

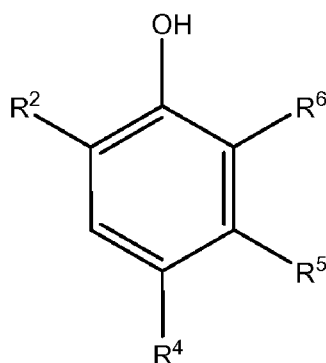


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- (71) **Applicant:** TANSNA THERAPEUTICS, INC. [US/US];
4320 Forest Park Avenue, Suite 304, Saint Louis, Missouri
63108 (US).
- (72) **Inventors:** BAKER, Max; c/o Tansna Therapeutics Inc.,
2500 Crosspark Road, Ste E141, Coralville, Iowa 52241
(US). MISHRA, Rajesh Kumar; c/o Tansna Therapeutics
Inc., 2500 Crosspark Road, Ste E141, Coralville, Iowa
52241 (US). TALLEY, John, J.; 6519 Walsh St., Saint
Louis, Missouri 63109 (US). MARTINEZ, Eduardo J.;
632 Dayton Road, Bryn Mawr, Pennsylvania 19010 (US).
- (74) **Agent:** DELASSUS, Gregory S.; Harness, Dickey &
Pierce, P.L.C., 7700 Bonhomme, Suite 400, Saint Louis,
Missouri 63105 (US).

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(54) **Title:** 2,5-DIALKYL-4-H/HALO/ETHER-PHENOL COMPOUNDS

(I)

(57) **Abstract:** The present disclosure provides phenolic compounds useful in the treatment of neurological conditions such as convulsions and tremors, having the structure of Formula (I): wherein R^2 , R^4 , R^5 , & R^6 , are as defined in the detailed description; pharmaceutical compositions comprising at least one of the compounds; and methods for treating neurological conditions.

2,5-DIALKYL-4-H/HALO/ETHER-PHENOL COMPOUNDS

[0001] This invention was made with government support under Grant Number 1R43NS076358-01 awarded by the National Institutes of Health. The government has
5 certain rights in the invention.

1. Field of the Invention

[0002] This invention relates to compounds having beneficial effects in the central nervous system (CNS) of mammals. More specifically, this invention relates to
10 compounds that prevent or halt ongoing seizures in mammals, and thus have antiepileptic/anticonvulsant activities that are useful for treating epileptics and other patients having seizures. In addition, the compounds described herein can have anti-inflammatory properties. The compounds disclosed exert anticonvulsant effects while having low side effects. In addition, this invention relates to compounds useful for treating
15 other pathological conditions of the CNS including anxiety, bipolar disorder, chronic or neuropathic pain, migraine headache, depression, schizophrenia, spasticity, tinnitus, and head trauma.

BACKGROUND

20 [0003] Epilepsy is a complex CNS condition involving excessive neuronal discharges that result in the occurrence of seizures (Stefan H, Feuerstein TJ, *Pharmacol Therapeut* 2007; 113:165–83).

[0004] Seizures may be localized (focal) or generalized within the brain. (Smith M, Wilcox KS, White HS, *Neurotherapeutics* 2007; 4:12–17)

25 [0005] Seizures may be expressed outwardly as convulsions or they may be non-convulsive (Kwan P, Brodie MJ, *Expert Opinion on Emerging Drugs* 2007; 12:407–22). Focal (partial) seizures are the most common in humans.

[0006] Epilepsy occurs in approximately 0.5 to 1% of the human population (Smith M, Wilcox KS, White HS, *Neurotherapeutics* 2007; 4:12–17). Chronic, daily treatment with
30 antiepileptic drugs (AEDs) continues to be the standard of care for these patients.

[0007] These existing AEDs, however, have varying degrees of effectiveness in suppressing seizures in humans (Stefan H, Feuerstein TJ, *Pharmacol Therapeut* 2007; 113:165–83).

[0008] In particular, it is estimated that 30% of all epilepsy patients are refractory to current AEDs (Malawska B, Kulig K., *Expert Opin Inv Drug* 2008; 17:361–69).

[0009] Epilepsy patients who are refractory, do not respond to the currently available AEDs (Hitiris N, Brodie MJ, *Curr Opin Neurol* 2006; 19:175–80).

[0010] Refractory epilepsy is defined as failure of adequate trials of two tolerated and appropriately chosen and used AED (anti-epilepsy drug) schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom (Kwan P, Arzimanoglou A, Berg AT, *et al.* (vol 51, pg 1069, 2010). *Epilepsia* 2010; 51:1922).

[0011] Although suboptimal, therapeutic strategies for refractory patients frequently include polytherapy and drug rotation performed on a trial-and-error fashion which usually has limited success (Pathan SA, Jain GK, Akhter S, Vohora D, Ahmad FJ, Khar RK, *Drug Discovery Today* 2010; 15:717–32). The percentage of epilepsy patients that remain refractory to available drugs has not improved appreciably over the decades.

[0012] Treatment of seizures with anticonvulsant drugs also has drawbacks due to the significant occurrence of side-effects. Common side effects of AEDs include sedation, somnolence, depression and other neuropsychological deficits (Wuttke TV, Lerche H, *Expert Opinion on Investigational Drugs* 2006; 15:1167–77) that interfere with a patient's quality and functioning in daily life. Side effects also are a major limitation to escalating patient doses in attempts to suppress seizures.

[0013] As described above, there is a significant need for new anticonvulsant drugs that are more efficacious and have lesser side effects than the currently available compounds. As a group antiseizure compounds are known to interact with a diversity of molecular targets that suppress nerve excitability and likely do so by exerting multiple mechanisms of action. Known mechanisms include effects on voltage-gated ion channels, non-specific cation channels, ligand-gated ion channels, excitatory amino acid receptors, neurotransmitter transporters, and neurotransmitters.

[0014] The alkyl substituted phenol, propofol, has good anticonvulsant activity in human *status epilepticus* (Kinirons P, Doherty CP, *Eur J Emerg Med* 2008; 15:187–95) the most debilitating form of human seizures.

[0015] Unfortunately, propofol cannot be used for more widespread and chronic/daily use. (Marik PE, Varon J, *Chest* 2004; 126:582–91).

[0016] Although approved for anesthesia, it is only used in acute care settings due to sedation and respiratory depression side-effects (Langley MS, Heel RC, *Drugs* 1988; 35:334–72).

[0017] The mechanisms by which propofol inhibits human *status epilepticus* are unknown. It is believed that propofol's anesthetic/sedative effects result from it being an agonist and potentiator of the GABA_A receptors (Bali M, Akabas MH, *Mol Pharmacol* 2004; 65:68–76)

10 [0018] The mode of action of propofol analogs is similarly elusive (Krasowski MD, Jenkins A, Flood P, Kung AY, Hopfinger AJ, Harrison NL, *Journal of Pharmacology and Experimental Therapeutics* 2001; 297:338–51).

[0019] GABA_A receptor agonism/potentialiation is also known to be a mechanism of some anticonvulsant compounds (Myhrer T, Nguyen NHT, Enger S, Aas P, *Arch Toxicol* 2006; 80:502–07).

[0020] GABA_A receptor agonism/potentialiation is presumed to be a component of propofol's anticonvulsant mechanism (Ragavendran JV, Sriram D, Kotapati S, Stables J, Yogeewari P, *European Journal of Medicinal Chemistry* 2008; 43:2650–55).

20 [0021] GABA_A receptor stimulation depresses nerve conduction by hyperpolarizing the neuronal membrane and suppressing impulse conduction. GABA receptors, which exist as multiple isoforms with different sensitivities to agonists (Atack JR, *Curr Top Med Chem* 2011; 11:1176–202).

[0022] GABA receptors are known to be present in nerves that excessively fire causing seizures. Other studies show that propofol can block sodium channels (Jones PJ, Wang YS, Smith MD, *et al.*, *J Pharmacol Exp Ther* 2007; 320:828–36).

[0023] Propofol has also been reported to down-regulate glutamatergic synaptic transmission (Snyder GL, Galdi S, Hendrick JP, Hemmings HC, *Neuropharmacology* 2007; 53:619–30), other known anticonvulsant mechanisms. Unlike the barbiturate or benzodiazepine drug families, which have different members useful for
30 anesthesia/sedation and anticonvulsant activity, propofol is the sole member of the alkyl phenolic class on the market.

[0024] Previously it has been shown that carvacrol, thymol, and other substituted phenols in essential oils have antibacterial and antifungal properties and cause. (Stefanakis *et al.*

(2013) *Food Control* 34:539–46).

[0025] Certain substituted phenols show bacteriostatic and bacteriocidal effects toward *Eschericia coli*, *Staphylococcus aureus*, *Listeria monocytogenes*, and *Bacillus cereus* (Klein *et al.* (2013) *Current Microbiology* 67: 200–08).

5

2. Description of the Related Art

[0026] Compounds useful as voltage-gated sodium channel inhibitors are described by Hadidah-Ruah *et al.*, in WO 2011/140425 published 10 November 2008. The compounds described therein include 4-iodo-2,5-dimethyl-phenol used as an intermediate to make 4-isopropoxy-2,5-dimethylbenzoic acid. 4-isopropoxy-2,5-dimethylbenzoic acid is used as an intermediate in a multi-step process to make compounds useful as voltage-gated sodium channel inhibitors.

[0027] Amine containing compounds useful for mainly excitatory CNS effects are described in Ermili *et al.*, *Edizione Scientifica*, 32(10):713–24 (1977). 4-chloro-2-isopropyl-5-methylphenol is used as an intermediate to make compounds which had mainly excitatory CNS effects. Two end product compounds, Ve (2-dimethylamino-6-methylchromone) and Vs (2-(dimethylamino)-4H-benzo[h]chromen-4-one), have weak anti-convulsant activity. 4-chloro-2-isopropyl-5-methylphenol is not used as an intermediate in the synthesis of these two compounds.

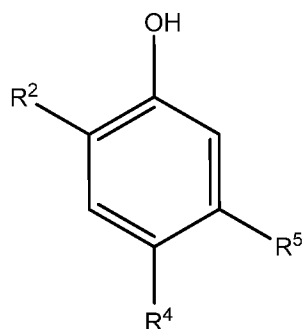
[0028] Phenol derivatives with known GABAnergic activity and structurally similar phenol derivatives were tested for lipophilic parameters because GABA receptors are present in cell membranes in Reiner *et al.*, *Colloids and Surfaces, B: Biointerfaces*, 101:61–67 (2013). Reiner *et al.* considered 4-chloro-2-isopropyl-5-methylphenol to be structurally related to the compound thymol, which has known GABAnergic activity, so 4-chloro-2-isopropyl-5-methylphenol was tested for membrane interaction. All five phenol derivatives tested were shown to interact with membranes.

SUMMARY OF THE INVENTION

[0029] In a first embodiment (Embodiment 1), a method is provided for treating and/or improving a condition selected from the group consisting of Alzheimer's Disease, anxiety, bipolar disorder, convulsions, dementia, depression, epilepsy, fibromyalgia, Huntington's Chorea, mania, memory, migraine, multiple sclerosis, neuropathic pain, Parkinson's Disease, seizures, tinnitus, Tourette's Syndrome, and tremors, comprising

administering a therapeutically effective amount of a compound or pharmaceutically acceptable salt of the compound, wherein the compound has the structure of Formula (I):

(I)



wherein:

R² is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

R⁴ is selected from the group consisting of H, halo, and alkoxy, wherein the alkoxy may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl and halo, and wherein R⁴ is not methyl; and

R⁵ is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl.

15

[0030] Embodiment 2 is the method of Embodiment 1 wherein each of R² and R⁵ has between one and five carbons.

20

[0031] Embodiment 3 is the method of Embodiment 1 wherein the condition is epilepsy, seizures, or convulsions.

[0032] Embodiment 4 is the method of Embodiment 1 wherein the condition is neuropathic pain or fibromyalgia.

25

[0033] Embodiment 5 is the method of Embodiment 1 wherein the condition is a psychological disorder.

30

[0034] Embodiment 6 is the method of Embodiment 5 wherein the psychological disorder is anxiety, mania, bipolar disorder, or depression.

[0035] Embodiment 7 is the method of Embodiment 1, wherein the condition is Alzheimer's Disease, Huntington's Disease, Multiple Sclerosis, Parkinson's disease, Tourette's Syndrome, tinnitus, and tremors.

[0036] Embodiment 8 is the method of Embodiment 1, wherein:

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

R^4 is halo.

5

[0037] Embodiment 9 is the method of Embodiment 8, wherein:

R^4 is selected from the group consisting of Br, Cl, and F.

[0038] Embodiment 10 is the method of Embodiment 9, wherein:

10 R^2 is alkyl; and

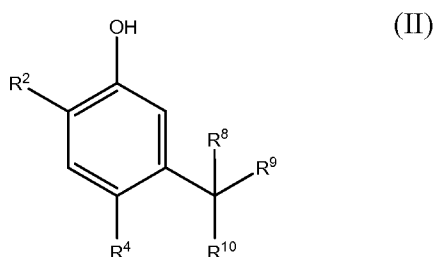
R^5 is alkyl having two or more carbons.

[0039] Embodiment 11 is the method of Embodiment 10, wherein the compound is selected from a group consisting of: 4-chloro-5-*tert*-butyl-2-methyl-phenol; 4-chloro-2-isopropyl-5-methyl-phenol; 4-fluoro-2-isopropyl-5-methyl-phenol; 4-chloro-2,5-diisopropyl-phenol; 4-bromo-5-isopropyl-2-methyl-phenol; 4-bromo-2-isopropyl-5-methyl-phenol; and 4-bromo-2-*tert*-butyl-5-isopropyl-phenol.

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[0040] Embodiment 12 is the method of Embodiment 1, wherein the compound has the structure of Formula (II):

20



25

wherein:

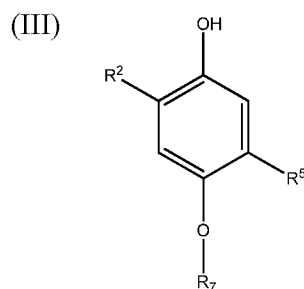
R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

R^4 is selected from the group consisting of Br, Cl, and F; and

R^8 , R^9 and R^{10} are each independently selected from the group consisting of H, alkyl,

30 and haloalkyl.

