide the desired concentration range for the EC₅₀ determination (agonist mode). 1 μ L of these dilution series were transferred to a flat bottom white opaque 96-well plate containing 49 μ L of assay media. Cells were injected automatically over the serial diluted test compounds and CP55,940 using a liquid dispenser, and the luminescence was recorded over 10-30 seconds in a microplate reader.

[0241] Sigmoidal dose-response curves were generated using average Luminescent Counts Per Second (LCPS) which were recorded immediately after cells were mixed with compounds in agonist mode.

[0242] Compound 62c of the present disclosure was tested and was found to exhibit an EC₅₀ towards human CB1 receptor of about 502 nM, with a relative efficacy in comparison to CP55,940 of about 117%.

Further Biological Examples

[0243] Example 40: Simulated Gastric Fluid (SGF) Assay

[0244] In a microcentrifuge tube, 626.5 μL of a solution containing 1.1x assay buffer (37.6 mM NaCl, pH 1.2-1.5) is diluted with 70 μL of a 10x pepsin solution (Sigma-Aldrich Co. Cat#: P7012, 80,000 U/mL in milliQ water). The resulting solution is incubated at 37°C and 1,200 rpm in an orbital mixer for 5 minutes, prior to the addition of 3.5 μL of the test compound (2 mM, DMSO). The sample is incubated in the same conditions for as long as required.

[0245] At the specified time points, 150 μL aliquots of the sample are transferred to microcentrifuge tubes containing 24 μL of acid quenching solution (0.5 M NaHCO_3). After vortexing the tube for 5 seconds, 348 μL of the protein precipitation solution containing an internal standard (25 μM Glyburide, ACN) are added. The tube is vortexed again for 20 seconds, and stored in ice.

[0246] Finally, the tubes are centrifuged at 5,000 $\times g$ and 4°C for 15 minutes. The percentage remaining of the test compound, compared to time zero, is quantified in the supernatant by HPLC / LC-MS or LC-MS/MS and the half-life is determined.

[0247] Example 41: TRPs activation: measurement of cation flux through intracellular calcium detection

[0248] The transient receptor potential ion channels (TRPs) are non-selective ligand-gated cation channels that integrate a variety of physical and chemical stimuli. When activated, these channels lead to the gating of cations, including Ca^{2+} , thus generating changes in intracellular calcium concentration. The single wavelength fluorescent indicator Fluo-4 acetoxymethyl (AM) is used to measure intracellular calcium flux and concentration in cells expressing TRPs and stimulated with cannabinoids. The Fluo-4 Direct™ calcium assay kit (Molecular Probes, Invitrogen, Carlsbad, CA, USA) allows the direct addition of the reagent into microplate wells containing cultured cells, without the requirement of media removal or a wash step, therefore facilitating the process of target screening.

[0249] As adapted from Moriello *et al.* ("Assay of TRPV1 Receptor Signaling" *Methods In Molecular Biology* (2016) 1412:65-76, herein incorporated by reference), human embryonic kidney (HEK-293) cells are used to express different TRPs, including TRPV1 and TRPV2. Cells are grown in Eagle's Minimum Essential Medium supplemented with 10% fetal bovine serum (FBS), 1% penicillin and streptomycin (pen/strep), and maintained in incubators at 37 °C in 5% CO_2 . Cells are seeded in 96-well plates and polyethylenimine (PEI) used to transiently transfect HEK-293 cells with expression vectors containing the open reading frame (ORF) of the TRPs of interest. Transfection using the empty expression vector is performed as a negative control.

[0250] 24-48 hours after transfection, cells are treated with Fluo-4 Direct™ (Molecular Probes) for 30-60 minutes and subsequently exposed to cannabinoids and benchmark compounds for different periods of time. Following incubations, fluorescence is measured using a microplate reader (excitation at 494 nm and emission at 516 nm).

[0251] Analysis of data is done by generating nonlinear regression curves and all data points corrected for background fluorescence and negative control. The response of agonists is normalized to the effect of a reference agonist and the response of antagonists normalized to the EC₈₀ of a reference agonist.

[0252] Example 42: PPAR_γ activation: nuclear hormone receptor activation assay

[0253] Peroxisome proliferator activated receptors (PPARs) are ligand-activated transcription factors of nuclear hormone receptors (NHRs). The PathHunter® PPAR_γ protein interaction assay (DiscoverX, Fremont, CA, USA) reports the activation of NHRs based on enzyme **complementation of β-galactosidase**, rendering a chemiluminescent signal.

[0254] CHO-K1 PPAR_γ cell lines (DiscoverX) stably expressing the target receptor is used. Cells are grown using reagents provided by the manufacturer (DiscoverX) and maintained in incubators at 37 °C in 5% CO₂. Cells are harvested and plated in black skirt, clear bottom 96-well plates and allowed to attach and recover overnight. Subsequently, cells are incubated with cannabinoids and/or benchmark compounds, such as troglitazone and rosiglitazone, for 30-90 minutes at 37 °C in 5 % CO₂. The detection reagent provided by the manufacturer (DiscoverX) is then added to the wells, and plates are incubated for 1 hour in the dark, followed by chemiluminescence detection using a microplate reader. Analysis of data is done by generating nonlinear regression curves and all data points are corrected for background luminescence and negative control. The response of agonists is normalized to the effect of a reference agonist and the response of antagonists normalized to the EC₈₀ of a reference agonist. Basal activity of the cells is set at 0 %.

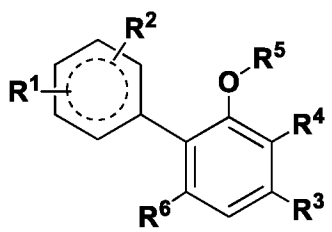
[0255] Numerous references have been made to patents and printed publications throughout this specification. Each of the cited references and printed publications are individually incorporated herein by reference in their entirety.

[0256] In closing, it is to be understood that the embodiments of the invention disclosed herein are illustrative of the principles of the present invention. Other modifications that may be employed are within the scope of the invention. Thus, by way of example, but not of limitation,

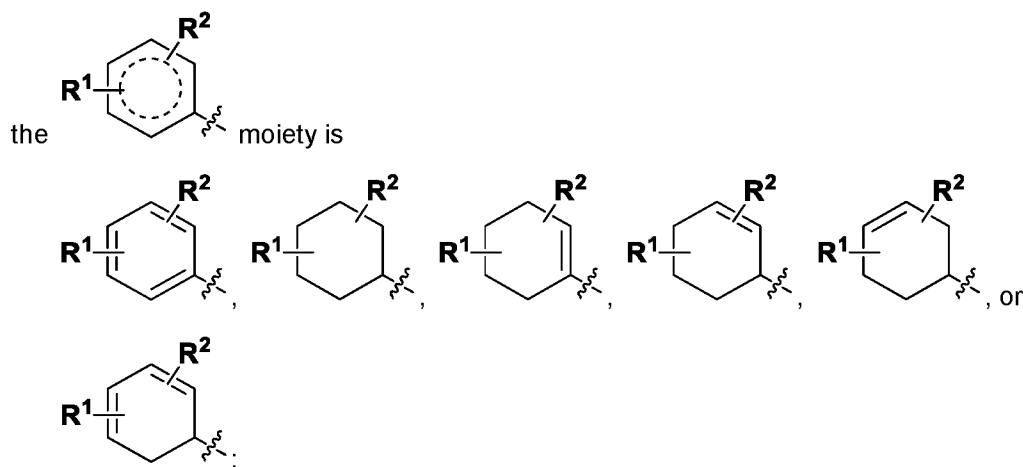
alternative configurations of the present invention may be utilized in accordance with the teachings herein. Accordingly, the present invention is not limited to that precisely as shown and described.

We claim:

1. A compound having structural formula:



or an enantiomer, diastereomer, racemate, tautomer, or metabolite thereof, or a pharmaceutically acceptable salt, solvate or hydrate of the compound, enantiomer, diastereomer, racemate, tautomer, or metabolite, wherein



R^1 is hydrogen, halo, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, C_2 - C_8 alkynyl, $-CO_2H$, $-(C_0-C_4 \text{ alkyl})-C(O)O(C_1-C_6 \text{ alkyl})$, $-(C_0-C_4 \text{ alkyl})-OC(O)O-(C_1-C_6 \text{ alkyl})$, $-OR^{1a}$, $-(C_1-C_4 \text{ alkyl})OR^{1a}$, $-SR^{1a}$, $-(C_1-C_4 \text{ alkyl})SR^{1a}$, $-NR^{1b}R^{1c}$, $-(C_1-C_4 \text{ alkyl})NR^{1b}R^{1c}$, $-(C_1-C_4 \text{ alkyl})C(O)NR^{1b}R^{1c}$, $-(C_0-C_4 \text{ alkyl})$ -aryl, $-(C_0-C_4 \text{ alkyl})$ -heteroaryl, $-(C_0-C_4 \text{ alkyl})$ -cycloalkyl, $-(C_0-C_4 \text{ alkyl})$ -heterocycloalkyl, or oxo when attached to a ring of appropriate saturation, wherein

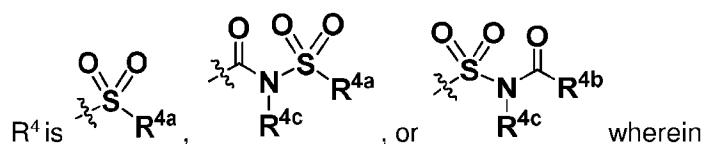
R^{1a} , R^{1b} , and R^{1c} are independently hydrogen, C_1 - C_4 alkyl, or $-C(O)(C_1-C_4 \text{ alkyl})$;