[0041] Embodiment 13 is the method of Embodiment 1, wherein the compound has the structure of Formula (III):



5

wherein:

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

R^5 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl; and

R^7 is selected from the group consisting of alkyl and haloalkyl.

10

[0042] Embodiment 14 is the method of Embodiment 13, wherein:

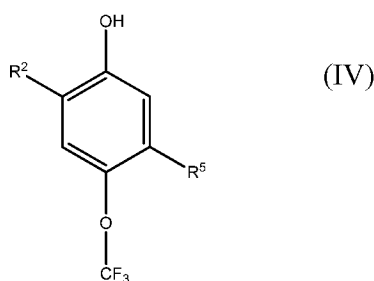
R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

R^5 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl; and

R^7 is alkyl.

15

[0043] Embodiment 15 is the method of Embodiment 14, wherein the compound has the structure of Formula (IV):



20

wherein:

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl; and

25

R^5 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl.

[0044] Embodiment 16 is the method of Embodiment 15, wherein:

R^2 is selected from the group consisting of alkyl and cycloalkyl; and

R^5 is selected from the group consisting of alkyl and cycloalkyl.

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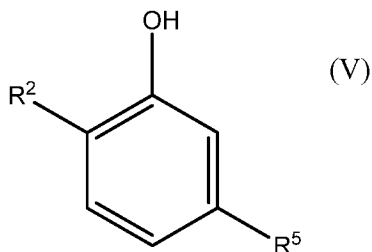
[0045] In yet another embodiment (Embodiment 17) a compound is provided, selected from the group consisting of: 4-bromo-5-ethyl-2-methyl-phenol; 4-fluoro-5-

isopropyl-2-methyl-phenol; 4-bromo-5-*tert*-butyl-2-methyl-phenol; 4-bromo-5-cyclopropyl-2-methyl-phenol; 4-bromo-2-ethyl-5-isopropyl-phenol; 4-chloro-2-ethyl-5-isopropyl-phenol; 2-ethyl-4-fluoro-5-isopropyl phenol; 4-bromo-5-isopropyl-2-propyl-phenol, 5-isopropyl-2-propyl-phenol; and 4-bromo-2,5-isopropyl-phenol.

5

[0046] In yet another embodiment (Embodiment 18) a compound is provided, selected from the group consisting of: 4-bromo-2-methyl-5-(2,2,2-trifluoro-1-methyl-ethyl)-phenol; 4-bromo-5-(2-fluoro-1-methyl-ethyl)-2-methyl -phenol; 4-bromo-2-methyl-5-(2,2,2-trifluoro-1-trifluoromethyl-ethyl)-phenol; 4-bromo-2-trifluoromethyl-5-(2,2,2-trifluoro-1-methyl-ethyl)-phenol; 4-bromo-2-cyclopropyl-5-isopropyl-phenol; 4-bromo-2,5-dicyclopropyl-phenol; 5-isopropyl-2-methyl-4-trifluoromethoxy-phenol; 2-cyclopropyl-5-isopropyl-4-trifluoromethoxy-phenol; 5-cyclopropyl-2-methyl-4-trifluoromethoxy -phenol; 2,5-dicyclopropyl-4-trifluoromethoxy-phenol; 4-*tert*-butoxy-5-cyclopropyl-2-methyl-phenol; 4-*tert*-butoxy-2-cyclopropyl-5-methyl-phenol; 4-*tert*-butoxy-2,5-dicyclopropyl-phenol; 4-isopropoxy-5-isopropyl-2-methyl-phenol; 4-bromo-5-isopropyl-2-trifluoromethyl-phenol; 4-bromo-5-(2-fluoro-1-methyl-ethyl)-2-methyl-phenol; and 4-*tert*-butoxy-5-isopropyl-2-methyl-phenol.

[0047] In yet another embodiment (Embodiment 19) a compound or pharmaceutically acceptable salt of the compound is provided, wherein the compound has the structure of Formula (V):



25

wherein:

R^2 is selected from the group consisting of haloalkyl and cycloalkyl.

R^5 is selected from the group consisting of haloalkyl and cycloalkyl.

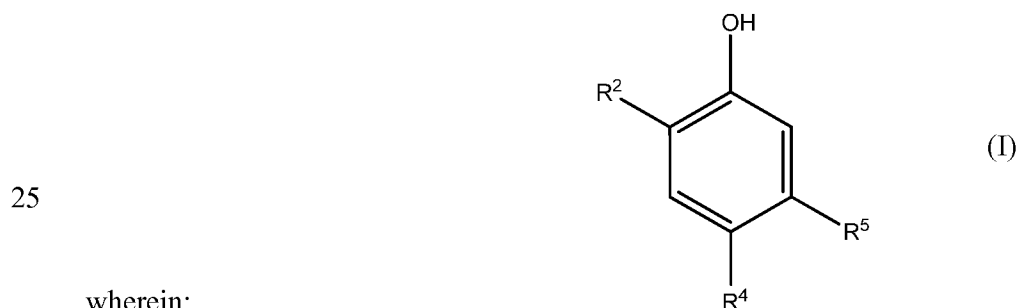
[0048] Embodiment 20 is the compound of Embodiment 19, wherein:

R^2 is selected from the group consisting of trifluoroalkyl and cycloalkyl

R^5 is selected from the group consisting of trifluoroalkyl and cycloalkyl.

5 [0049] In yet another embodiment (Embodiment 21) a compound is provided, selected from the group consisting of: 5-(1,2-dimethyl-propyl)-2-methyl-phenol; 5-isobutyl-2-methyl-phenol; 5-cyclopentyl-2-methyl-phenol; 5-*sec*-butyl-2-ethyl-phenol; 5-butyl-2-propyl-phenol; 5-isopropyl-2-propyl-phenol; 5-*sec*-butyl-2-propyl-phenol; 5-*tert*-butyl-2-propyl-phenol; 2-butyl-5-isopropyl-phenol; 2-butyl-5-*sec*-butyl-phenol; 5-(*tert*-butyl)-2-butylphenol; 2-isopropyl-5-propyl-phenol; 5-*sec*-butyl-2-isopropyl-phenol; 2-*sec*-butyl-5-ethyl-phenol; 2-*sec*-butyl-5-propyl-phenol; 5-butyl-2-*sec*-butyl-phenol; 2-*sec*-butyl-5-isopropyl-phenol; 5-*sec*-butyl-2-*tert*-butyl-phenol; 2-methyl-5-(2,2,2-trifluoro-1-methyl-ethyl)-phenol; 5-(2-fluoro-1-methyl-ethyl)-2-methyl-phenol; 2-methyl-5-(2,2,2-trifluoro-1-trifluoromethyl-ethyl)-phenol; 2-trifluoromethyl-5-(2,2,2-trifluoro-1-methyl-ethyl)-phenol; 5-isopropyl-2-(1-methyl-butyl)-phenol; 2-isopropyl-5-isopropyl-phenol; 2-cyclopropyl-5-isopropyl-phenol; and 2,5-dicyclopropyl-phenol.

[0050] In yet another embodiment (Embodiment 22), a compound or pharmaceutically acceptable salt of the compound is provided, wherein the compound has
20 the structure of Formula (I):



wherein:

R^2 is selected from the group consisting of methyl, cycloalkyl, and $-CF_3$;

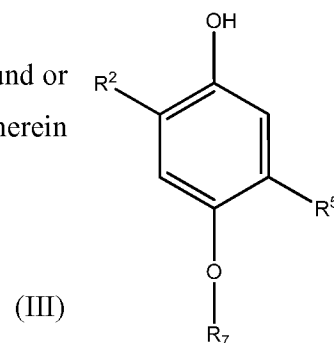
R^4 is halo;

30 R^5 is selected from the group consisting of fluoroalkyl and a three, four, or five carbon cycloalkyl.

[0051] Embodiment 23 is the compound of Embodiment 22, wherein:

R^4 is selected from the group consisting of Br, Cl, and F.

[0052] In yet another embodiment (Embodiment 24) a compound or pharmaceutically acceptable salt of the compound is provided, wherein
5 the compound has the structure of Formula (III):



wherein,

R^2 and R^5 are each independently selected from the group consisting of alkyl and
10 cycloalkyl; wherein at least one of R^2 and R^5 is cycloalkyl.

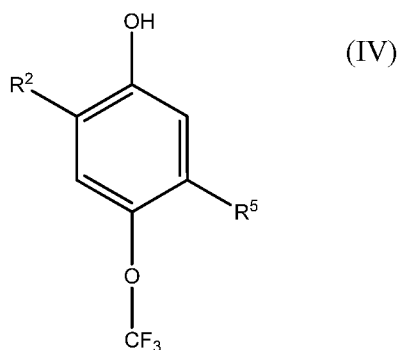
R^7 is selected from the group consisting of isopropyl, *tert*-butyl, and haloalkyl.

[0053] Embodiment 25 is the compound of Embodiment 24, wherein:

R^7 is selected from the group consisting of isopropyl and *tert*-butyl.

15

[0054] Embodiment 26 is the compound or pharmaceutically acceptable salt of the compound of Embodiment 22, wherein the compound has the structure of Formula (IV):



20

25 wherein:

R^2 is selected from the group consisting of alkyl, and cycloalkyl; and

R^5 is selected from the group consisting of alkyl, and cycloalkyl.

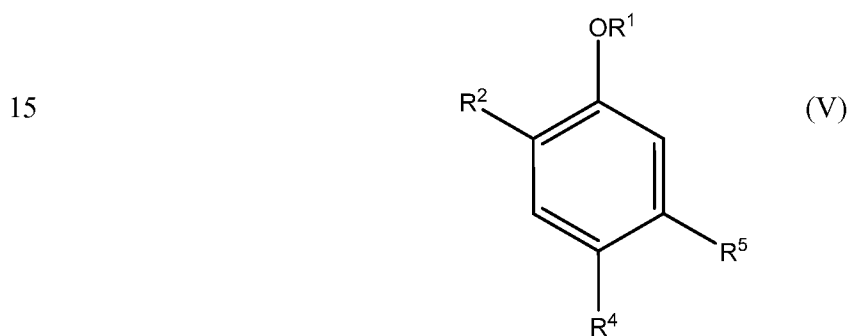
[0055] In yet a further embodiment (Embodiment 27), a method is provided for
30 treating epilepsy, seizures, or convulsions, the method comprising administering a therapeutically effective amount of a compound or of a pharmaceutically acceptable salt of the compound, wherein the compound has the structure of Formula (I), wherein R^2 and

R^5 are each independently selected from the group consisting of methyl, isopropyl, and tert-butyl; and R^4 is selected from the group consisting of Br, Cl, and F.

[0056] Embodiment 28 is the method of any one of Embodiments 1–16 or 27,
5 wherein the compound is deuterated.

[0057] Embodiment 29 is the compound or pharmaceutically acceptable salt of any one of Embodiments 17–26, wherein the compound is deuterated.

10 [0058] Embodiment 30 provides a method for treating a neurological or an inflammatory condition comprising administering a therapeutically effective amount of a compound or pharmaceutically acceptable salt of the compound, wherein the compound has a structure of Formula (V):



20

wherein:

R^1 is selected from the group consisting of an ester, a carbonate, a phosphate, a carbamate, a sulfamate, and an acylmethylester;

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

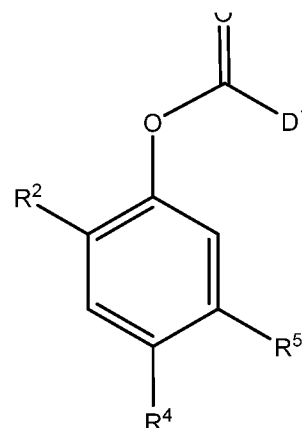
25 R^4 is selected from the group consisting of H, halo, and alkoxy, wherein the alkoxy may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl and halo, and wherein R^4 is not methyl; and

R^5 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl.

30 [0059] Embodiment 31 is the method of Embodiment 30, wherein the compound has a structure of Formula (VI):

(VI)

wherein D¹ is alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroalkyl, heteroaryl, heteroaralkyl, carbonylalkyl, or phosphonooxyalkyl, optionally substituted with one or more substituents selected from the group consisting of
 5 alkyl, carboxylate, heteroalkyl, monocyclic ring, bicyclic ring, and hydroxyl moieties.



DETAILED DESCRIPTION

[0060] The following description is merely exemplary in nature and is not intended to limit the present disclosure, application, or uses.

10

A. Definitions

[0061] The use of generic terms in the description of the compounds are herein defined for clarity. The terms “substituent”, “radical”, “group”, “moiety” and “fragment” may be used interchangeably.

[0062] If a substituent is described as being “optionally substituted,” the substituent may
 15 be either (1) not substituted or (2) substituted on a substitutable position. If a substitutable position is not substituted, the default substituent is H.

[0063] Singular forms “a” and “an” may include plural reference unless the context clearly dictates otherwise.

[0064] The number of carbon atoms in a substituent can be indicated by the prefix “C_{A-B}”
 20 where A is the minimum and B is the maximum number of carbon atoms in the substituent.

[0065] The terms “hydroxyl” and “hydroxy” may be used interchangeably.

[0066] The term “halo” refers to fluoro (–F), chloro (–Cl), bromo (–Br), or iodo (–I).

[0067] The term “alkyl” denotes a linear or branched acyclic alkyl radical containing from
 25 1 to about 15 carbon atoms. In some embodiments, alkyl is a C₁₋₁₀alkyl, C₁₋₇alkyl, C₁₋₆alkyl or C₁₋₅alkyl radical. Examples of alkyl include, but are not limited to, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, *tert*-butyl, *sec*-butyl, pentan-3-yl and the like.

[0068] The term “heteroatom” denotes an atom other than carbon or hydrogen, found in the context of an organic compound. Non-limiting exemplary heteroatoms
 30 include N, O, P, and S.

[0069] The term “heteroalkyl” denotes an alkyl that comprises one or more heteroatoms. A heteroatom in a heteroalkyl can be found in the middle and/or at the distal terminus of the alkyl chain.

[0070] The term “alkylcarbonyl” denotes an alkyl radical attached to carbonyl.

5 [0071] The term "hydroxyalkyl" embraces a radical wherein any one or more of an alkyl carbon is substituted with a hydroxyl radical as defined above, for example, monohydroxyalkyl, dihydroxyalkyl and trihydroxyalkyl. More specific examples of hydroxyalkyl include hydroxymethyl, hydroxyethyl and hydroxypropyl.

10 [0072] Hydroxyalkyl may be substituted with, for example, alkyl, hydroxyalkoxy, hydroxyalkoxyalkyl, amino, aminoalkyl, aryl, aralkyl, and heterocyclyl. Further non-limiting examples include hydroxyalkyl substituted with methyl, isobutyl, benzyl, isopropyl, benzyl and *sec*-butyl.

[0073] The term “hydroxyalkoxy” denotes a hydroxy radical attached to an alkoxy radical.

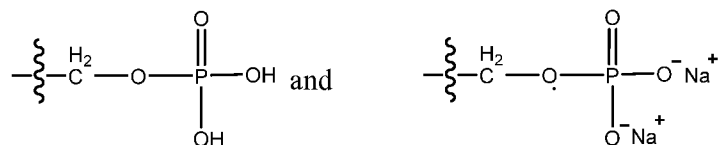
15 [0074] The term “hydroxyalkoxyalkyl” denotes a hydroxyalkoxy radical attached to an alkyl radical. Non-limiting examples include hydroxyethyl-O-ethyl and hydroxymethyl-O-ethyl.

[0075] Hydroxyalkoxyalkyl may, for example, be substituted with alkyl, hydroxyalkyl, hydroxyalkoxy, amino, aminoalkyl, aryl, aralkyl, and heterocyclyl. Further non-limiting examples include hydroxyalkoxyalkyl substituted with methyl, isobutyl, benzyl, isopropyl and *sec*-butyl. More specific non-limiting examples of substituted hydroxyalkoxyalkyl include hydroxyethyl-O-ethyl substituted with methyl, isobutyl, benzyl, isopropyl and *sec*-butyl.

25 [0076] The term “haloalkyl” embraces an alkyl radical wherein any one or more of the alkyl carbon atoms is substituted with halo as defined above. For example, monohaloalkyl, dihaloalkyl and trihaloalkyl. A monohaloalkyl radical, for one example, may have either a bromo, chloro or a fluoro atom within the radical. A dihalo radical may have two of the same halo radicals or a combination of different halo radicals. A trihaloalkyl radical may have three of the same halo radicals or a combination of different halo radicals. Non-limiting examples of haloalkyl include fluoromethyl, difluoromethyl, trifluoromethyl, chloromethyl, dichloromethyl, trichloromethyl, trifluoroethyl, pentafluoroethyl, heptafluoropropyl, difluorochloromethyl, dichlorofluoromethyl, difluoroethyl, difluoropropyl, dichloroethyl, dichloropropyl, iodomethyl, diiodomethyl and triiodomethyl.

[0077] The term “alkoxy” is RO— where R is alkyl as defined above. Non-limiting examples of alkoxy radicals include methoxy, ethoxy and propoxy. The terms “alkyloxy” and “alkoxy” and “alkyl-O-” may be used interchangeably.

[0078] The term “phosphonooxyalkyl” is —RO—P(O)(OH)₂, where R is alkyl as defined above. The term “phosphonooxyalkyl” should also be understood to include salts. Non-limiting examples of phosphonooxyalkyl radicals include



[0079] The term “alkoxyalkyl” refers to an alkyl moiety substituted with an alkoxy radical. Examples of alkoxyalkyl radicals include methoxymethyl, methoxyethyl, methoxypropyl and ethoxyethyl.

[0080] The term “alkoxycarbonyl” refers to a carbonyl radical substituted with alkoxy. Non-limiting examples include methoxycarbonyl and ethoxycarbonyl.

[0081] The term “alkoxycarbonylalkyl” refers to an alkoxycarbonyl radical substituted with alkyl.

[0082] The term “carbonyl” denotes a carbon radical having two of four covalent bonds shared with a single oxygen atom.

[0083] The term “alkylcarbonyl” denotes an alkyl radical attached to a carbonyl radical.

[0084] The term “carbonylalkyl” denotes a carbonyl radical attached to an alkyl radical.

[0085] The term “carbonylalkylcarbonyl” denotes a carbonylalkyl radical attached to a carbonyl radical.

[0086] The term “cyclic ring” embraces any aromatic or non-aromatic cyclized carbon radical (e.g., aryl and cycloalkyl respectively) which may contain one or more ring heteroatoms (e.g., heteroaryl and heterocyclyl). A cyclic ring may be unsaturated, partially unsaturated, or saturated.

[0087] The term “cycloalkyl” embraces any monocyclic, bicyclic or tricyclic cyclized carbon radical of 3 to about 15 carbon atoms that is fully or partially saturated. Cycloalkyl may be attached to an aryl, cycloalkyl or a heterocyclyl radical in a fused or pendant manner.

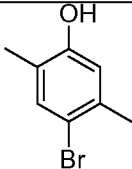
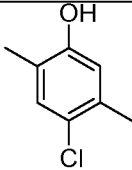
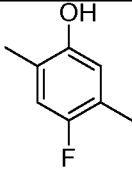
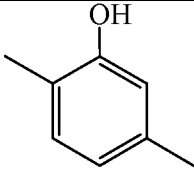
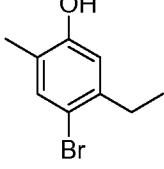
[0088] Cycloalkyl may be substituted with alkyl, alkoxy, carboxyalkyl, hydroxyalkyl, amino, acylamino, amido, alkylamino, nitrooxyalkyl, nitrooxy, carbonyl, acyl, aralkyl, aryl, heterocyclyl or cycloalkyl.

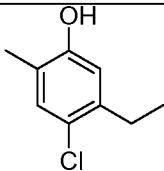
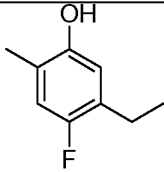
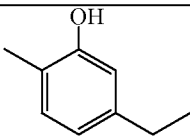
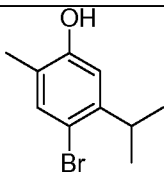
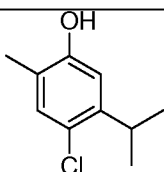
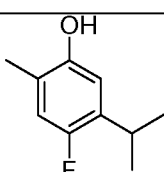
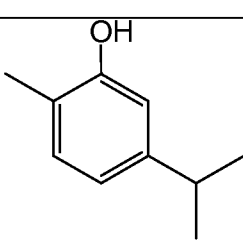
- [0089] The term “aryl” refers to any monocyclic, bicyclic or tricyclic cyclized carbon radical, wherein at least one ring is aromatic. An aromatic radical may be attached to a non-aromatic cycloalkyl or heterocyclyl radical in a fused or pendant manner. Examples of aryl radicals include, but are not limited to, phenyl and naphthyl.
- 5 [0090] The term “aralkyl” embraces aryl attached to an alkyl radical and may be used interchangeably with arylalkyl. Examples of aralkyl include benzyl, diphenylmethyl, triphenylmethyl, phenylethyl and diphenylethyl. The terms “benzyl” and “phenylmethyl” may be used interchangeably.
- 10 [0091] The term “aralkoxy” embraces an arylalkyl radical attached through an oxygen atom to the parent molecular scaffold. The terms “arylalkoxy” and “aralkoxy” may be used interchangeably.
- [0092] The term “aryloxy” is RO-, where R is aryl.
- [0093] The term “aryloxyalkyl” embraces an aryloxy radical attached to an alkyl radical.
- 15 [0094] The term “pharmaceutically-acceptable” means suitable for use in pharmaceutical preparations, generally considered as safe for such use, officially approved by a regulatory agency of a national or state government for such use, or being listed in the U. S. Pharmacopoeia or other generally recognized pharmacopoeia for use in animals, and more particularly in humans.
- 20 [0095] The term “pharmaceutically-acceptable salt” refers to a salt which is suitable for use in pharmaceutical preparations. The term “therapeutically-effective amount” refers to an amount of a compound that, when administered to a subject for treating a disease, is sufficient to effect treatment for the disease. “Therapeutically effective amount” can vary depending on the compound, the disease and its severity, the age, the weight, etc. of the subject to be treated.
- 25 [0096] The term “solvate” denotes a molecular or ionic complex of molecules or ions of solvent with those of a compound of the present invention. The term “solvate” embraces the term “hydrate”.
- [0097] The term “hydrate” denotes a compound of the present invention containing water combined in the molecular form.
- 30 [0098] Some of the compounds described contain one or more stereocenters and are meant to include R, S and mixtures of R and S forms for each stereocenter present.
- [0099] The term “AED” refers to “Anti-Epileptic Drug.” AED can be used interchangeably with “ASD,” which means “Anti-Seizure Drug.”

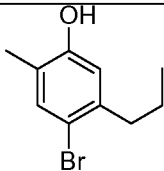
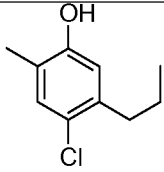
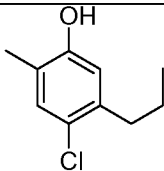
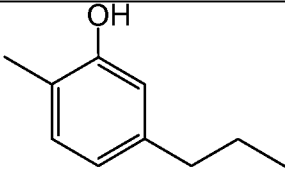
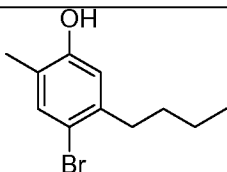
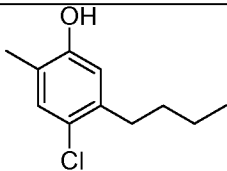
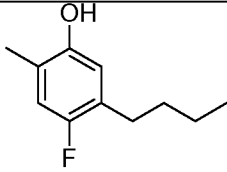
B. Compounds

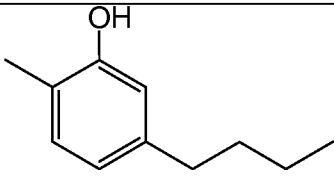
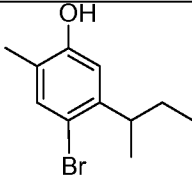
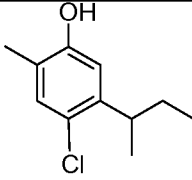
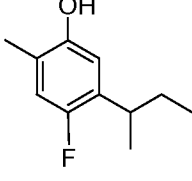
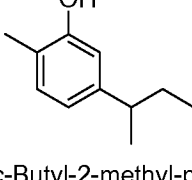
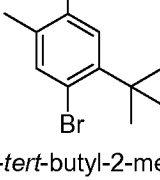
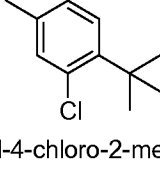
[0100] The present disclosure provides a compound having the structure of Formula (I). All compounds shown in the tables below should be understood optionally to include one or more deuterium or tritium hydridos wherever a hydrogen atom is indicated or implied:

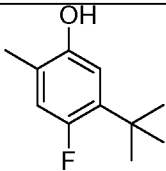
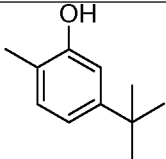
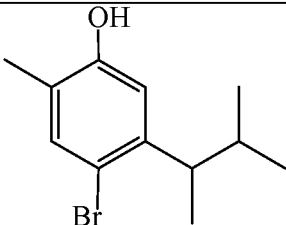
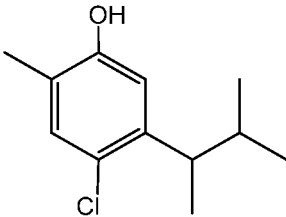
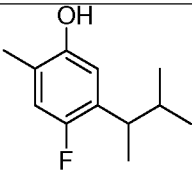
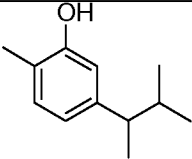
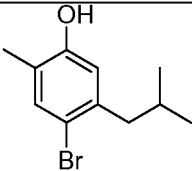
Family 1a Species

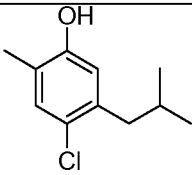
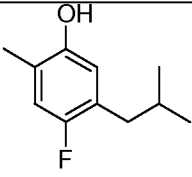
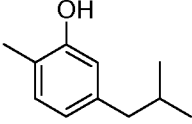
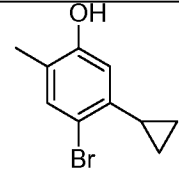
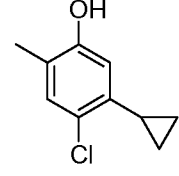
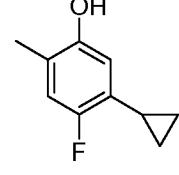
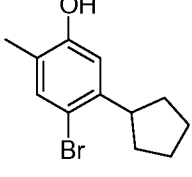
Example Number	Species Structure Species Name
Methyl series 1	 4-Bromo-2,5-dimethyl-phenol
2	 4-Chloro-2,5-dimethyl-phenol
3	 4-Fluoro-2,5-dimethyl-phenol
4	 2,5-Dimethyl-phenol
5	 4-Bromo-5-ethyl-2-methyl-phenol

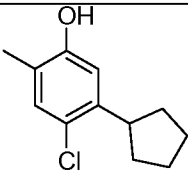
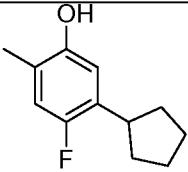
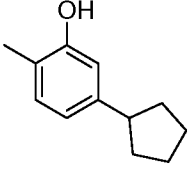
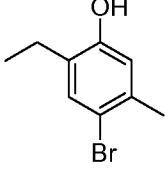
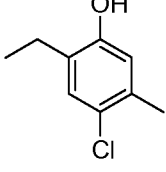
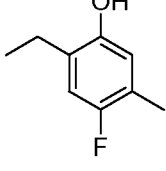
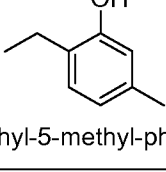
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7	 5-Ethyl-4-fluoro-2-methyl-phenol
8	 5-Ethyl-2-methyl-phenol
9	 4-Bromo-5-isopropyl-2-methyl-phenol
10	 4-Chloro-5-isopropyl-2-methyl-phenol
11	 4-Fluoro-5-isopropyl-2-methyl-phenol
12	 5-Isopropyl-2-methyl-phenol