R^2 is hydrogen, halo, C_1 - C_8 alkyl, C_2 - C_8 alkenyl, C_2 - C_8 alkynyl, $-CO_2H$, $-(C_0-C_4 \text{ alkyl})-C(O)O(C_1-C_6 \text{ alkyl})$, $-(C_0-C_4 \text{ alkyl})-OC(O)O-(C_1-C_6 \text{ alkyl})$, $-OR^{2a}$, $-(C_1-C_4 \text{ alkyl})OR^{2a}$, $-SR^{2a}$, $-(C_1-C_4 \text{ alkyl})SR^{2a}$, $-NR^{2b}R^{2c}$, $-(C_1-C_4 \text{ alkyl})NR^{2b}R^{2c}$, $-(C_1-C_4 \text{ alkyl})C(O)NR^{2b}R^{2c}$, $-(C_0-C_4 \text{ alkyl})$ -aryl, $-(C_0-C_4 \text{ alkyl})$ -heteroaryl, $-(C_0-C_4 \text{ alkyl})$ -cycloalkyl, $-(C_0-C_4 \text{ alkyl})$ -heterocycloalkyl, or oxo when attached to a ring of appropriate saturation, wherein

R^{2a} , R^{2b} , and R^{2c} are independently hydrogen, C_1 - C_4 alkyl, or $-C(O)(C_1-C_4 \text{ alkyl})$;

A8142866WO

R³ is hydrogen, C₁-C₁₂ alkyl, C₂-C₁₂ alkenyl, C₂-C₁₂ alkynyl, -(OCH₂CH₂)₀₋₆O(C₁-C₈ alkyl), -(C₀-C₄ alkyl)-NR^{3a}R^{3b}, -(C₀-C₄ alkyl)-aryl, -(C₀-C₄ alkyl)-heteroaryl, -(C₀-C₄ alkyl)-cycloalkyl or -(C₀-C₄ alkyl)-heterocycloalkyl, wherein R^{3a} and R^{3b} are each independently hydrogen or C₁-C₆ alkyl;



R^{4a} is C₁-C₈ alkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, -OR^{4e}, -(C₁-C₄ alkyl)OR^{4e}, -(C₁-C₄ alkyl)-C(O)(C₁-C₄ alkyl), -(C₀-C₄ alkyl)-aryl, -(C₀-C₄ alkyl)-heteroaryl, -(C₀-C₄ alkyl)-cycloalkyl, -(C₀-C₄ alkyl)-heterocycloalkyl, -NR^{4d}R^{4e}, or -(C₁-C₄ alkyl)NR^{4d}R^{4e}, and

R^{4b} is C₁-C₈ alkyl, C₂-C₈ alkenyl, C₂-C₈ alkynyl, -CH₂-(OCH₂CH₂)₀₋₆O(C₁-C₈ alkyl), -(C₁-C₄ alkyl)OR^{4e}, -(C₁-C₄ alkyl)-C(O)(C₁-C₄ alkyl), -(C₁-C₄ alkyl)-C(O)O(R^{4e}), -(C₀-C₄ alkyl)-aryl, -(C₀-C₄ alkyl)-heteroaryl, -(C₀-C₄ alkyl)-cycloalkyl, -(C₀-C₄ alkyl)-heterocycloalkyl, or -(C₁-C₄ alkyl)NR^{4d}R^{4e}, wherein

R^{4d} is hydrogen, C₁-C₆ alkyl, -(C₁-C₄ alkyl)-C(O)(C₁-C₄ alkyl), -(C₁-C₄ alkyl)-C(O)O(R^{4e}), -(C₁-C₄ alkyl)-OC(O)(R^{4e}), -(C₀-C₄ alkyl)-aryl, -(C₀-C₄ alkyl)-heteroaryl, -(C₀-C₄ alkyl)-cycloalkyl, or -(C₀-C₄ alkyl)-heterocycloalkyl,

R^{4e} is hydrogen or C₁-C₄ alkyl, and

R^{4c} is hydrogen or C₁-C₄ alkyl;

R⁵ is hydrogen, C₁-C₈ alkyl, -(C₁-C₄ alkyl)-O-(C₀-C₄ alkyl), -C(O)(C₁-C₄ alkyl), -C(O)O(C₁-C₄ alkyl), -C(O)NH₂, -C(O)NH(C₁-C₄ alkyl), -C(O)N(C₁-C₄ alkyl)₂, -(C₁-C₄ alkyl)C(O)O(C₁-C₄ alkyl), or -(C₁-C₄ alkyl)OC(O)(C₁-C₄ alkyl); and

R⁶ is hydrogen or -OR^{6a}, wherein R^{6a} is hydrogen, C₁-C₈ alkyl, -(C₁-C₄ alkyl)-O-(C₀-C₄ alkyl), -C(O)(C₁-C₄ alkyl), -C(O)O(C₁-C₄ alkyl), -C(O)NH₂, -C(O)NH(C₁-C₄ alkyl), -C(O)N(C₁-C₄ alkyl)₂, -(C₁-C₄ alkyl)C(O)O(C₁-C₄ alkyl), or -(C₁-C₄ alkyl)OC(O)(C₁-C₄ alkyl); wherein each alkyl, alkenyl and alkynyl is unsubstituted, halogenated (e.g., fluorinated, chlorinated), substituted with one or two hydroxyl or C₁-C₆ alkoxy groups, or substituted with one or two oxo groups;

each cycloalkyl has 3-10 ring carbons and is saturated or partially unsaturated, and optionally includes one or two fused cycloalkyl rings, each fused ring having 3-8 ring members, and is substituted with 0-6 R⁷;

each heterocycloalkyl has 3-10 ring members and 1-3 heteroatoms where each is independently nitrogen, oxygen or sulfur and is saturated or partially unsaturated, and

optionally includes one or two fused cycloalkyl rings, each having 3-8 ring members, and is substituted with 0-6 R⁷;

each aryl is a phenyl or a naphthyl, and optionally includes one or two fused cycloalkyl or heterocycloalkyl rings, each fused cycloalkyl or heterocycloalkyl ring having 4-8 ring members, and is substituted with 0-5 R⁸;

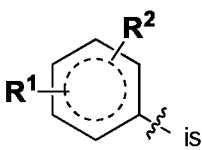
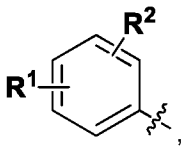
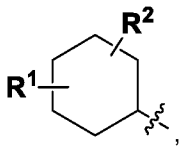
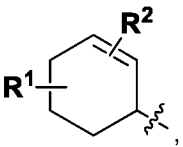
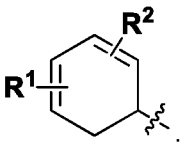
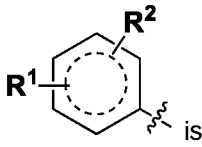
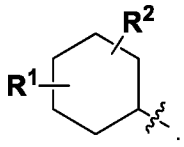
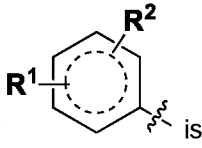
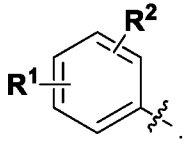
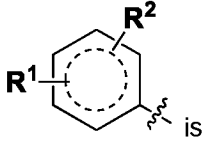
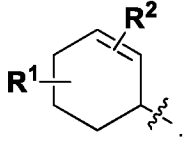
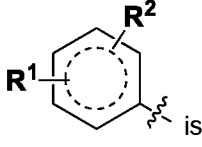
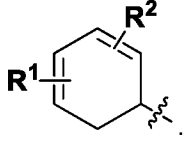
each heteroaryl is a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms, where each is independently nitrogen, oxygen or sulfur or a 8-10 membered bicyclic heteroaryl having 1-5 heteroatoms where each is independently nitrogen, oxygen or sulfur, and optionally includes one or two fused cycloalkyl or heterocycloalkyl rings, each fused cycloalkyl or heterocycloalkyl ring having 4-8 ring members, and is substituted with 0-5 R⁸,

in which

each R⁷ is independently oxo, C₁-C₄ alkyl, -Cl, -F, -Br, -CN, -SF₅, -N₃, nitro, -SR^A, -S(O)₁₋₂R^A, -OR^A, -(C₀-C₃ alkyl)-OR^B, -NR^BR^A, -C(O)R^A, -C(O)NR^BR^A, -NR^BC(O)R^A, -C(S)NR^BR^A, -NR^BC(S)R^A, -CO₂R^A, -OC(O)R^A, -C(O)SR^A, -SC(O)R^A, -C(S)OR^A, -OC(S)R^A, -C(S)SR^A, -SC(S)R^A, -S(O)₁₋₂OR^A, -OS(O)₁₋₂R^A, -S(O)₁₋₂NR^BR^A, -NR^BS(O)₁₋₂R^A, -OCO₂R^A, -OC(O)NR^BR^A, -NR^BCO₂R^A, -NR^BC(O)NR^BR^A, -SCO₂R^A, -OC(O)SR^A, -SC(O)SR^A, -SC(O)NR^BR^A, -NR^BC(O)SR^A, -OC(S)OR^A, -OC(S)NR^BR^A, -NR^BC(S)OR^A, -NR^BC(S)NR^BR^A, -SC(S)OR^A, -OC(S)SR^A, -SC(S)SR^A, -SC(S)NR^BR^A, -NR^BC(S)SR^A, -NR^BC(NR^B)NR^BR^A, -NR^BS(O)₁₋₂NR^BR^A, phenyl, C₃-C₈ cycloalkyl, a five to six-membered heteroaryl, or a five to six-membered heterocycloalkyl; and

each R⁸ is independently optionally-substituted C₁-C₄ alkyl, -Cl, -F, -Br, -CN, -SF₅, -N₃, nitro, -SR^A, -S(O)₁₋₂R^A, -OR^A, -(C₀-C₃ alkyl)-OR^B, -NR^BR^A, -C(O)R^A, -C(O)NR^BR^A, -NR^BC(O)R^A, -C(S)NR^BR^A, -NR^BC(S)R^A, -CO₂R^A, -OC(O)R^A, -SO₃H, -C(O)SR^A, -SC(O)R^A, -C(S)OR^A, -OC(S)R^A, -C(S)SR^A, -SC(S)R^A, -S(O)₁₋₂OR^A, -OS(O)₁₋₂R^A, -S(O)₁₋₂NR^BR^A, -NR^BS(O)₁₋₂R^A, -OCO₂R^A, -OC(O)NR^BR^A, -NR^BCO₂R^A, -NR^BC(O)NR^BR^A, -SCO₂R^A, -OC(O)SR^A, -SC(O)SR^A, -SC(O)NR^BR^A, -NR^BC(O)SR^A, -OC(S)OR^A, -OC(S)NR^BR^A, -NR^BC(S)OR^A, -NR^BC(S)NR^BR^A, -SC(S)OR^A, -OC(S)SR^A, -SC(S)SR^A, -SC(S)NR^BR^A, -NR^BC(S)SR^A, -NR^BC(NR^B)NR^BR^A, -NR^BS(O)₁₋₂NR^BR^A; phenyl, C₃-C₈ cycloalkyl, a five to six-membered heteroaryl, or a five to six-membered heterocycloalkyl;

wherein each R^A is independently H or C₁-C₃ alkyl, and each R^B is independently H, C₁-C₃ alkyl, C₁-C₃ fluoroalkyl, C₁-C₃ hydroxyalkyl, -S(O)₁₋₂(C₁-C₃ alkyl), -C(O)(C₁-C₃ alkyl) or -CO₂(C₁-C₃ alkyl).