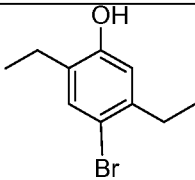
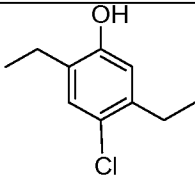
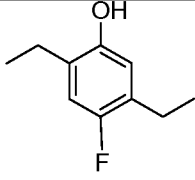
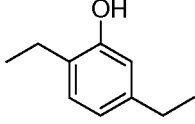
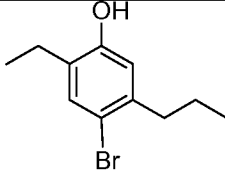
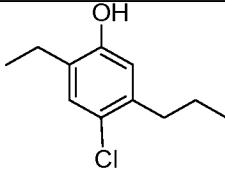
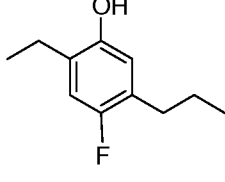
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14	 2-methyl, 4-chloro, 5- <i>n</i> -propyl phenol
15	 4-Chloro-2-methyl-5-propyl-phenol
16	 2-Methyl-5-propyl-phenol
17	 4-Bromo-5-butyl-2-methyl-phenol
18	 5-Butyl-4-chloro-2-methyl-phenol
19	 5-Butyl-4-fluoro-2-methyl-phenol

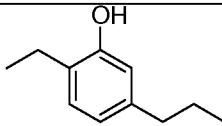
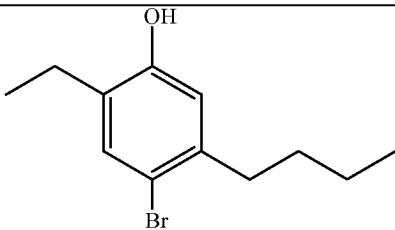
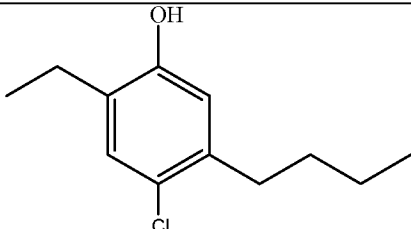
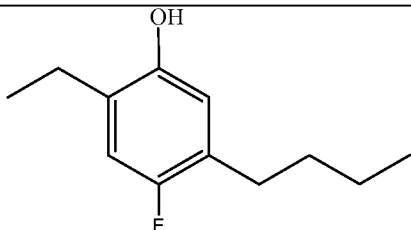
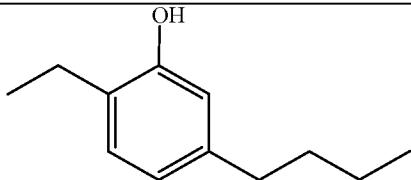
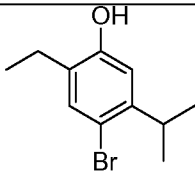
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21	 4-Bromo-5-sec-butyl-2-methyl-phenol
22	 5-sec-Butyl-4-chloro-2-methyl-phenol
23	 5-sec-Butyl-4-fluoro-2-methyl-phenol
24	 5-sec-Butyl-2-methyl-phenol
25	 4-Bromo-5-<i>tert</i>-butyl-2-methyl-phenol
26	 5-<i>tert</i>-Butyl-4-chloro-2-methyl-phenol

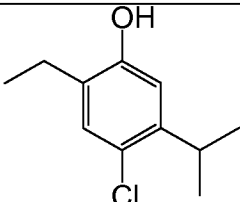
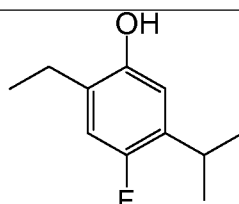
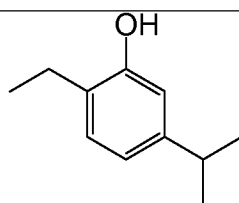
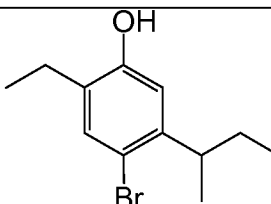
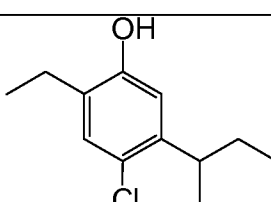
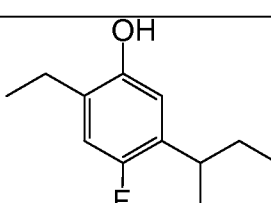
26	 5- <i>tert</i> -Butyl-4-fluoro-2-methyl-phenol
28	 5- <i>tert</i> -Butyl-2-methyl-phenol
29	 4-Bromo-5-(1,2-dimethyl-propyl)-2-methyl-phenol
30	 4-Chloro-5-(1,2-dimethyl-propyl)-2-methyl-phenol
31	 5-(1,2-Dimethyl-propyl)-4-fluoro-2-methyl-phenol
32	 5-(1,2-Dimethyl-propyl)-2-methyl-phenol
33	 4-Bromo-5-isobutyl-2-methyl-phenol

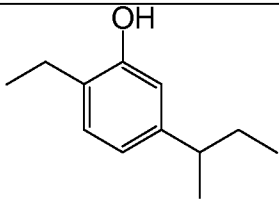
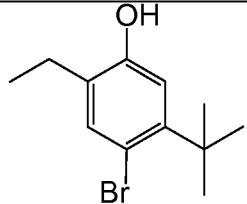
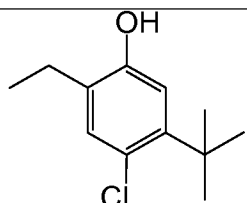
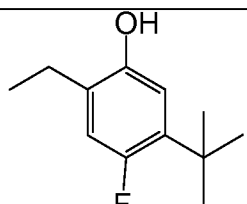
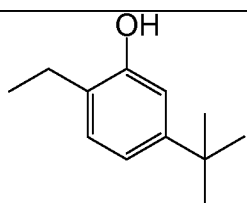
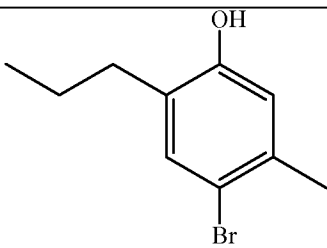
34	 4-Chloro-5-isobutyl-2-methyl-phenol
35	 4-Fluoro-5-isobutyl-2-methyl-phenol
40	 5-Isobutyl-2-methyl-phenol
41	 4-Bromo-5-cyclopropyl-2-methyl-phenol
42	 4-Chloro-5-cyclopropyl-2-methyl-phenol
43	 5-Cyclopropyl-4-fluoro-2-methyl-phenol
44	 4-Bromo-5-cyclopentyl-2-methyl-phenol

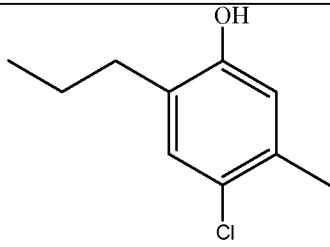
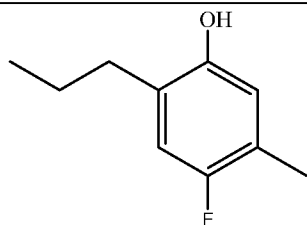
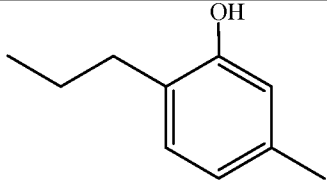
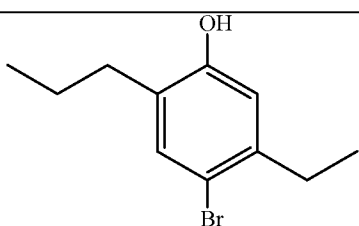
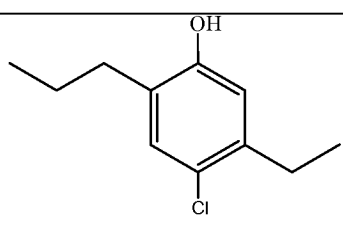
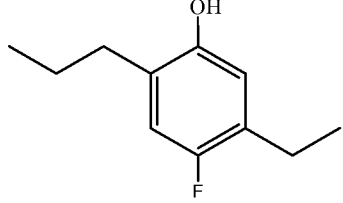
45	 4-Chloro-5-cyclopentyl-2-methyl-phenol
46	 5-Cyclopentyl-4-fluoro-2-methyl-phenol
47	 5-Cyclopentyl-2-methyl-phenol
Ethyl Series 48	 4-Bromo-2-ethyl-5-methyl-phenol
49	 4-Chloro-2-ethyl-5-methyl-phenol
50	 2-Ethyl-4-fluoro-5-methyl-phenol
51	 2-Ethyl-5-methyl-phenol

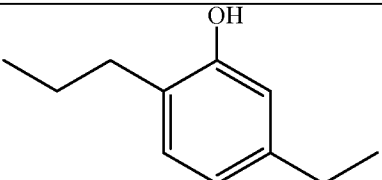
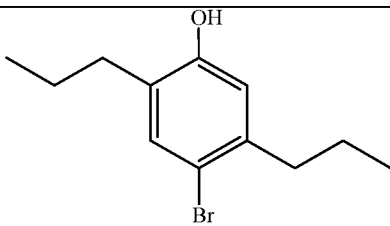
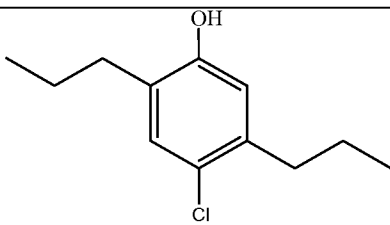
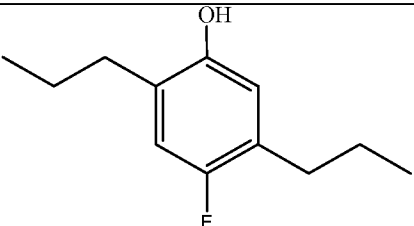
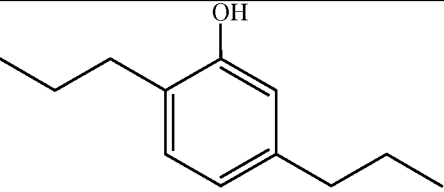
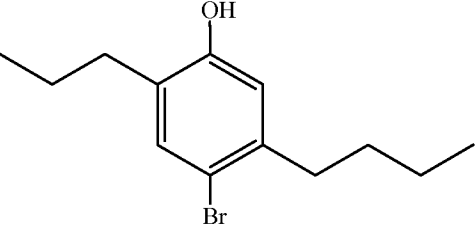
52	 4-Bromo-2,5-diethyl-phenol
53	 4-Chloro-2,5-diethyl-phenol
54	 2,5-Diethyl-4-fluoro-phenol
55	 2,5-Diethyl-phenol
56	 4-Bromo-2-ethyl-5-propyl-phenol
57	 4-Chloro-2-ethyl-5-propyl-phenol
58	 2-Ethyl-4-fluoro-5-propyl-phenol

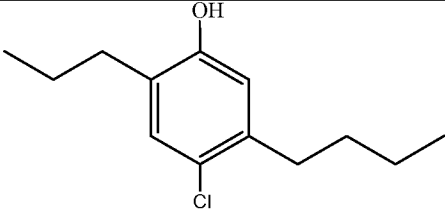
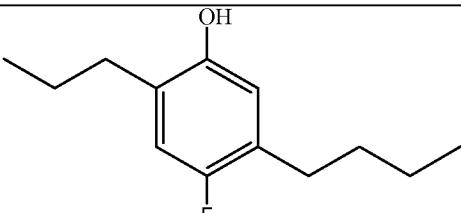
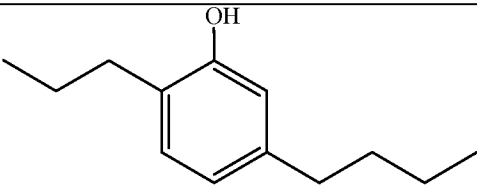
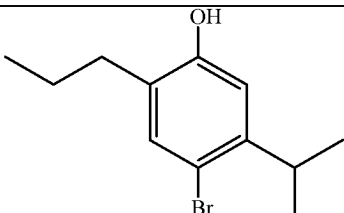
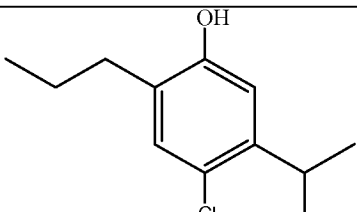
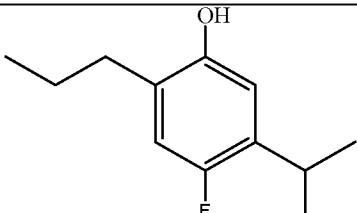
59	 2-Ethyl-5-propyl-phenol
60	 4-Bromo-5-butyl-2-ethyl-phenol
61	 5-Butyl-4-chloro-2-ethyl-phenol
62	 5-Butyl-2-ethyl-4-fluoro-phenol
63	 5-Butyl-2-ethyl-phenol
64	 4-Bromo-2-ethyl-5-isopropyl-phenol

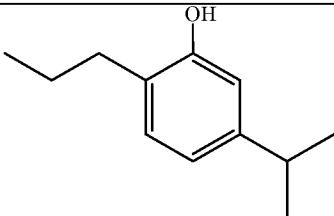
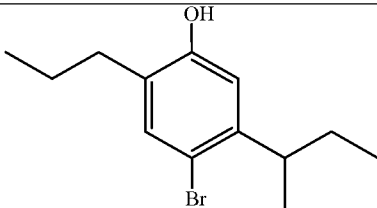
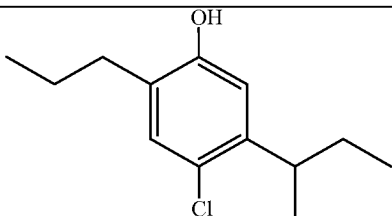
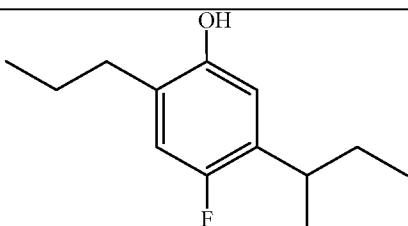
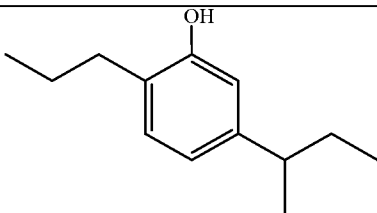
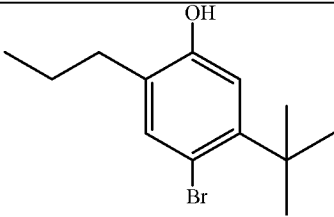
65	 4-Chloro-2-ethyl-5-isopropyl-phenol
66	 2-Ethyl-4-fluoro-5-isopropyl-phenol
67	 2-Ethyl-5-isopropyl-phenol
68	 4-Bromo-5-sec-butyl-2-ethyl-phenol
69	 5-sec-Butyl-4-chloro-2-ethyl-phenol
70	 5-sec-Butyl-2-ethyl-4-fluoro-phenol

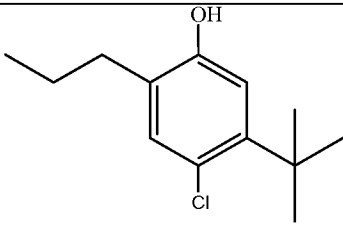
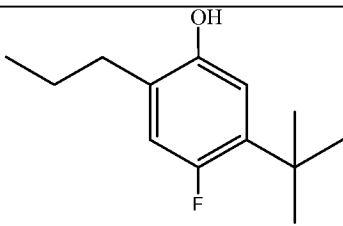
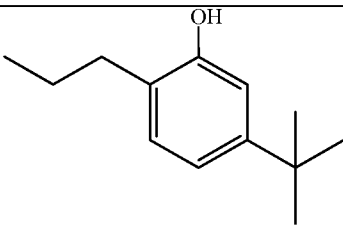
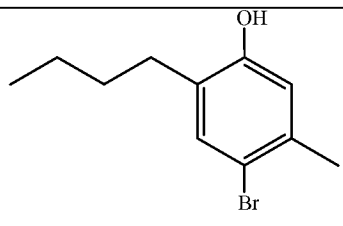
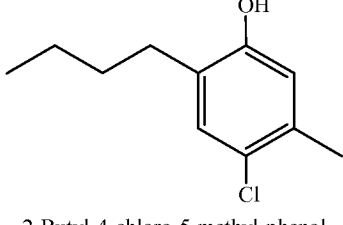
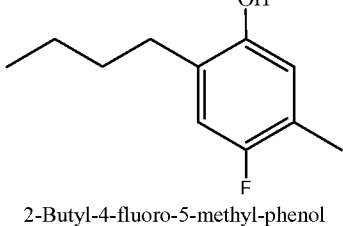
71	 5-sec-Butyl-2-ethyl-phenol
72	 4-Bromo-5-<i>tert</i>-butyl-2-ethyl-phenol
73	 5-<i>tert</i>-Butyl-4-chloro-2-ethyl-phenol
74	 5-<i>tert</i>-Butyl-2-ethyl-4-fluoro-phenol
75	 5-<i>tert</i>-Butyl-2-ethyl-phenol
Propyl series 76	 4-Bromo-5-methyl-2-propyl-phenol

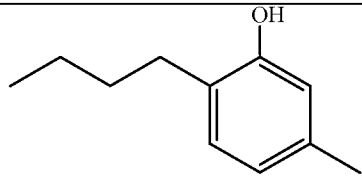
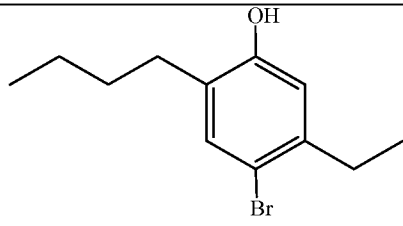
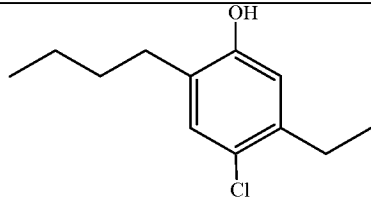
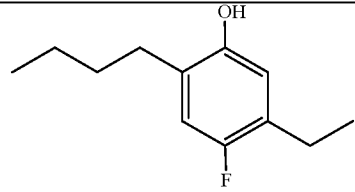
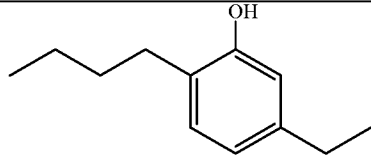
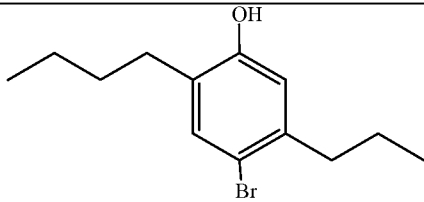
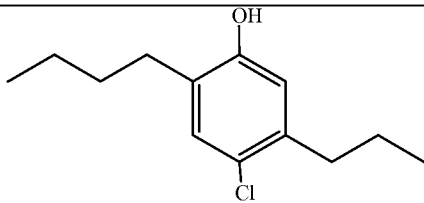
77	 4-Chloro-5-methyl-2-propyl-phenol
78	 4-fluoro-5-methyl-2-propylphenol
79	 5-Methyl-2-propyl-phenol
80	 4-Bromo-5-ethyl-2-propyl-phenol
81	 4-Chloro-5-ethyl-2-propyl-phenol
82	 5-Ethyl-4-fluoro-2-propyl-phenol

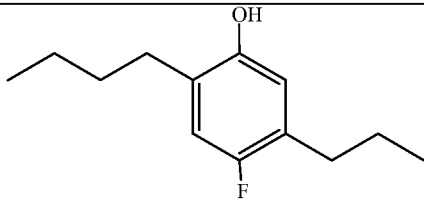
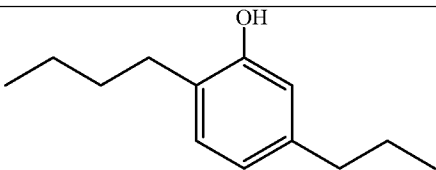
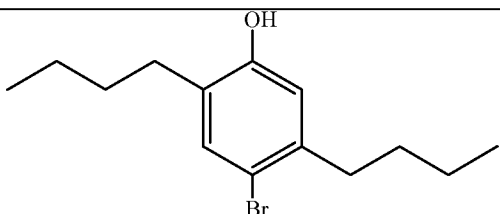
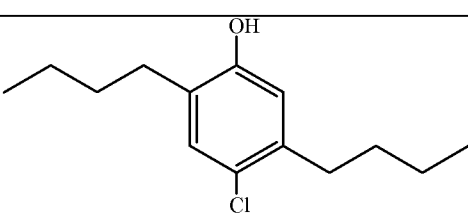
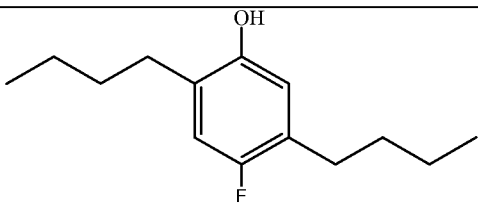
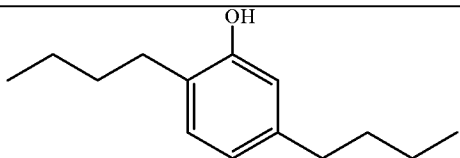
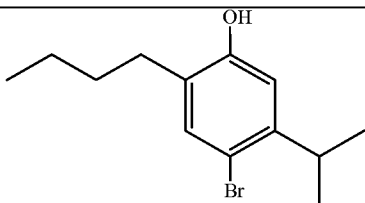
83	 5-Ethyl-2-propyl-phenol
84	 4-Bromo-2,5-dipropyl-phenol
85	 4-Chloro-2,5-dipropyl-phenol
86	 4-Fluoro-2,5-dipropyl-phenol
87	 2,5-Dipropyl-phenol
88	 4-Bromo-5-butyl-2-propyl-phenol

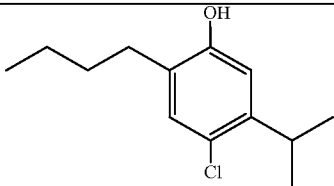
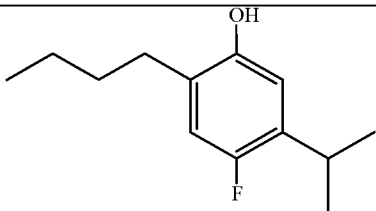
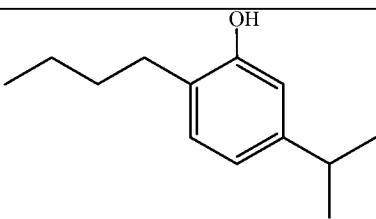
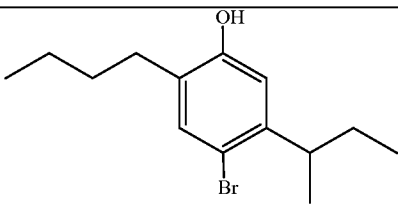
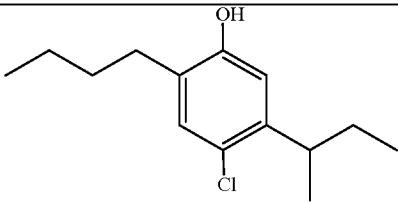
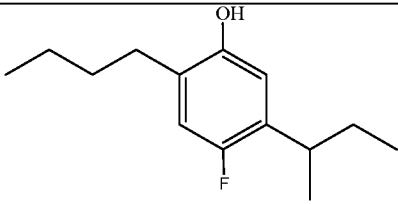
89	 5-Butyl-4-chloro-2-propyl-phenol
90	 5-Butyl-4-fluoro-2-propyl-phenol
91	 5-Butyl-2-propyl-phenol
92	 4-Bromo-5-isopropyl-2-propyl-phenol
93	 4-Chloro-5-isopropyl-2-propyl-phenol
94	 4-Fluoro-5-isopropyl-2-propyl-phenol

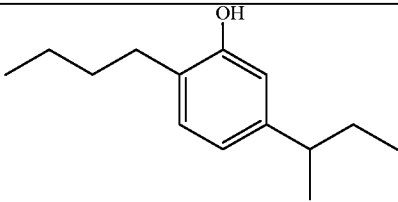
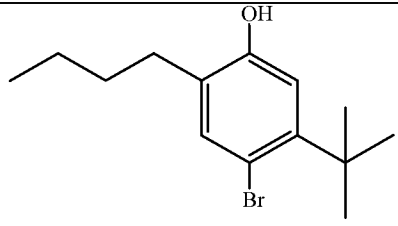
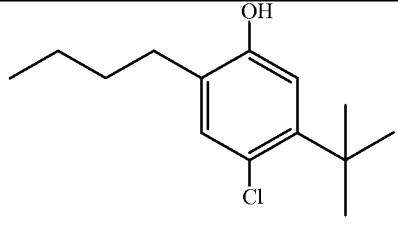
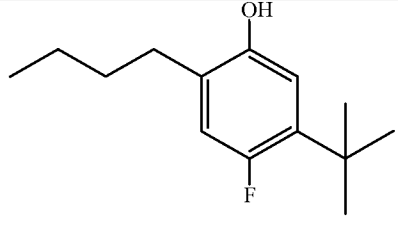
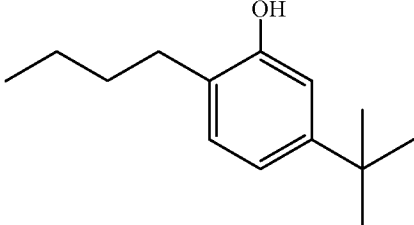
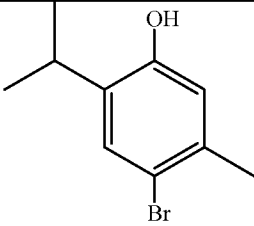
95	 5-Isopropyl-2-propyl-phenol
96	 4-Bromo-5-sec-butyl-2-propyl-phenol
97	 5-sec-Butyl-4-chloro-2-propyl-phenol
98	 5-sec-Butyl-4-fluoro-2-propyl-phenol
99	 5-sec-Butyl-2-propyl-phenol
100	 4-Bromo-5-tert-butyl-2-propyl-phenol

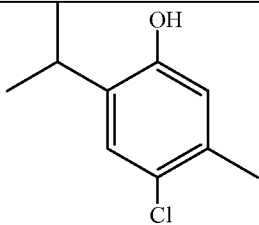
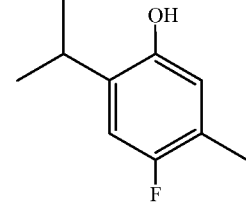
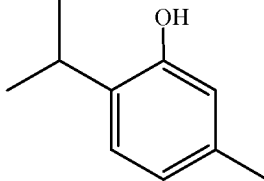
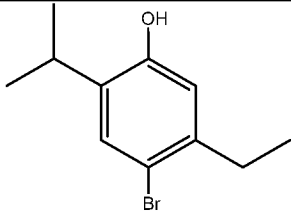
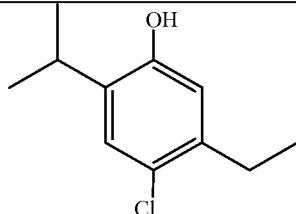
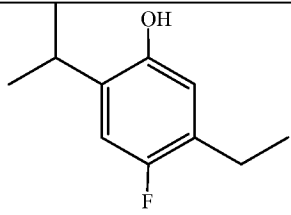
101	 5-<i>tert</i>-Butyl-4-chloro-2-propyl-phenol
102	 5-<i>tert</i>-Butyl-4-fluoro-2-propyl-phenol
103	 5-<i>tert</i>-Butyl-2-propyl-phenol
n-Butyl series 104	 4-Bromo-2-butyl-5-methyl-phenol
105	 2-Butyl-4-chloro-5-methyl-phenol
106	 2-Butyl-4-fluoro-5-methyl-phenol