2. The compound according to claim 1, wherein the moiety  is
- , , , or .
3. The compound according to claim 1, wherein the moiety  is .
4. The compound according to claim 1, wherein the moiety  is .
5. The compound according to claim 1, wherein the moiety  is .
6. The compound according to claim 1, wherein the moiety  is .
7. The compound according to any one of claims 1-6, wherein R^1 is hydrogen, halo, C₁-C₈ alkyl, C₂-C₈ alkenyl, -CO₂H, -(C₀-C₄ alkyl)-C(O)O(C₁-C₆ alkyl), -OR^{1a}, -(C₁-C₄ alkyl)OR^{1a}, -SR^{1a}, -(C₁-C₄ alkyl)SR^{1a}, -NR^{1b}R^{1c}, -(C₁-C₄ alkyl)NR^{1b}R^{1c}, -(C₁-C₄ alkyl)C(O)NR^{1b}R^{1c}, -(C₀-C₄ alkyl)-aryl, -(C₀-C₄ alkyl)-heteroaryl, -(C₀-C₄ alkyl)-cycloalkyl, -(C₀-C₄ alkyl)-heterocycloalkyl, or oxo.
8. The compound according to any one of claims 1-6, wherein R^1 is hydrogen, -F, -Cl, C₁-C₈ alkyl, C₂-C₈ alkenyl, -CO₂H, -(C₀-C₄ alkyl)-C(O)O(C₁-C₆ alkyl), -(C₀-C₄ alkyl)-aryl, -(C₀-C₄ alkyl)-heteroaryl, -(C₀-C₄ alkyl)-cycloalkyl, -(C₀-C₄ alkyl)-heterocycloalkyl, or oxo.

9. The compound according to any one of claims 1-6, wherein R^1 is hydrogen, -F, -Cl, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, $-CO_2H$, $-(C_0$ - C_2 alkyl)- $C(O)O(C_1$ - C_6 alkyl), or oxo.
10. The compound according to any one of claims 1-6, wherein R^1 is hydrogen.
11. The compound according to any one of claims 1-6, wherein R^1 is hydrogen, C_1 - C_4 alkyl, or C_2 - C_4 alkenyl.
12. The compound according to any one of claims 1-6, wherein R^1 is C_1 - C_4 alkyl, or C_2 - C_4 alkenyl.
13. The compound according to any one of claims 1-6, wherein R^1 is C_1 - C_4 alkyl optionally substituted with hydroxy.
14. The compound according to any one of claims 1-6, wherein R^1 is methyl, ethyl, or propyl.
15. The compound according to any one of claims 1-6, wherein R^1 is C_2 - C_4 alkenyl.
16. The compound according to any one of claims 1-6, wherein R^1 is $-CO_2H$, $-C(O)O(C_1$ - C_4 alkyl), or oxo.
17. The compound according to any one of claims 1-6, wherein R^1 is $-CO_2H$.
18. The compound according to any one of claims 1-6, wherein R^1 is oxo.
19. The compound according to any one of claims 1-6, wherein R^1 is $-CH_2OH$.
20. The compound according to any one of claims 1-6, wherein R^1 is $-(C_0$ - C_4 alkyl)-aryl, $-(C_0$ - C_4 alkyl)-heteroaryl, $-(C_0$ - C_4 alkyl)-cycloalkyl, or $-(C_0$ - C_4 alkyl)-heterocycloalkyl.
21. The compound according to any one of claims 1-6, wherein R^1 is $-OR^{1a}$, $-(C_1$ - C_4 alkyl) OR^{1a} , $-SR^{1a}$, $-(C_1$ - C_4 alkyl) SR^{1a} , $-NR^{1b}R^{1c}$, $-(C_1$ - C_4 alkyl) $NR^{1b}R^{1c}$, or $-(C_1$ - C_4 alkyl) $C(O)NR^{1b}R^{1c}$.
22. The compound according to any one of claims 1-6, wherein R^1 is $-OR^{1a}$, $-(C_1$ - C_4 alkyl) OR^{1a} , $-NR^{1b}R^{1c}$, $-(C_1$ - C_4 alkyl) $NR^{1b}R^{1c}$, or $-(C_1$ - C_4 alkyl) $C(O)NR^{1b}R^{1c}$.
23. The compound according to claim 21 or 22, wherein R^{1a} , R^{1b} , and R^{1c} are independently hydrogen, C_1 - C_4 alkyl, or $-C(O)CH_3$.

24. The compound according to claim 21 or 22, wherein R^{1a} , R^{1b} , and R^{1c} are independently hydrogen or C₁-C₄ alkyl.
25. The compound according to any one of claims 1-24, wherein R^2 is hydrogen, halo, C₁-C₈ alkyl, C₂-C₈ alkenyl, -CO₂H, -(C₀-C₄ alkyl)-C(O)O(C₁-C₆ alkyl), -OR^{2a}, -(C₁-C₄ alkyl)OR^{2a}, -SR^{2a}, -(C₁-C₄ alkyl)SR^{2a}, -NR^{2b}R^{2c}, -(C₁-C₄ alkyl)NR^{2b}R^{2c}, -(C₁-C₄ alkyl)C(O)NR^{2b}R^{2c}, -(C₀-C₄ alkyl)-aryl, -(C₀-C₄ alkyl)-heteroaryl, -(C₀-C₄ alkyl)-cycloalkyl, -(C₀-C₄ alkyl)-heterocycloalkyl, or oxo.
26. The compound according to any one of claims 1-24, wherein R^2 is hydrogen, -F, -Cl, C₁-C₈ alkyl, C₂-C₈ alkenyl, -CO₂H, hydroxy, -(C₀-C₄ alkyl)-C(O)O(C₁-C₆ alkyl), -(C₀-C₄ alkyl)-aryl, -(C₀-C₄ alkyl)-heteroaryl, -(C₀-C₄ alkyl)-cycloalkyl, -(C₀-C₄ alkyl)-heterocycloalkyl, or oxo.
27. The compound according to any one of claims 1-24, wherein R^2 is hydrogen, -F, -Cl, C₁-C₆ alkyl, C₂-C₆ alkenyl, hydroxy, -CO₂H, -(C₀-C₂ alkyl)-C(O)O(C₁-C₆ alkyl), or oxo.
28. The compound according to any one of claims 1-24, wherein R^2 is hydrogen.
29. The compound according to any one of claims 1-24, wherein R^2 is C₁-C₄ alkyl or C₂-C₄ alkenyl.
30. The compound according to any one of claims 1-24, wherein R^2 is hydrogen, C₁-C₄ alkyl or C₂-C₄ alkenyl.
31. The compound according to any one of claims 1-24, wherein R^2 is C₁-C₄ alkyl optionally substituted with hydroxy.
32. The compound according to any one of claims 1-24, wherein R^2 is methyl, ethyl, or propyl.
33. The compound according to any one of claims 1-24, wherein R^2 is C₂-C₄ alkenyl.
34. The compound according to any one of claims 1-24, wherein R^2 is -CO₂H, -C(O)O(C₁-C₄ alkyl), or oxo.
35. The compound according to any one of claims 1-24, wherein R^2 is -CO₂H.
36. The compound according to any one of claims 1-24, wherein R^2 is oxo.

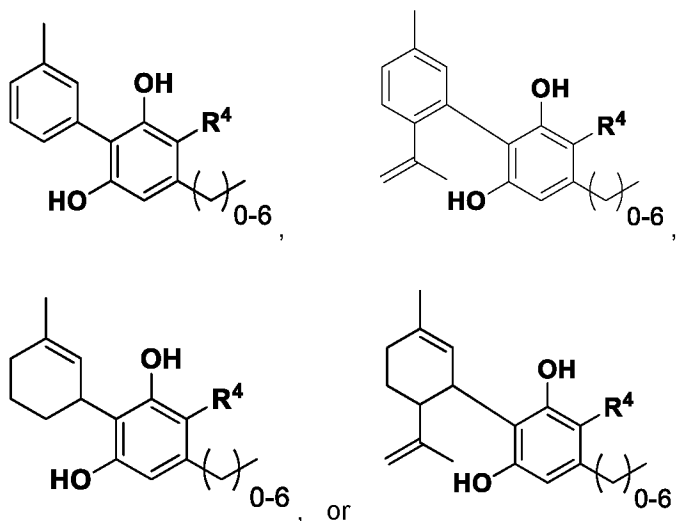
37. The compound according to any one of claims 1-24, wherein R^2 is $-\text{CH}_2\text{OH}$.
38. The compound according to any one of claims 1-24, wherein R^2 is $-(\text{C}_0\text{-C}_4 \text{ alkyl})\text{-aryl}$, $-(\text{C}_0\text{-C}_4 \text{ alkyl})\text{-heteroaryl}$, $-(\text{C}_0\text{-C}_4 \text{ alkyl})\text{-cycloalkyl}$, or $-(\text{C}_0\text{-C}_4 \text{ alkyl})\text{-heterocycloalkyl}$.
39. The compound according to any one of claims 1-24, wherein R^2 is $-\text{OR}^{2a}$, $-(\text{C}_1\text{-C}_4 \text{ alkyl})\text{OR}^{2a}$, $-\text{SR}^{2a}$, $-(\text{C}_1\text{-C}_4 \text{ alkyl})\text{SR}^{2a}$, $-\text{NR}^{2b}\text{R}^{2c}$, $-(\text{C}_1\text{-C}_4 \text{ alkyl})\text{NR}^{2b}\text{R}^{2c}$, or $-(\text{C}_1\text{-C}_4 \text{ alkyl})\text{C(O)NR}^{2b}\text{R}^{2c}$.
40. The compound according to any one of claims 1-24, wherein R^2 is $-\text{OR}^{2a}$, $-(\text{C}_1\text{-C}_4 \text{ alkyl})\text{OR}^{2a}$, $-\text{NR}^{2b}\text{R}^{2c}$, $-(\text{C}_1\text{-C}_4 \text{ alkyl})\text{NR}^{2b}\text{R}^{2c}$, or $-(\text{C}_1\text{-C}_4 \text{ alkyl})\text{C(O)NR}^{2b}\text{R}^{2c}$.
41. The compound according to any one of claims 1-24, wherein R^2 is $-\text{OR}^{2a}$.
42. The compound according to any one of claims 1-24, wherein R^2 is $-\text{NR}^{2b}\text{R}^{2c}$.
43. The compound according to any one of claims 39-42, wherein R^{2a} , R^{2b} , and R^{2c} are independently hydrogen, $\text{C}_1\text{-C}_4$ alkyl, or $-\text{C(O)CH}_3$.
44. The compound according to any one of claims 39-42, wherein R^{2a} , R^{2b} , and R^{2c} are independently hydrogen or $\text{C}_1\text{-C}_4$ alkyl.
45. The compound according to any one of claims 1-44, wherein R^3 is hydrogen, $\text{C}_1\text{-C}_{12}$ alkyl, $\text{C}_2\text{-C}_{12}$ alkenyl, $\text{C}_2\text{-C}_{12}$ alkynyl, $-(\text{OCH}_2\text{CH}_2)_{0-6}\text{OCH}_3$, $-(\text{C}_0\text{-C}_4 \text{ alkyl})\text{-aryl}$, $-(\text{C}_0\text{-C}_4 \text{ alkyl})\text{-heteroaryl}$, $-(\text{C}_0\text{-C}_4 \text{ alkyl})\text{-cycloalkyl}$ or $-(\text{C}_0\text{-C}_4 \text{ alkyl})\text{-heterocycloalkyl}$.
46. The compound according to any one of claims 1-44, wherein R^3 is hydrogen, $\text{C}_1\text{-C}_{12}$ alkyl, $-(\text{C}_0\text{-C}_4 \text{ alkyl})\text{-heteroaryl}$, $-(\text{C}_0\text{-C}_4 \text{ alkyl})\text{-cycloalkyl}$ or $-(\text{C}_0\text{-C}_4 \text{ alkyl})\text{-heterocycloalkyl}$.
47. The compound according to any one of claims 1-44, wherein R^3 is hydrogen, $\text{C}_1\text{-C}_8$ alkyl, $-(\text{C}_1\text{-C}_4 \text{ alkyl})\text{-heteroaryl}$ or $-(\text{C}_1\text{-C}_4 \text{ alkyl})\text{-heterocycloalkyl}$.
48. The compound according to any one of claims 1-44, wherein R^3 is hydrogen, $\text{C}_4\text{-C}_9$ alkyl, $-(\text{C}_1\text{-C}_2 \text{ alkyl})\text{-heteroaryl}$ or $-(\text{C}_1\text{-C}_2 \text{ alkyl})\text{-heterocycloalkyl}$.
49. The compound according to any one of claims 1-44, wherein R^3 is hydrogen, or $\text{C}_1\text{-C}_{10}$ alkyl.
50. The compound according to any one of claims 1-44, wherein R^3 is hydrogen.

51. The compound according to any one of claims 1-44, wherein R^3 is an unsubstituted $n\text{-C}_3\text{-C}_6$ alkyl.
52. The compound according to any one of claims 1-44, wherein R^3 is n-propyl.
53. The compound according to any one of claims 1-44, wherein R^3 is n-pentyl.
54. The compound according to any one of claims 1-44, wherein R^3 is 1,1-dimethylheptyl.
55. The compound according to any one of claims 1-44, wherein R^3 is $-(\text{C}_0\text{-C}_4 \text{ alkyl})\text{-aryl}$, $-(\text{C}_0\text{-C}_4 \text{ alkyl})\text{-heteroaryl}$, $-(\text{C}_0\text{-C}_4 \text{ alkyl})\text{-cycloalkyl}$ or $-(\text{C}_0\text{-C}_4 \text{ alkyl})\text{-heterocycloalkyl}$.
56. The compound according to claim 55, wherein the heterocycloalkyl has 3-8 ring members and 1-3 heteroatoms that are nitrogen, oxygen or sulfur and is substituted with 0-4 R^7 .
57. The compound according to claim 55, wherein the heterocycloalkyl is piperidinyl, pyrrolidinyl, azetidiny, or aziridinyl.
58. The compound according to claim 55, wherein the heterocycloalkyl is azetidiny and is substituted with 1-2 R^7 which are independently oxo, $\text{C}_1\text{-C}_4$ alkyl, $-\text{Cl}$, $-\text{F}$, $-\text{Br}$, $-\text{C}(\text{O})\text{R}^A$, or $-\text{CO}_2\text{R}^A$, wherein R^A is H or $\text{C}_1\text{-C}_3$ alkyl.
59. The compound according to claim 58, wherein R^7 is $-\text{C}(\text{O})\text{CH}_3$.
60. The compound according to any one of claims 1-59, wherein R^5 is hydrogen, $\text{C}_1\text{-C}_6$ alkyl, $-(\text{C}_1\text{-C}_4 \text{ alkyl})\text{-O-(C}_0\text{-C}_4 \text{ alkyl)}$, $-\text{C}(\text{O})(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{C}(\text{O})\text{O}(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{C}(\text{O})\text{NH}_2$, $-\text{C}(\text{O})\text{NH}(\text{C}_1\text{-C}_4 \text{ alkyl})$, or $-\text{C}(\text{O})\text{N}(\text{C}_1\text{-C}_4 \text{ alkyl})_2$.
61. The compound according to any one of claims 1-59, wherein R^5 is hydrogen, $\text{C}_1\text{-C}_8$ alkyl, or $-(\text{C}_1\text{-C}_4 \text{ alkyl})\text{-O-(C}_0\text{-C}_4 \text{ alkyl)}$.
62. The compound according to any one of claims 1-59, wherein R^5 is hydrogen.
63. The compound according to any one of claims 1-62, wherein R^6 is hydrogen.
64. The compound according to any one of claims 1-62, wherein R^6 is $-\text{OR}^{6a}$.
65. The compound according to any one of claims 1-62, wherein R^6 is $-\text{OR}^{6a}$, wherein R^{6a} is hydrogen, $\text{C}_1\text{-C}_6$ alkyl, $-(\text{C}_1\text{-C}_4 \text{ alkyl})\text{-O-(C}_0\text{-C}_4 \text{ alkyl)}$, $-\text{C}(\text{O})(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{C}(\text{O})\text{O}(\text{C}_1\text{-C}_4 \text{ alkyl})$, $-\text{C}(\text{O})\text{NH}_2$, $-\text{C}(\text{O})\text{NH}(\text{C}_1\text{-C}_4 \text{ alkyl})$, or $-\text{C}(\text{O})\text{N}(\text{C}_1\text{-C}_4 \text{ alkyl})_2$.

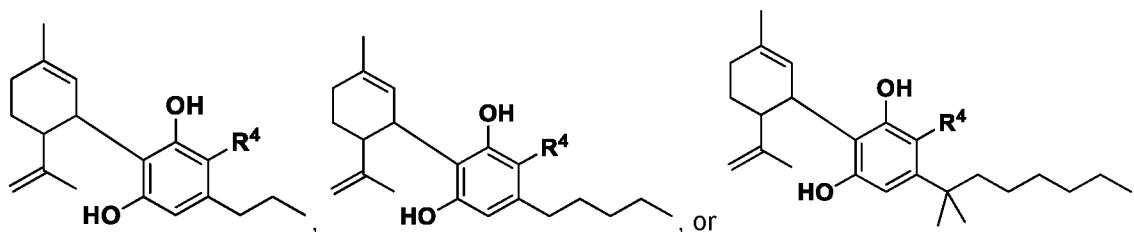
66. The compound according to any one of claims 1-62, wherein R^6 is $-OR^{6a}$, wherein R^{6a} is hydrogen, C_1 - C_6 alkyl, or $-(C_1$ - C_4 alkyl)- O -(C_0 - C_4 alkyl).