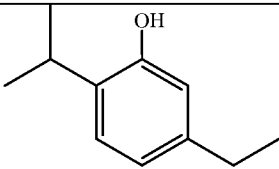
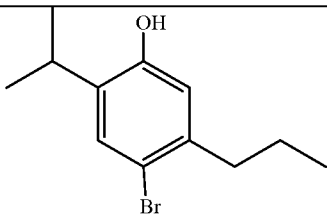
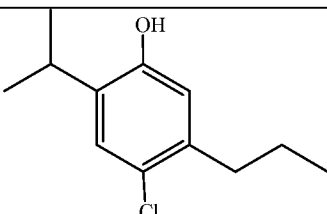
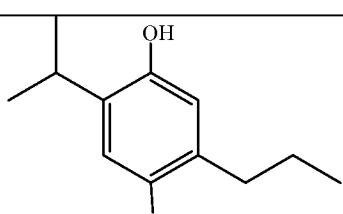
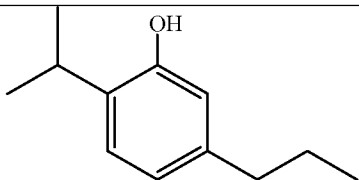
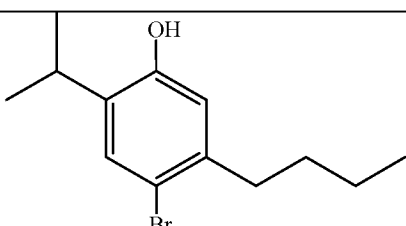
107	 2-Butyl-5-methyl-phenol
108	 4-Bromo-2-butyl-5-ethyl-phenol
109	 2-Butyl-4-chloro-5-ethyl-phenol
110	 2-Butyl-5-ethyl-4-fluoro-phenol
111	 2-Butyl-5-ethyl-phenol
112	 4-Bromo-2-butyl-5-propyl-phenol
113	 2-Butyl-4-chloro-5-propyl-phenol

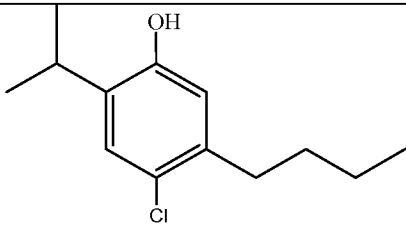
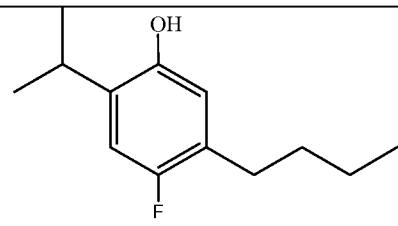
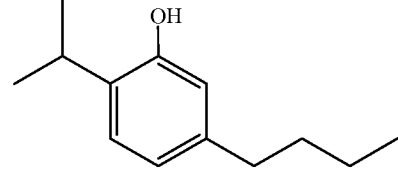
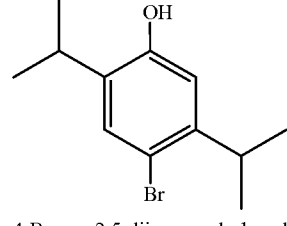
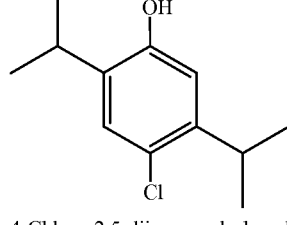
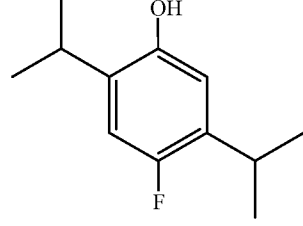
114	 2-Butyl-4-fluoro-5-propyl-phenol
115	 2-Butyl-5-propyl-phenol
116	 4-Bromo-2,5-dibutyl-phenol
117	 2,5-Dibutyl-4-chloro-phenol
118	 2,5-Dibutyl-4-fluoro-phenol
119	 2,5-Dibutyl-phenol
120	 4-Bromo-2-butyl-5-isopropyl-phenol

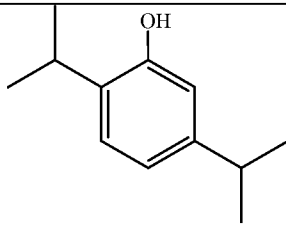
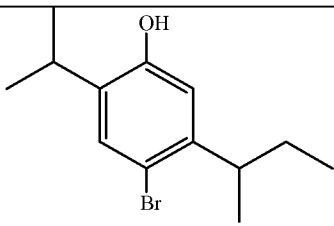
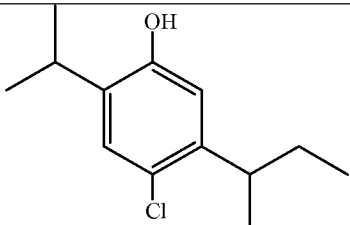
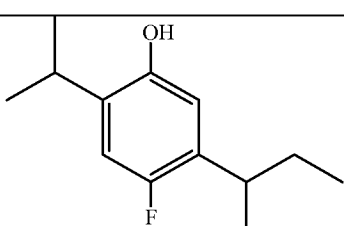
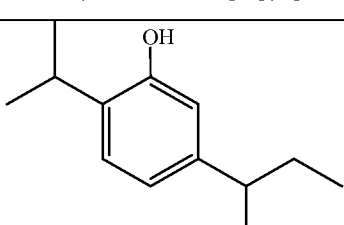
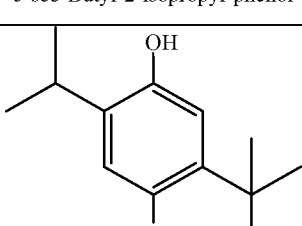
121	 2-Butyl-4-chloro-5-isopropyl-phenol
122	 2-Butyl-4-fluoro-5-isopropyl-phenol
123	 2-Butyl-5-isopropyl-phenol
124	 4-Bromo-2-butyl-5-<i>sec</i>-butyl-phenol
125	 2-Butyl-5-<i>sec</i>-butyl-4-chloro-phenol
126	 2-Butyl-5-<i>sec</i>-butyl-4-fluoro-phenol

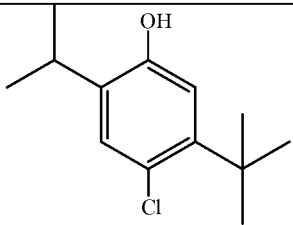
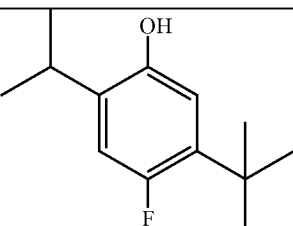
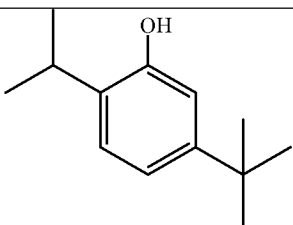
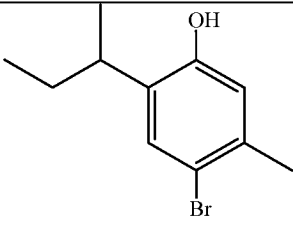
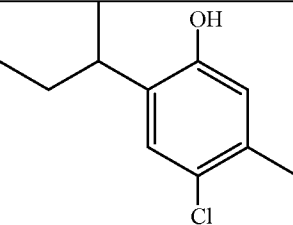
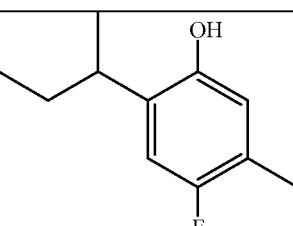
127	 2-Butyl-5-<i>sec</i>-butyl-phenol
128	 4-Bromo-2-butyl-5-<i>tert</i>-butyl-phenol
129	 2-Butyl-5-<i>tert</i>-butyl-4-chloro-phenol
130	 2-Butyl-5-<i>tert</i>-butyl-4-fluoro-phenol
131	
Isopropyl Series 132	 4-Bromo-2-isopropyl-5-methyl-phenol

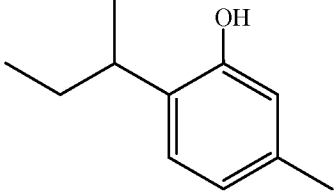
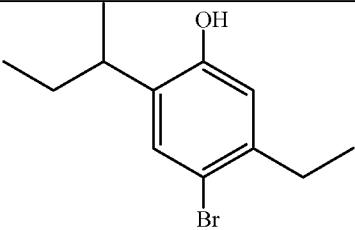
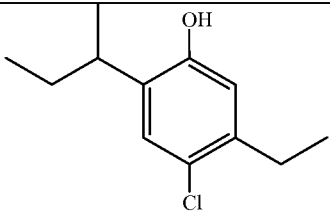
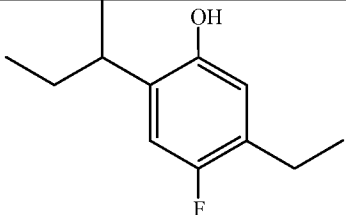
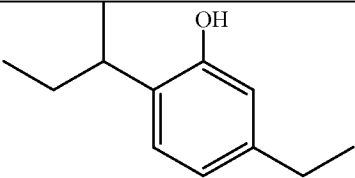
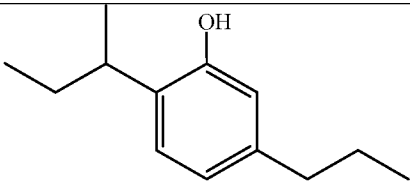
133	 4-Chloro-2-isopropyl-5-methyl-phenol
134	 4-Fluoro-2-isopropyl-5-methyl-phenol
135	 2-Isopropyl-5-methyl-phenol
136	 4-Bromo-5-ethyl-2-isopropyl-phenol
137	 4-Chloro-5-ethyl-2-isopropyl-phenol
138	 5-Ethyl-4-fluoro-2-isopropyl-phenol

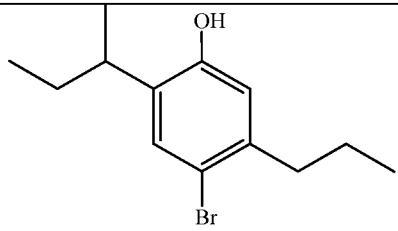
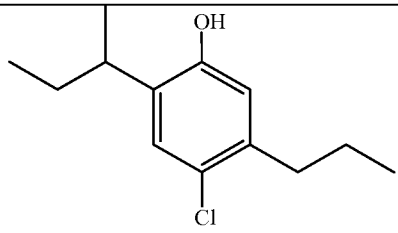
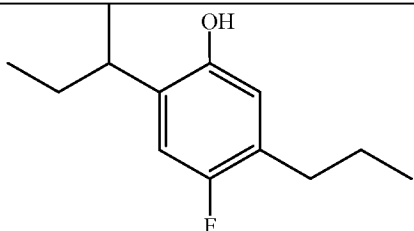
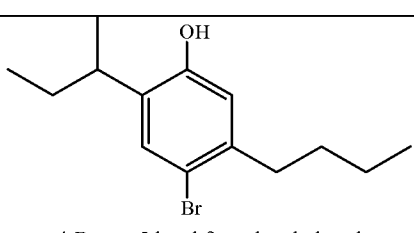
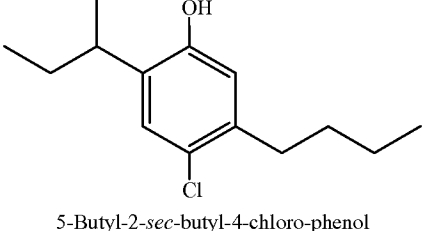
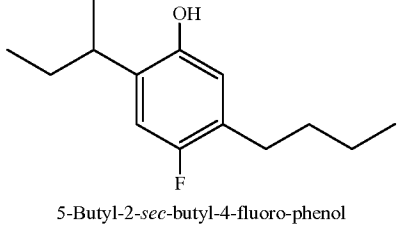
139	 5-Ethyl-2-isopropyl-phenol
140	 4-Bromo-2-isopropyl-5-propyl-phenol
141	 4-Chloro-2-isopropyl-5-propyl-phenol
142	 4-Fluoro-2-isopropyl-5-propyl-phenol
143	 2-Isopropyl-5-propyl-phenol
144	 4-Bromo-5-butyl-2-isopropyl-phenol

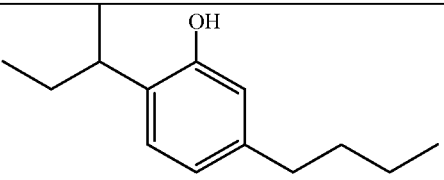
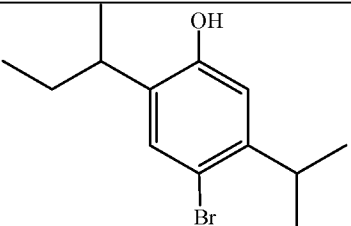
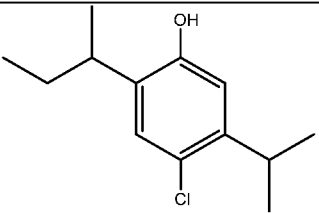
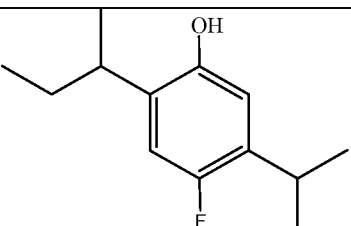
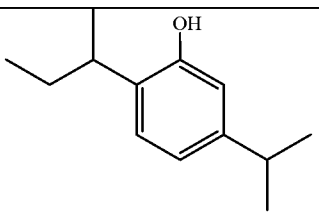
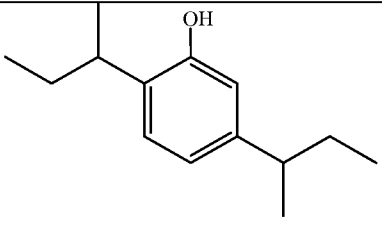
145	 5-Butyl-4-chloro-2-isopropyl-phenol
146	 5-Butyl-4-fluoro-2-isopropyl-phenol
147	 5-Butyl-2-isopropyl-phenol
148	 4-Bromo-2,5-diisopropyl-phenol
149	 4-Chloro-2,5-diisopropyl-phenol
150	 4-Fluoro-2,5-diisopropyl-phenol