67. The compound according to any one of claims 1-62, wherein R^6 is $-OH$.

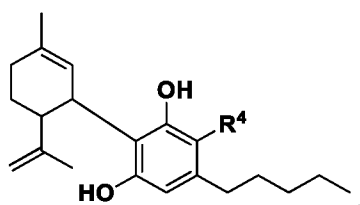
68. The compound according to claim 1, wherein the compound is of formula:



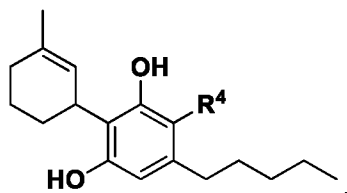
69. The compound according to claim 1, wherein the compound is of formula:



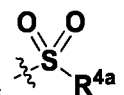
70. The compound according to claim 1, wherein the compound is of formula:



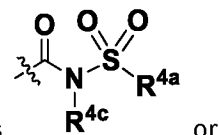
71. The compound according to claim 1, wherein the compound is of formula:



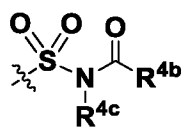
72. The compound according to any one of claims 1-71, wherein R^4 is



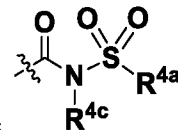
73. The compound according to any one of claims 1-71, wherein R^4 is



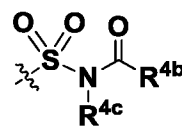
or



74. The compound according to any one of claims 1-71, wherein R^4 is



75. The compound according to any one of claims 1-71, wherein R^4 is



76. The compound according to any one of claims 1-74, wherein R^{4a} is C_1 - C_8 alkyl, C_2 - C_8 alkenyl, $-OR^{4e}$, $-(C_1-C_4 \text{ alkyl})OR^{4e}$, $-(C_1-C_4 \text{ alkyl})-C(O)(C_1-C_4 \text{ alkyl})$, $-(C_0-C_4 \text{ alkyl})$ -aryl, $-(C_0-C_4 \text{ alkyl})$ -heteroaryl, $-(C_0-C_4 \text{ alkyl})$ -cycloalkyl, $-(C_0-C_4 \text{ alkyl})$ -heterocycloalkyl, $-NR^{4d}R^{4e}$, or $-(C_1-C_4 \text{ alkyl})NR^{4d}R^{4e}$.

77. The compound according to any one of claims 1-74, wherein R^{4a} is C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or $-OR^{4e}$.

78. The compound according to any one of claims 1-74, wherein R^{4a} is C_2 - C_6 alkenyl.

79. The compound according to any one of claims 1-74, wherein R^{4a} is C_1-C_4 alkyl.
80. The compound according to any one of claims 1-74, wherein R^{4a} is $-OR^{4e}$.
81. The compound according to any one of claims 1-74, wherein R^{4a} is C_1-C_8 alkyl, C_2-C_8 alkenyl, $-(C_0-C_4 \text{ alkyl})\text{-aryl}$, $-(C_0-C_4 \text{ alkyl})\text{-heteroaryl}$, $-(C_0-C_4 \text{ alkyl})\text{-cycloalkyl}$, or $-(C_0-C_4 \text{ alkyl})\text{-heterocycloalkyl}$.
82. The compound according to any one of claims 1-74, wherein R^{4a} is $-(C_0-C_4 \text{ alkyl})\text{-aryl}$, $-(C_0-C_4 \text{ alkyl})\text{-heteroaryl}$, $-(C_0-C_4 \text{ alkyl})\text{-cycloalkyl}$, or $-(C_0-C_4 \text{ alkyl})\text{-heterocycloalkyl}$.
83. The compound according to any one of claims 1-74, wherein R^{4a} is monocyclic $-(C_0-C_1 \text{ alkyl})\text{-aryl}$, monocyclic or bicyclic $-(C_0-C_1 \text{ alkyl})\text{-heteroaryl}$, monocyclic $-(C_0-C_1 \text{ alkyl})\text{-cycloalkyl}$ or monocyclic $-(C_0-C_2 \text{ alkyl})\text{-heterocycloalkyl}$.
84. The compound according to any one of claims 1-74, wherein R^{4a} is monocyclic $-(C_0-C_1 \text{ alkyl})\text{-aryl}$ or monocyclic $-(C_0-C_1 \text{ alkyl})\text{-cycloalkyl}$.
85. The compound according to any one of claims 1-74, wherein R^{4a} is monocyclic or bicyclic $-(C_0-C_1 \text{ alkyl})\text{-heteroaryl}$ or monocyclic $-(C_0-C_2 \text{ alkyl})\text{-heterocycloalkyl}$.
86. The compound according to any one of claims 83-85, wherein each R^8 is independently C_1-C_4 alkyl, $-F$, $-Cl$, nitro, amino, methoxymethyl, cyclopropyl, phenyl, pyridyl, or $-NR^B C(O)R^A$, wherein R^B is hydrogen or methyl and R^A is hydrogen or C_1-C_4 alkyl.
87. The compound according to any one of claims 83-86, wherein each R^7 is independently C_1-C_4 alkyl, methoxymethyl, $-F$, $-Cl$, hydroxy, oxo, cyclopropyl, phenyl, or pyridyl.
88. The compound according to any one of claims 1-74, wherein R^{4a} is $-(C_1-C_4 \text{ alkyl})NR^{4d}R^{4e}$.
89. The compound according to any one of claims 1-74, wherein R^{4a} is $-NR^{4d}R^{4e}$.
90. The compound according to any one of claims 1-74, wherein R^{4a} is $-NR^{4d}R^{4e}$, wherein R^{4d} is hydrogen, C_1-C_4 alkyl, $-(C_1-C_4 \text{ alkyl})\text{-C(O)O}(R^{4e})$, $-(C_0-C_2 \text{ alkyl})\text{-aryl}$, $-(C_0-C_2 \text{ alkyl})\text{-heteroaryl}$, $-(C_0-C_2 \text{ alkyl})\text{-cycloalkyl}$, or $-(C_0-C_2 \text{ alkyl})\text{-heterocycloalkyl}$ and R^{4e} is hydrogen or C_1-C_4 alkyl.

91. The compound according to any one of claims 1-74, wherein R^{4a} is $-NR^{4d}R^{4e}$, wherein R^{4d} is hydrogen or C_1 - C_4 alkyl and R^{4e} is hydrogen or methyl.
92. The compound according to any one of claims 1-74, wherein R^{4a} is $-NR^{4d}R^{4e}$, wherein R^{4d} is $-(C_0$ - C_1 alkyl)-aryl, $-(C_0$ - C_1 alkyl)-heteroaryl, $-(C_0$ - C_1 alkyl)-cycloalkyl, or $-(C_0$ - C_1 alkyl)-heterocycloalkyl and R^{4e} is hydrogen or methyl.
93. The compound according to claim 1-71, 73 or 75, wherein R^{4b} is C_1 - C_8 alkyl, C_2 - C_8 alkenyl, $-\text{CH}_2-(\text{OCH}_2\text{CH}_2)_{0-6}\text{O}(C_1$ - C_6 alkyl), $-(C_1$ - C_4 alkyl)- $\text{C}(\text{O})\text{O}(R^{4e})$, $-(C_1$ - C_4 alkyl) OR^{4e} , $-(C_1$ - C_4 alkyl)- $\text{C}(\text{O})(C_1$ - C_4 alkyl), $-(C_0$ - C_4 alkyl)-aryl, $-(C_0$ - C_4 alkyl)-heteroaryl, $-(C_0$ - C_4 alkyl)-cycloalkyl, $-(C_0$ - C_4 alkyl)-heterocycloalkyl, or $-(C_1$ - C_4 alkyl) $\text{NR}^{4d}R^{4e}$.
94. The compound according to claim 1-71, 73 or 75, wherein R^{4b} is C_1 - C_8 alkyl, C_2 - C_8 alkenyl, or $-(C_1$ - C_4 alkyl) OR^{4e} .
95. The compound according to claim 1-71, 73 or 75, wherein R^{4b} is C_1 - C_4 alkyl.
96. The compound according to claim 1-71, 73 or 75, wherein R^{4b} is $-\text{CH}_2-(\text{OCH}_2\text{CH}_2)_{0-4}\text{O}(C_1$ - C_6 alkyl), $-(C_1$ - C_4 alkyl)- $\text{C}(\text{O})\text{O}(R^{4e})$, or $-(C_1$ - C_4 alkyl)- $\text{C}(\text{O})(C_1$ - C_4 alkyl).
97. The compound according to claim 1-71, 73 or 75, wherein R^{4b} is C_1 - C_8 alkyl, C_2 - C_8 alkenyl, $-(C_0$ - C_4 alkyl)-aryl, $-(C_0$ - C_4 alkyl)-heteroaryl, $-(C_0$ - C_4 alkyl)-cycloalkyl, or $-(C_0$ - C_4 alkyl)-heterocycloalkyl.
98. The compound according to claim 1-71, 73 or 75, wherein R^{4b} is $-(C_0$ - C_4 alkyl)-aryl, $-(C_0$ - C_4 alkyl)-heteroaryl, $-(C_0$ - C_4 alkyl)-cycloalkyl, or $-(C_0$ - C_4 alkyl)-heterocycloalkyl.
99. The compound according to claim 1-71, 73 or 75, wherein R^{4b} is monocyclic $-(C_0$ - C_1 alkyl)-aryl, monocyclic or bicyclic $-(C_0$ - C_1 alkyl)-heteroaryl, monocyclic $-(C_0$ - C_1 alkyl)-cycloalkyl or monocyclic $-(C_0$ - C_2 alkyl)-heterocycloalkyl.
100. The compound according to claim 1-71, 73 or 75, wherein R^{4b} is monocyclic $-(C_0$ - C_1 alkyl)-aryl or monocyclic $-(C_0$ - C_1 alkyl)-cycloalkyl.
101. The compound according to claim 1-71, 73 or 75, wherein R^{4b} is monocyclic or bicyclic $-(C_0$ - C_1 alkyl)-heteroaryl or monocyclic $-(C_0$ - C_2 alkyl)-heterocycloalkyl.

102. The compound according to claim 97-101, wherein each R^8 is independently C_1 - C_4 alkyl, -F, -Cl, nitro, amino, methoxymethyl, cyclopropyl, phenyl, pyridyl, or $-NR^B C(O)R^A$, wherein R^B is hydrogen or methyl and R^A is hydrogen or C_1 - C_4 alkyl.
103. The compound according to any one of claims 97-102, wherein each R^7 is independently C_1 - C_4 alkyl, methoxymethyl, -F, -Cl, hydroxy, oxo, cyclopropyl, phenyl, or pyridyl.
104. The compound according to claim 1-71, 73 or 75, wherein R^{4b} is $-(C_1-C_4 \text{ alkyl})NR^{4d}R^{4e}$.
105. The compound according to claim 1-72 or 73-104, wherein R^{4c} is hydrogen.
106. The compound according to claim 1-72 or 73-104, wherein R^{4c} is C_1 - C_4 alkyl.
107. The compound according to claim 1-106, wherein R^{4d} is hydrogen or C_1 - C_6 alkyl.
108. The compound according to any one of claims 1-107, wherein R^{4e} is hydrogen or methyl.
109. The compound according to any one of claims 1-108, wherein each alkyl is unsubstituted.
110. The compound according to any one of claims 1-109, wherein each cycloalkyl is a cyclopropane, a cyclobutane, a cyclopentane or a cyclohexane.
111. The compound according to any one of claims 1-110, wherein each heterocycloalkyl is a pyrrolidine, a piperidine, a piperazine, a tetrahydrofuran, a (1H) dihydropyran, or a morpholine.
112. The compound according to any one of claims 1-111, wherein each aryl is a phenyl.
113. The compound according to claim 112, wherein the phenyl is substituted with 0-3 R^8 .
114. The compound according to any one of claims 1-113, wherein each heteroaryl is a monocyclic or bicyclic heteroaryl.
115. The compound according to claim 114, wherein the monocyclic or bicyclic heteroaryl is substituted with 0-3 R^8 .
116. The compound according to any one of claims 1-115, wherein each R^7 is independently oxo, C_1 - C_4 alkyl, -Cl, -F, -Br, -CN, $-SF_5$, $-N_3$, nitro, $-SR^A$, $-S(O)_{1-2}R^A$, $-OR^A$, $-NR^B R^A$, $-C(O)R^A$, $-C(O)NR^B R^A$, $-NR^B C(O)R^A$, $-C(S)NR^B R^A$, $-NR^B C(S)R^A$, $-CO_2R^A$, $-OC(O)R^A$, $-C(O)SR^A$, $-SC(O)R^A$,

-C(S)OR^A, -OC(S)R^A, -C(S)SR^A, -SC(S)R^A, -S(O)₁₋₂OR^A, -OS(O)₁₋₂R^A, -S(O)₁₋₂NR^BR^A, or -NR^BS(O)₁₋₂R^A.

117. The compound according to any one of claims 1-116, wherein each R⁷ is independently oxo, C₁-C₄ alkyl, -Cl, -F, -Br, -CN, -SF₅, -N₃, nitro, -SR^A, -S(O)₁₋₂R^A, -OR^A, -NR^BR^A, or -C(O)R^A.

118. The compound according to any one of claims 1-117, wherein each R⁸ is independently C₁-C₄ alkyl, -Cl, -F, -Br, -CN, -SF₅, -N₃, nitro, -SR^A, -S(O)₁₋₂R^A, -OR^A, -NR^BR^A, -C(O)R^A, -C(O)NR^BR^A, -NR^BC(O)R^A, -C(S)NR^BR^A, -NR^BC(S)R^A, -CO₂R^A, -OC(O)R^A, -C(O)SR^A, -SC(O)R^A, -C(S)OR^A, -OC(S)R^A, -C(S)SR^A, -SC(S)R^A, -S(O)₁₋₂OR^A, -OS(O)₁₋₂R^A, -S(O)₁₋₂NR^BR^A, or -NR^BS(O)₁₋₂R^A.

119. The compound according to any one of claims 1-118, wherein each R⁸ is independently C₁-C₄ alkyl, -Cl, -F, -Br, -CN, -SF₅, -N₃, nitro, -SR^A, -S(O)₁₋₂R^A, -OR^A, -NR^BR^A, or -C(O)R^A.

120. The compound of claim 1, which is:

2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonic acid;

sodium 2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonate;

3'-methyl-3-(methylsulfonyl)-4-pentyl-[1,1'-biphenyl]-2,6-diol;

3-(cyclopropylsulfonyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-2,6-diol;

3-(tert-butylsulfonyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-2,6-diol;

3-(benzylsulfonyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-2,6-diol;

3'-methyl-4-pentyl-3-(phenylsulfonyl)-[1,1'-biphenyl]-2,6-diol;

3'-methyl-3-((4-nitrophenyl)sulfonyl)-4-pentyl-[1,1'-biphenyl]-2,6-diol;

3'-methyl-4-pentyl-3-(pyridin-3-ylsulfonyl)-[1,1'-biphenyl]-2,6-diol;

3-(furan-3-ylsulfonyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-2,6-diol;

3-((1H-imidazol-4-yl)sulfonyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-2,6-diol;

3'-methyl-3-(oxetan-3-ylsulfonyl)-4-pentyl-[1,1'-biphenyl]-2,6-diol;

3'-methyl-4-pentyl-3-((perfluorophenyl)sulfonyl)-[1,1'-biphenyl]-2,6-diol;

4-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)cyclohexan-1-one;

1-(2-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)ethyl)pyrrolidine-2,5-dione;

3-((2-(dimethylamino)ethyl)sulfonyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-2,6-diol;

1-(3-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)piperidin-1-yl)ethan-1-one;

3-((2-chloropyrimidin-5-yl)sulfonyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-2,6-diol;

2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N,3'-dimethyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N,N,3'-trimethyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;

N-cyclopropyl-2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N-isopropyl-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-3'-methyl-4-pentyl-N-phenyl-[1,1'-biphenyl]-3-sulfonamide;

N-benzyl-2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;

3'-methyl-3-((4-methylpiperazin-1-yl)sulfonyl)-4-pentyl-[1,1'-biphenyl]-2,6-diol;

3'-methyl-4-pentyl-3-(piperidin-1-ylsulfonyl)-[1,1'-biphenyl]-2,6-diol;

3'-methyl-3-(morpholinosulfonyl)-4-pentyl-[1,1'-biphenyl]-2,6-diol;

2,6-dihydroxy-3'-methyl-4-pentyl-N-(pyridin-3-yl)-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-3'-methyl-4-pentyl-N-(pyrimidin-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-3'-methyl-N-(2-oxopropyl)-4-pentyl-[1,1'-biphenyl]-3-sulfonamide; _

1-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)azetidin-3-one;

2,6-dihydroxy-3'-methyl-N-(oxetan-2-ylmethyl)-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-3'-methyl-N-(oxetan-2-ylmethyl)-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-3'-methyl-N-(oxetan-2-ylmethyl)-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;
2,6-dihydroxy-3'-methyl-N-(oxetan-2-ylmethyl)-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;
methyl ((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)alaninate;
N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-3-morpholinopropanamide;
4-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl])-3-sulfonamido)-4-oxobutanoic acid;
4-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl])-3-sulfonamido)-4-oxobutanoic acid;
2-amino-N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide;
N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(2-methoxyethoxy)acetamide;
2-amino-N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-3-hydroxypropanamide;
2-amino-N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)propanamide;
3-amino-N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-2-methylpropanamide;
N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide;
N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-3-oxobutanamide;
N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(3-methyl-1H-1,2,4-triazol-5-yl)acetamide;
N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-1H-1,2,4-triazole-5-carboxamide;
N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)oxetane-2-carboxamide;
N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)benzamide;
N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)nicotinamide;

N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-2-phenylacetamide;

N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(furan-2-yl)acetamide;

N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(oxazol-2-yl)acetamide;

N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(thiazol-2-yl)acetamide;

2-(1H-benzo[d]imidazol-2-yl)-N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide;

2,6-dihydroxy-3'-methyl-4-pentyl-N-(phenylsulfonyl)-[1,1'-biphenyl]-3-carboxamide;

N-(cyclohexylsulfonyl)-2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-carboxamide;

(E)-2,6-dihydroxy-3'-methyl-4-pentyl-N-(prop-1-en-1-ylsulfonyl)-[1,1'-biphenyl]-3-carboxamide;

N-((1H-benzo[d]imidazol-2-yl)sulfonyl)-2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-carboxamide;

N,N-diethyl-2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;

N-(2-bromoethyl)-2,6-dihydroxy-N-(2-hydroxyethyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonamide;

2,2,2-trifluoroethyl 2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-sulfonate;

-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)-4-(trifluoromethyl)benzamide;

N-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)pivalamide;

2,6-dihydroxy-N,N,3'-trimethyl-4-propyl-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N-isopropyl-3'-methyl-4-propyl-[1,1'-biphenyl]-3-sulfonamide;

3-(ethylsulfonyl)-3'-methyl-4-pentyl-[1,1'-biphenyl]-2,6-diol;

tert-butyl 4-((2,6-dihydroxy-3'-methyl-4-pentyl-[1,1'-biphenyl]-3-yl)sulfonyl)piperazine-1-carboxylate;

2,6-dihydroxy-3'-methyl-4-pentyl-N-(pyridin-3-ylsulfonyl)-[1,1'-biphenyl]-3-carboxamide;

2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonic acid;

sodium 2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonate;

5'-methyl-3-(methylsulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;

3-(cyclopropylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;

3-(tert-butylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;

3-(benzylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;

5'-methyl-4-pentyl-3-(phenylsulfonyl)-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;

5'-methyl-3-((4-nitrophenyl)sulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;

5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-3-(pyridin-3-ylsulfonyl)-[1,1'-biphenyl]-2,6-diol;

3-(furan-3-ylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;

3-((1H-imidazol-4-yl)sulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;

5'-methyl-3-(oxetan-3-ylsulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;

5'-methyl-4-pentyl-3-((perfluorophenyl)sulfonyl)-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;

4-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)cyclohexan-1-one;

1-(2-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)ethyl)pyrrolidine-2,5-dione;

3-((2-(dimethylamino)ethyl)sulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;

1-(3-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)piperidin-1-yl)ethan-1-one;

3-((2-chloropyrimidin-5-yl)sulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;

2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N,5'-dimethyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N,N,5'-trimethyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

N-cyclopropyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N-isopropyl-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-5'-methyl-4-pentyl-N-phenyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

N-benzyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

5'-methyl-3-((4-methylpiperazin-1-yl)sulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;

5'-methyl-4-pentyl-3-(piperidin-1-ylsulfonyl)-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;

5'-methyl-3-(morpholinosulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;

2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-N-(pyridin-3-yl)-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-N-(pyrimidin-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-N-(pyrimidin-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

1-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)azetidin-3-one;