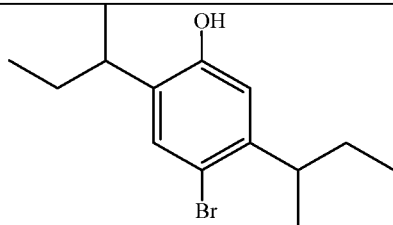
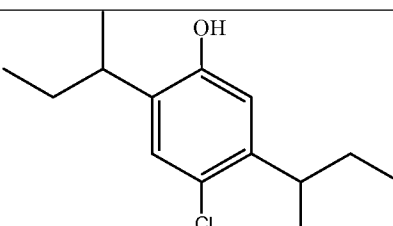
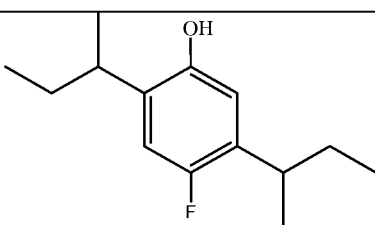
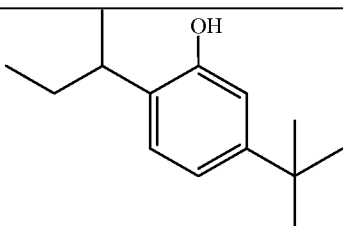
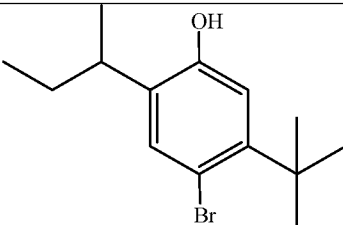
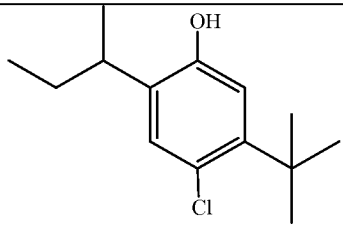
151	 2,5-Diisopropyl-phenol
152	 4-Bromo-5-<i>sec</i>-butyl-2-isopropyl-phenol
153	 5-<i>sec</i>-Butyl-4-chloro-2-isopropyl-phenol
154	 5-<i>sec</i>-Butyl-4-fluoro-2-isopropyl-phenol
155	 5-<i>sec</i>-Butyl-2-isopropyl-phenol
156	 4-Bromo-5-<i>tert</i>-butyl-2-isopropyl-phenol

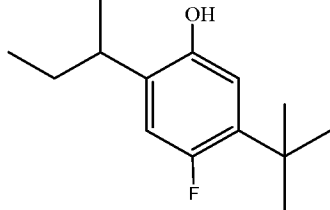
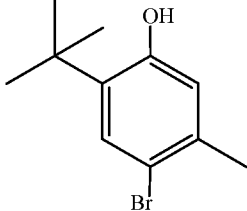
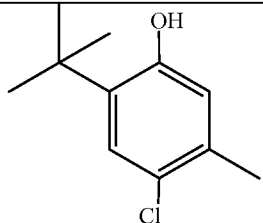
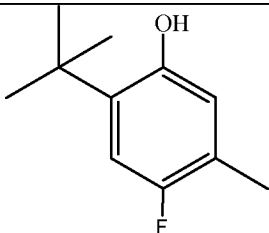
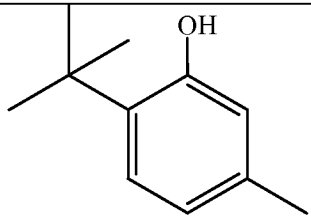
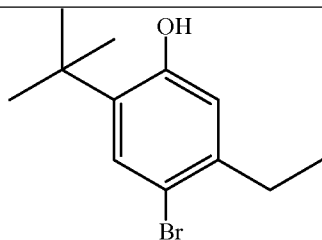
157	 5-<i>tert</i>-Butyl-4-chloro-2-isopropyl-phenol
158	 5-<i>tert</i>-Butyl-4-fluoro-2-isopropyl-phenol
159	 5-<i>tert</i>-Butyl-2-isopropyl-phenol
<i>Sec</i>-butyl Series 160	 4-Bromo-2-<i>sec</i>-butyl-5-methyl-phenol
161	 2-<i>sec</i>-Butyl-4-chloro-5-methyl-phenol
162	 2-<i>sec</i>-Butyl-4-fluoro-5-methyl-phenol

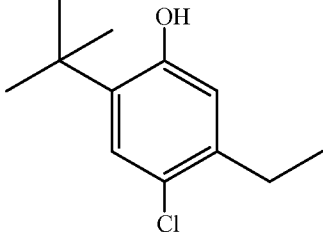
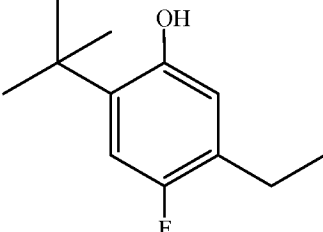
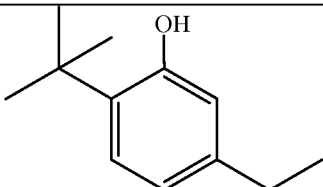
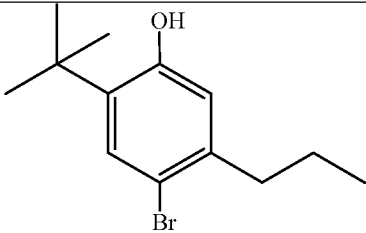
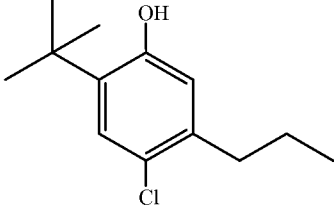
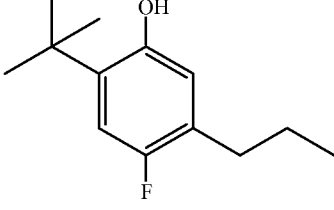
163	 2-sec-Butyl-5-methyl-phenol
164	 4-Bromo-2-sec-butyl-5-ethyl-phenol
165	 2-sec-Butyl-4-chloro-5-ethyl-phenol
166	 2-sec-Butyl-5-ethyl-4-fluoro-phenol
167	 2-sec-Butyl-5-ethyl-phenol
168	 2-sec-Butyl-5-propyl-phenol

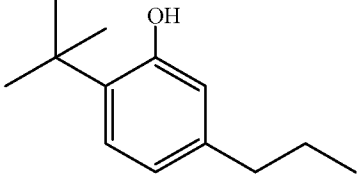
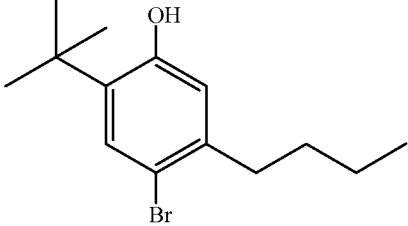
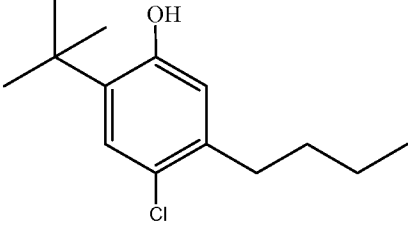
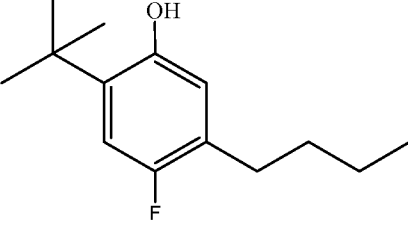
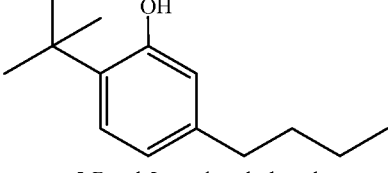
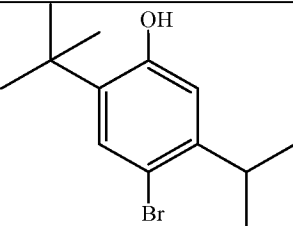
169	 4-Bromo-2-<i>sec</i>-butyl-5-propyl-phenol
170	 2-<i>sec</i>-Butyl-4-chloro-5-propyl-phenol
171	 2-<i>sec</i>-Butyl-4-fluoro-5-propyl-phenol
172	 4-Bromo-5-butyl-2-<i>sec</i>-butyl-phenol
173	 5-Butyl-2-<i>sec</i>-butyl-4-chloro-phenol
174	 5-Butyl-2-<i>sec</i>-butyl-4-fluoro-phenol

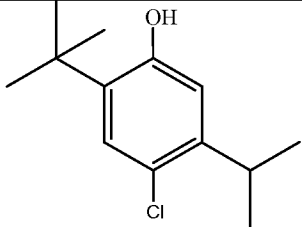
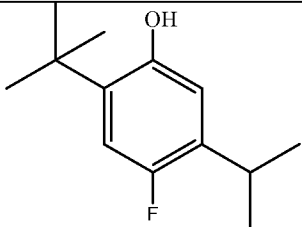
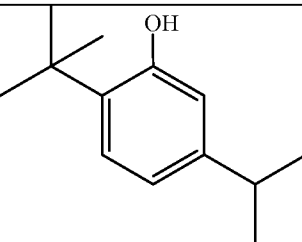
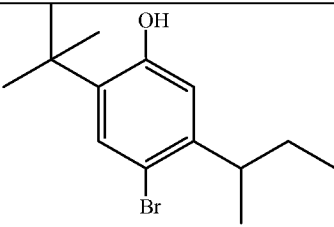
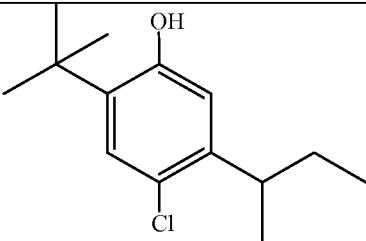
175	 5-Butyl-2-sec-butyl-phenol
176	 4-Bromo-2-sec-butyl-5-isopropyl-phenol
177	 2-sec-Butyl-4-chloro-5-isopropyl-phenol
178	 2-sec-Butyl-4-fluoro-5-isopropyl-phenol
179	 2-sec-Butyl-5-isopropyl-phenol
180	 2,5-Di-sec-butyl-phenol

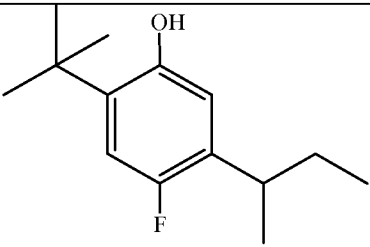
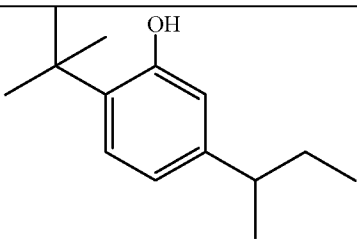
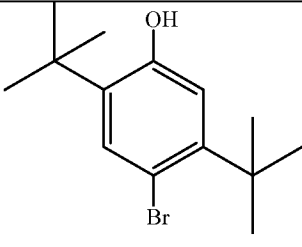
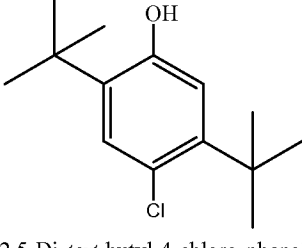
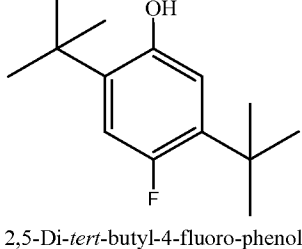
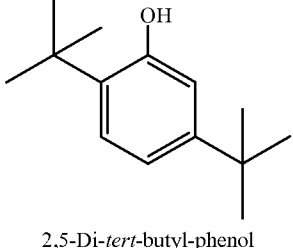
181	 4-Bromo-2,5-di-sec-butyl-phenol
182	 2,5-Di-sec-butyl-4-chloro-phenol
183	 2,5-Di-sec-butyl-4-fluoro-phenol
184	 2-sec-Butyl-5-tert-butyl-phenol
185	 4-Bromo-2-sec-butyl-5-tert-butyl-phenol
186	 2-sec-Butyl-5-tert-butyl-4-chloro-phenol

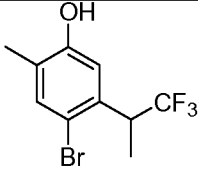
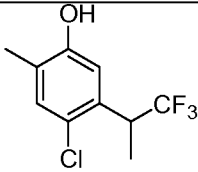
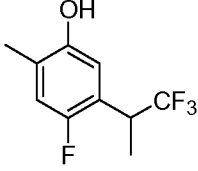
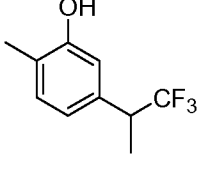
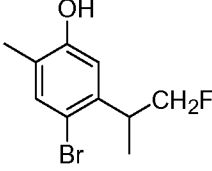
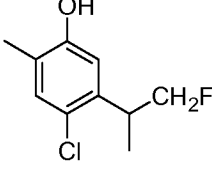
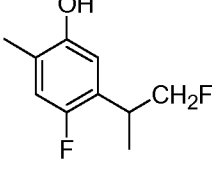
187	 2-sec-Butyl-5-tert-butyl-4-fluoro-phenol
<i>tert</i> -butyl series 188	 4-Bromo-2-tert-butyl-5-methyl-phenol
189	 2-tert-Butyl-4-chloro-5-methyl-phenol
190	 2-tert-Butyl-4-fluoro-5-methyl-phenol
191	 2-tert-Butyl-5-methyl-phenol
192	 4-Bromo-2-tert-butyl-5-ethyl-phenol