2,6-dihydroxy-5'-methyl-N-(oxetan-2-ylmethyl)-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

3-((2-azaspiro[3.3]heptan-2-yl)sulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;

3-((2,6-diazaspiro[3.3]heptan-2-yl)sulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;

((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)alanine;

methyl ((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)alaninate;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-3-morpholinopropanamide;

4-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl])-3-sulfonamido)-4-oxobutanoic acid;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-3-(4-methylpiperazin-1-yl)propanamide;

2-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(2-methoxyethoxy)acetamide;

2-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-3-hydroxypropanamide;

2-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)propanamide;

3-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-2-methylpropanamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-3-oxobutanamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-3-oxobutanamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-3-oxobutanamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-3-oxobutanamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-3-oxobutanamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)nicotinamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-2-phenylacetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(furan-2-yl)acetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(oxazol-2-yl)acetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(thiazol-2-yl)acetamide;

2-(1H-benzo[d]imidazol-2-yl)-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide;

2,6-dihydroxy-5'-methyl-4-pentyl-N-(phenylsulfonyl)-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-carboxamide;

N-(cyclohexylsulfonyl)-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-carboxamide;

(E)-2,6-dihydroxy-5'-methyl-4-pentyl-N-(prop-1-en-1-ylsulfonyl)-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-carboxamide;

N-((1H-benzo[d]imidazol-2-yl)sulfonyl)-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-carboxamide;

N,N-diethyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

N-(2-bromoethyl)-2,6-dihydroxy-N-(2-hydroxyethyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonamide;

2,2,2-trifluoroethyl 2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-sulfonate;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)-4-(trifluoromethyl)benzamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)pivalamide;

2,6-dihydroxy-N,N,5'-trimethyl-2'-(prop-1-en-2-yl)-4-propyl-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N,N,5'-trimethyl-2'-(prop-1-en-2-yl)-4-propyl-[1,1'-biphenyl]-3-sulfonamide;

3-(ethylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-2,6-diol;

tert-butyl 4-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-[1,1'-biphenyl]-3-yl)sulfonyl)piperazine-1-carboxylate;

2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-N-(pyridin-3-ylsulfonyl)-[1,1'-biphenyl]-3-carboxamide;

2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonic acid;

sodium 2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonate;

5'-methyl-3-(methylsulfonyl)-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

3-(cyclopropylsulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

3-(tert-butylsulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

3-(benzylsulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

5'-methyl-4-pentyl-3-(phenylsulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

5'-methyl-3-((4-nitrophenyl)sulfonyl)-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

5'-methyl-4-pentyl-3-(pyridin-3-ylsulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

3-(furan-3-ylsulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

3-((1H-imidazol-4-yl)sulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

5'-methyl-3-(oxetan-3-ylsulfonyl)-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

5'-methyl-4-pentyl-3-((perfluorophenyl)sulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

4-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)cyclohexan-1-one;

1-(2-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)ethyl)pyrrolidine-2,5-dione;

3-((2-(dimethylamino)ethyl)sulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

1-(3-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)piperidin-1-yl)ethan-1-one;

3-((2-chloropyrimidin-5-yl)sulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N,N,5'-trimethyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

N-cyclopropyl-2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N-isopropyl-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-5'-methyl-4-pentyl-N-phenyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

N-benzyl-2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

5'-methyl-3-((4-methylpiperazin-1-yl)sulfonyl)-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

5'-methyl-4-pentyl-3-(piperidin-1-ylsulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

5'-methyl-3-(morpholinosulfonyl)-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

2,6-dihydroxy-5'-methyl-4-pentyl-N-(pyridin-3-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-5'-methyl-4-pentyl-N-(pyrimidin-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-5'-methyl-N-(2-oxopropyl)-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

1-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)azetidin-3-one;

2,6-dihydroxy-5'-methyl-N-(oxetan-2-ylmethyl)-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

3-((2-azaspiro[3.3]heptan-2-yl)sulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

3-((2,6-diazaspiro[3.3]heptan-2-yl)sulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

3-((2,6-diazaspiro[3.3]heptan-2-yl)sulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

methyl ((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)alaninate;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-3-morpholinopropanamide;

4-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl])-3-sulfonamido)-4-oxobutanoic acid;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-3-(4-methylpiperazin-1-yl)propanamide;

2-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(2-methoxyethoxy)acetamide;

2-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-3-hydroxypropanamide;

2-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)propanamide;

3-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-methylpropanamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-3-oxobutanamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(3-methyl-1H-1,2,4-triazol-5-yl)acetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-1H-1,2,4-triazole-5-carboxamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)oxetane-2-carboxamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)benzamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)nicotinamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-phenylacetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(furan-2-yl)acetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(oxazol-2-yl)acetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(thiazol-2-yl)acetamide;

2-(1H-benzo[d]imidazol-2-yl)-N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide;

2,6-dihydroxy-5'-methyl-4-pentyl-N-(phenylsulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide;

N-(cyclohexylsulfonyl)-2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide;

(E)-2,6-dihydroxy-5'-methyl-4-pentyl-N-(prop-1-en-1-ylsulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide;

N-((1H-benzo[d]imidazol-2-yl)sulfonyl)-2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide;

N,N-diethyl-2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

N-(2-bromoethyl)-2,6-dihydroxy-N-(2-hydroxyethyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,2,2-trifluoroethyl 2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonate;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-4-(trifluoromethyl)benzamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)pivalamide;

2,6-dihydroxy-N,N,5'-trimethyl-4-propyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N-isopropyl-5'-methyl-4-propyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

3-(ethylsulfonyl)-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

tert-butyl 4-((2,6-dihydroxy-5'-methyl-4-pentyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)piperazine-1-carboxylate;

2,6-dihydroxy-5'-methyl-4-pentyl-N-(pyridin-3-ylsulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide;

2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonic acid;

sodium 2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonate;

5'-methyl-3-(methylsulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

3-(cyclopropylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

3-(tert-butylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

3-(benzylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

5'-methyl-4-pentyl-3-(phenylsulfonyl)-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

5'-methyl-4-pentyl-3-(phenylsulfonyl)-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-3-(pyridin-3-ylsulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

3-(furan-3-ylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

3-((1H-imidazol-4-yl)sulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

5'-methyl-3-(oxetan-3-ylsulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

5'-methyl-3-(oxetan-3-ylsulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

4-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)cyclohexan-1-one;

1-(2-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)ethyl)pyrrolidine-2,5-dione;

3-((2-(dimethylamino)ethyl)sulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

1-(3-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)piperidin-1-yl)ethan-1-one;

3-((2-chloropyrimidin-5-yl)sulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N,5'-dimethyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N,N,5'-trimethyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

N-cyclopropyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N-isopropyl-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-5'-methyl-4-pentyl-N-phenyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

N-benzyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

5'-methyl-3-((4-methylpiperazin-1-yl)sulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

5'-methyl-4-pentyl-3-(piperidin-1-ylsulfonyl)-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

5'-methyl-3-(morpholinosulfonyl)-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-N-(pyrimidin-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-5'-methyl-N-(2-oxopropyl)-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

1-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)azetidin-3-one;

2,6-dihydroxy-5'-methyl-N-(oxetan-2-ylmethyl)-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

3-((2-azaspiro[3.3]heptan-2-yl)sulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

3-((2,6-diazaspiro[3.3]heptan-2-yl)sulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)alanine;

methyl ((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)alaninate;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-3-morpholinopropanamide;

4-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamido)-4-oxobutanoic acid;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-3-(4-methylpiperazin-1-yl)propanamide;

2-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(2-methoxyethoxy)acetamide;

2-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-3-hydroxypropanamide;

2-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)propanamide;

3-amino-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-methylpropanamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-3-oxobutanamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(3-methyl-1H-1,2,4-triazol-5-yl)acetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-1H-1,2,4-triazole-5-carboxamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)oxetane-2-carboxamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)oxetane-2-carboxamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)nicotinamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-phenylacetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(furan-2-yl)acetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(oxazol-2-yl)acetamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-2-(thiazol-2-yl)acetamide;

2-(1H-benzo[d]imidazol-2-yl)-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide;

2-(1H-benzo[d]imidazol-2-yl)-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide;

2-(1H-benzo[d]imidazol-2-yl)-N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)acetamide;

(E)-2,6-dihydroxy-5'-methyl-4-pentyl-N-(prop-1-en-1-ylsulfonyl)-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide;

(E)-2,6-dihydroxy-5'-methyl-4-pentyl-N-(prop-1-en-1-ylsulfonyl)-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide;

N,N-diethyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

N-(2-bromoethyl)-2,6-dihydroxy-N-(2-hydroxyethyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,2,2-trifluoroethyl-2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonate;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)-4-(trifluoromethyl)benzamide;

N-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)pivalamide;

2,6-dihydroxy-N,N,5'-trimethyl-2'-(prop-1-en-2-yl)-4-propyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

2,6-dihydroxy-N-isopropyl-5'-methyl-2'-(prop-1-en-2-yl)-4-propyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-sulfonamide;

3-(ethylsulfonyl)-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-2,6-diol;

tert-butyl 4-((2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-yl)sulfonyl)piperazine-1-carboxylate; or

2,6-dihydroxy-5'-methyl-4-pentyl-2'-(prop-1-en-2-yl)-N-(pyridin-3-ylsulfonyl)-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide.

121. A pharmaceutical composition comprising a compound of any one of claims 1 to 120, or an enantiomer, diastereomer, racemate, tautomer, or metabolite thereof, or a pharmaceutically acceptable salt, solvate or hydrate of the compound, enantiomer, diastereomer, racemate, tautomer, or metabolite, together with a pharmaceutically acceptable excipient, diluent, or carrier.

122. A method of treating or preventing a disease associated with cannabinoid receptor in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of a compound according to any one of claims 1 to 120 or a composition according to claim 121.

123. The method of claim 122, wherein the cannabinoid receptor is one or more of CB1, CB2, 5HT1A, 5HT2A, GPR18, GPR55, GPR119, TRPV1, TRPV2, PPAR γ or a μ -opioid receptor.

124. The method of claim 122 or 123, wherein the cannabinoid receptor is CB1 or CB2.

125. A method of treating or preventing a disease in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of a compound according to any one of claims 1 to 120 or a composition according to claim 121, wherein the disease is acute pain, ADHD/ADD, alcohol use disorder, allergic asthma, ALS, Alzheimer's,

anorexia (e.g. HIV-related cachexia), anxiety disorders (e.g., social anxiety disorder, specific phobia, test anxiety, generalized anxiety disorder), arthritis, atherosclerosis, autism, bipolar disorder, burns, cancer, cancer pain, Charcot-Marie-Tooth disease, chronic inflammatory demyelinating polyneuropathies, chronic pain, chronic allograft nephropathy, cocaine use disorder, complex regional pain syndrome, congestive heart failure, depression, fibromyalgia, fragile X syndrome/FXTAS, frontotemporal dementias (behavioural variant), gingivitis pyrexia, glaucoma, glioblastoma, glomerulonephropathy, Huntington's disease, hypertrophic scars, IBD/IBS, inflammation, Inflammatory myopathies, ischemia, kidney fibrosis, keloids, leukodystrophies, liver fibrosis, liver cirrhosis, lung fibrosis, migraine, multiple sclerosis, myocardial infarction, nausea (e.g. CINV, motion sickness), neuropathic pain (e.g., postherpetic neuralgia, painful diabetic neuropathy), nightmare disorder, non-alcoholic fatty liver disease, obesity, obsessive-compulsive disorder, opioid sparing, opioid use disorder, osteoarthritis, osteoporosis, Parkinson's, post-concussion syndrome/traumatic brain injury, psychosis/schizophrenia, PTSD, regulation of bone mass, REM sleep behaviour disorder, reperfusion injury, Rett syndrome, rheumatoid arthritis, skin conditions (e.g. acne, psoriatic arthritis), sleep disorders (e.g., insomnia, RLS), spinocerebellar ataxias, systemic fibrosis, systemic sclerosis, thermal injury, tobacco use disorder/nicotine dependence, Tourette's, tumors, or trigeminal neuralgia.

126. Use of a compound according to any one of claims 1 to 120 or a composition according to claim 121 for the treatment or prevention of a disease associated with a cannabinoid receptor.

127. The use according to claim 126, wherein the cannabinoid receptor is one or more of CB1, CB2, 5HT1A, 5HT2A, GPR18, GPR55, GPR119, TRPV1, TRPV2, PPAR γ , or a μ -opioid receptor.

128. The use according to claim 126 or 127, wherein the cannabinoid receptor is CB1 or CB2.

129. Use of a compound according to any one of claims 1 to 120 or a composition according to claim 121 for selectively modulating the activity of a CB1 or CB2 receptor.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/CA2020/050969

A. CLASSIFICATION OF SUBJECT MATTER

IPC: **C07C 311/29** (2006.01), **A61K 31/18** (2006.01), **A61K 31/185** (2006.01), **A61K 31/335** (2006.01), **A61K 31/395** (2006.01), **A61K 31/41** (2006.01) (more IPCs on the last page)

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC: **C07C 311/29** (2006.01), **A61K 31/18** (2006.01), **A61K 31/185** (2006.01), **A61K 31/335** (2006.01), **A61K 31/395** (2006.01), **A61K 31/41** (2006.01) (more IPCs on the last page)

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

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

STN (Registry File, CAPLUS), Questel Orbit, Canadian Patent Database (search terms: Cannabinoids, CB1 receptor, CB2 receptor, serotonin receptor, sulfonic acid, sulfonate, sulfonyl, sulfonamide, sulfonamido, biphenyl)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2018/035450 A1 (ROSCOW) 22 February 2018 (22-02-2018) *pg. 17, 18, 23, 24*	1-129
A	US 2003/0232802 A1 (HEIL et al.) 18 December 2003 (18-12-2003) *pg. 21, Ex. 1, and Table 2*	1-129
A	WO 2011/006099 A1 (MARRIYNNIS et al.) 13 January 2011 (13-01-2011) *pg. 27, Table 1, compd. 3.14; pg. 31, Table 2, compd. 4.14; pg. 33, Table 3, compd. 5.14*	1-129
P, X	US 10683265 B1 (QU et al.) 16 June 2020 (16-06-2020) *col. 6, 7, 8, 9; claim 1*	1, 2, 5, 7-9, 11-14, 25-28, 30, 45-49, 51, 53, 60-62, 64-72, 76, 89, 90, 91, 109, 120-129

☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

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

Date of the actual completion of the international search
02 September 2020 (02-09-2020)

Date of mailing of the international search report
08 October 2020 (08-10-2020)

Name and mailing address of the ISA/CA
Canadian Intellectual Property Office
Place du Portage I, C114 - 1st Floor, Box PCT
50 Victoria Street
Gatineau, Quebec K1A 0C9
Facsimile No.: 819-953-2476

Authorized officer

Olusola Womiloju (819) 639-9409

INTERNATIONAL SEARCH REPORT

International application No.

PCT/CA2020/050969

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, X	WO 2020/002587 A1 (STUPPLE et al.) 2 January 2020 (02-01-2020) *pg. 102, Table A, Ex. 10*	1, 2, 4, 7-11, 25-28, 30, 45, 60, 61, 63, 72, 76, 89, 90, 92, 114, 115, 121-129
P, X	WO 2019/243491 A1 (STUPPLE et al.) 26 December 2019 (26-12-2019) *pg. 156, Table F, compd. 96	1, 2, 4, 7-11, 25-28, 30, 45, 60, 61, 63, 72, 76, 89, 90, 92, 114, 115, 121-129

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.

PCT/CA2020/050969

Patent Document Cited in Search Report	Publication Date	Patent Family Member(s)	Publication Date
WO2018035450A1	22 February 2018 (22-02-2018)	AU2017313843A1 BR112019003024A2 BR112019003024A8 CA3033875A1 CL2019000434A1 CN109890202A CO2019002123A2 EP3500090A1 EP3500090A4 MX2019001968A PE20190654A1 US2020181631A1 ZA201900986B	07 March 2019 (07-03-2019) 14 May 2019 (14-05-2019) 10 September 2019 (10-09-2019) 22 February 2018 (22-02-2018) 24 May 2019 (24-05-2019) 14 June 2019 (14-06-2019) 31 May 2019 (31-05-2019) 26 June 2019 (26-06-2019) 08 January 2020 (08-01-2020) 02 October 2019 (02-10-2019) 08 May 2019 (08-05-2019) 11 June 2020 (11-06-2020) 18 December 2019 (18-12-2019)
US2003232802A1	18 December 2003 (18-12-2003)	US6919470B2 AR027982A1 AU6211101A BG107118A BR0109698A CA2404545A1 CN1430602A CZ20023257A3 DE10015866A1 DOP2001000140A EE200200563A EP1278722A1 GT200100047A HU0300265A2 IL151679D0 JP2003529580A KR20020091165A MA25741A1 MXPA02009618A NO20024617D0 NO20024617L PE20011224A1 PL359652A1 SK14032002A3 SV2002000355A WO0174763A1 ZA200207091B	19 July 2005 (19-07-2005) 23 April 2003 (23-04-2003) 15 October 2001 (15-10-2001) 30 April 2003 (30-04-2003) 11 February 2003 (11-02-2003) 11 October 2001 (11-10-2001) 16 July 2003 (16-07-2003) 16 April 2003 (16-04-2003) 11 October 2001 (11-10-2001) 15 July 2002 (15-07-2002) 15 April 2004 (15-04-2004) 29 January 2003 (29-01-2003) 31 December 2001 (31-12-2001) 28 June 2003 (28-06-2003) 10 April 2003 (10-04-2003) 07 October 2003 (07-10-2003) 05 December 2002 (05-12-2002) 01 April 2003 (01-04-2003) 14 May 2003 (14-05-2003) 26 September 2002 (26-09-2002) 13 November 2002 (13-11-2002) 01 February 2002 (01-02-2002) 23 August 2004 (23-08-2004) 01 April 2003 (01-04-2003) 07 June 2002 (07-06-2002) 11 October 2001 (11-10-2001) 04 September 2003 (04-09-2003)
WO2011006099A1	13 January 2011 (13-01-2011)	US2012172339A1	05 July 2012 (05-07-2012)
US10683265B1	16 June 2020 (16-06-2020)	DE102019133627B3	23 July 2020 (23-07-2020)
WO2020002587A1	02 January 2020 (02-01-2020)	GB201810581D0 TW202012379A	15 August 2018 (15-08-2018) 01 April 2020 (01-04-2020)
WO2019243491A1	26 December 2019 (26-12-2019)	GB201810092D0 TW202016103A US2020039945A1 UY38270A	08 August 2018 (08-08-2018) 01 May 2020 (01-05-2020) 06 February 2020 (06-02-2020) 31 January 2020 (31-01-2020)

A61K 31/4196 (2006.01), *A61K 31/421* (2006.01), *A61K 31/426* (2006.01), *A61K 31/44* (2006.01),
A61K 31/445 (2006.01), *A61K 31/495* (2006.01), *A61K 31/505* (2006.01), *A61K 31/5375* (2006.01),
C07C 309/42 (2006.01), *C07C 317/22* (2006.01), *C07C 317/24* (2006.01), *C07D 205/06* (2006.01),
C07D 205/12 (2006.01), *C07D 207/404* (2006.01), *C07D 211/54* (2006.01), *C07D 213/61* (2006.01),
C07D 213/71 (2006.01), *C07D 233/84* (2006.01), *C07D 235/04* (2006.01), *C07D 239/38* (2006.01),
C07D 249/08 (2006.01), *C07D 263/32* (2006.01), *C07D 277/30* (2006.01), *C07D 295/15* (2006.01),
C07D 295/26 (2006.01), *C07D 305/06* (2006.01), *C07D 305/08* (2006.01), *C07D 307/64* (2006.01),
C07D 487/04 (2006.01)