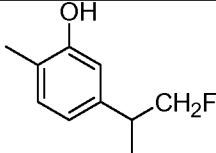
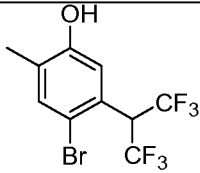
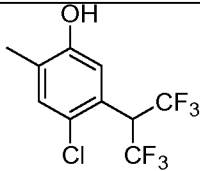
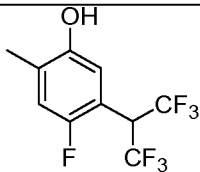
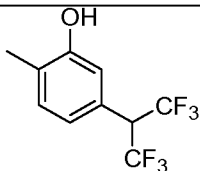
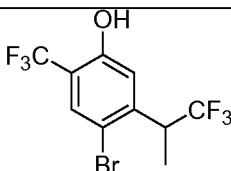
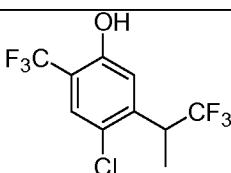
193	 2-<i>tert</i>-Butyl-4-chloro-5-ethyl-phenol
194	 2-<i>tert</i>-Butyl-5-ethyl-4-fluoro-phenol
195	 2-<i>tert</i>-Butyl-5-ethyl-phenol
196	 4-Bromo-2-<i>tert</i>-butyl-5-propyl-phenol
197	 2-<i>tert</i>-Butyl-4-chloro-5-propyl-phenol
198	 2-<i>tert</i>-Butyl-4-fluoro-5-propyl-phenol

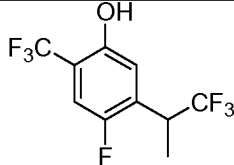
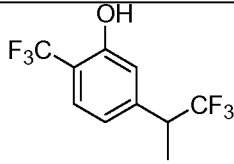
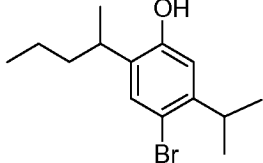
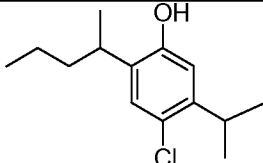
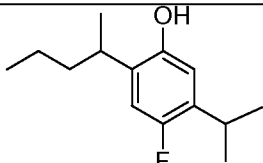
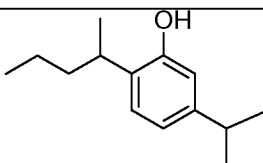
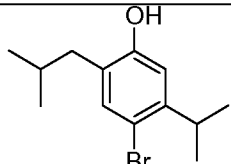
199	 2-<i>tert</i>-Butyl-5-propyl-phenol
200	 4-Bromo-5-butyl-2-<i>tert</i>-butyl-phenol
201	 5-Butyl-2-<i>tert</i>-butyl-4-chloro-phenol
202	 5-Butyl-2-<i>tert</i>-butyl-4-fluoro-phenol
203	 5-Butyl-2-<i>tert</i>-butyl-phenol
204	 4-Bromo-2-<i>tert</i>-butyl-5-isopropyl-phenol

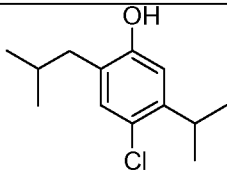
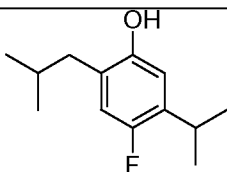
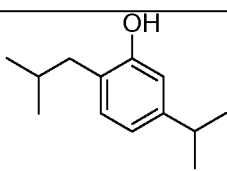
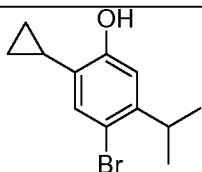
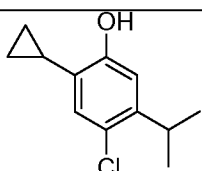
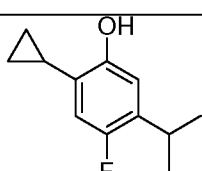
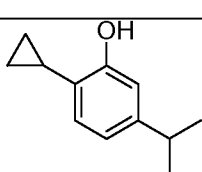
205	 2-<i>tert</i>-Butyl-4-chloro-5-isopropyl-phenol
206	 2-<i>tert</i>-Butyl-4-fluoro-5-isopropyl-phenol
207	 2-<i>tert</i>-Butyl-5-isopropyl-phenol
208	 4-Bromo-5-<i>sec</i>-butyl-2-<i>tert</i>-butyl-phenol
209	 5-<i>sec</i>-Butyl-2-<i>tert</i>-butyl-4-chloro-phenol

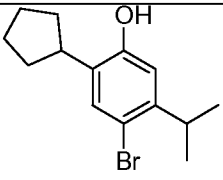
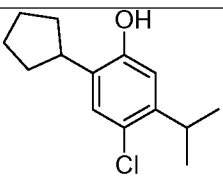
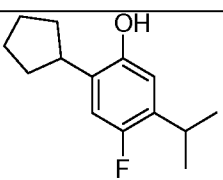
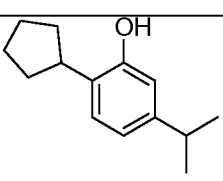
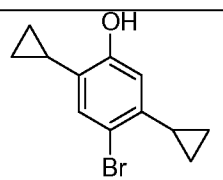
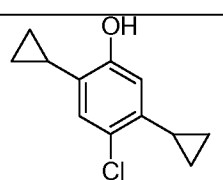
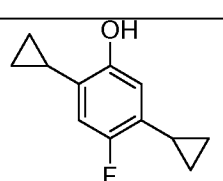
210	 5-sec-Butyl-2-tert-butyl-4-fluoro-phenol
211	 5-sec-Butyl-2-tert-butyl-phenol
212	 4-Bromo-2,5-di-tert-butyl-phenol
213	 2,5-Di-tert-butyl-4-chloro-phenol
214	 2,5-Di-tert-butyl-4-fluoro-phenol
215	 2,5-Di-tert-butyl-phenol

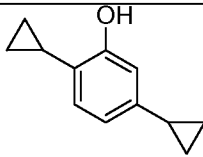
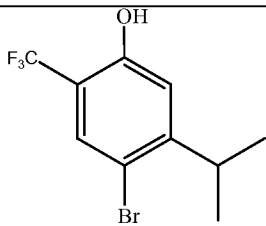
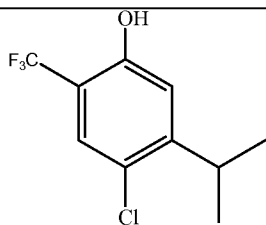
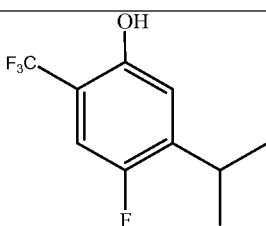
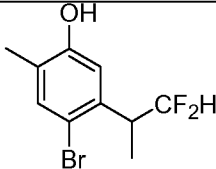
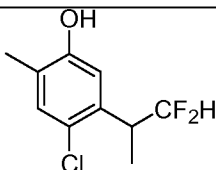
5- trifluoroisopropyl Series 216	 4-Bromo-2-methyl-5-(2,2,2-trifluoro-1-methyl-ethyl)-phenol
217	 4-Chloro-2-methyl-5-(2,2,2-trifluoro-1-methyl-ethyl)-phenol
218	 4-Fluoro-2-methyl-5-(2,2,2-trifluoro-1-methyl-ethyl)-phenol
219	 2-Methyl-5-(2,2,2-trifluoro-1-methyl-ethyl)-phenol
5-Fluoroisopropyl series 220	 4-Bromo-5-(2-fluoro-1-methyl-ethyl)-2-methyl-phenol
221	 4-Chloro-5-(2-fluoro-1-methyl-ethyl)-2-methyl-phenol
222	 4-Fluoro-5-(2-fluoro-1-methyl-ethyl)-2-methyl-phenol

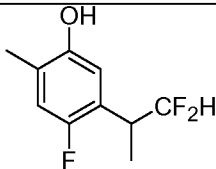
223	 5-(2-Fluoro-1-methyl-ethyl)-2-methyl-phenol
5-Hexafluoroiso propyl series 224	 4-Bromo-2-methyl-5-(2,2,2-trifluoro-1-trifluoromethyl-ethyl)-phenol
225	 4-Chloro-2-methyl-5-(2,2,2-trifluoro-1-trifluoromethyl-ethyl)-phenol
226	 4-Fluoro-2-methyl-5-(2,2,2-trifluoro-1-trifluoromethyl-ethyl)-phenol
227	 2-Methyl-5-(2,2,2-trifluoro-1-trifluoromethyl-ethyl)-phenol
2-trifluoro Methyl, 5-trifluoro Isopropyl series 228	 4-Bromo-2-trifluoromethyl-5-(2,2,2-trifluoro-1-methyl-ethyl)-phenol
229	 4-Chloro-2-trifluoromethyl-5-(2,2,2-trifluoro-1-methyl-ethyl)-phenol

230	 4-Fluoro-2-trifluoromethyl-5-(2,2,2-trifluoro-1-methyl-ethyl)-phenol
231	 2-Trifluoromethyl-5-(2,2,2-trifluoro-1-methyl-ethyl)-phenol
<i>Sec-pentyl</i> Series 232	 4-Bromo-5-isopropyl-2-(1-methyl-butyl)-phenol
233	 4-Chloro-5-isopropyl-2-(1-methyl-butyl)-phenol
234	 4-Fluoro-5-isopropyl-2-(1-methyl-butyl)-phenol
235	 5-Isopropyl-2-(1-methyl-butyl)-phenol
<i>Isobutyl series</i> 236	 4-Bromo-2-isobutyl-5-isopropyl-phenol

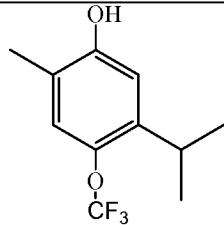
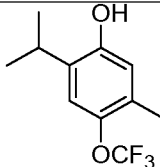
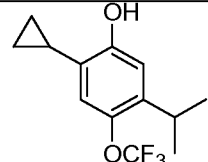
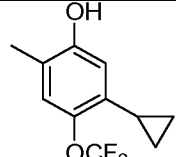
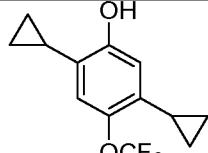
237	 4-Chloro-2-isobutyl-5-isopropyl-phenol
238	 4-Fluoro-2-isobutyl-5-isopropyl-phenol
239	 2-Isobutyl-5-isopropyl-phenol
Cyclopropyl Series 240	 4-Bromo-2-cyclopropyl-5-isopropyl-phenol
241	 4-Chloro-2-cyclopropyl-5-isopropyl-phenol
241	 2-Cyclopropyl-4-fluoro-5-isopropyl-phenol
242	 2-Cyclopropyl-5-isopropyl-phenol

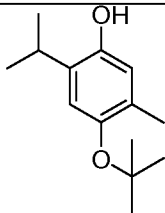
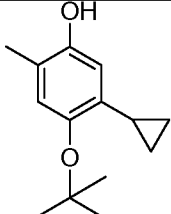
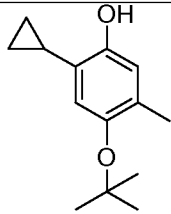
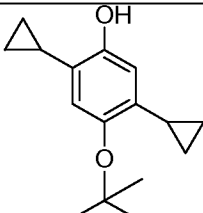
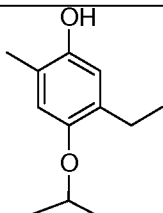
Cyclopentyl Series 243	 4-Bromo-2-cyclopentyl-5-isopropyl-phenol
244	 4-Chloro-2-cyclopentyl-5-isopropyl-phenol
245	 2-Cyclopentyl-4-fluoro-5-isopropyl-phenol
246	 2-Cyclopentyl-5-isopropyl-phenol
2,5-dicyclopropyl Series 247	 4-Bromo-2,5-dicyclopropyl-phenol
248	 4-Chloro-2,5-dicyclopropyl-phenol
249	 2,5-Dicyclopropyl-4-fluoro-phenol

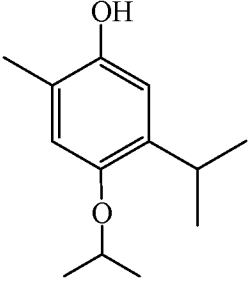
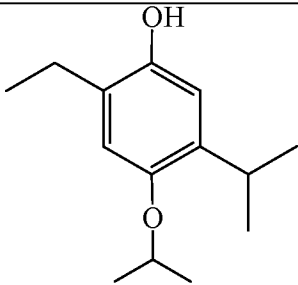
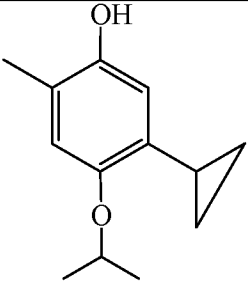
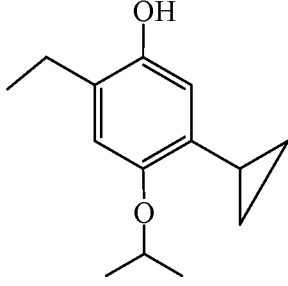
250	 2,5-Dicyclopropyl-phenol
251	 4-Bromo-5-isopropyl-2-trifluoromethyl-phenol
252	 4-Chloro-5-isopropyl-2-trifluoromethyl-phenol
253	 4-Fluoro-5-isopropyl-2-trifluoromethyl-phenol
254	 4-Bromo-5-(2,2-difluoro-1-methyl-ethyl)-2-methyl-phenol
255	 4-Chloro-5-(2,2-difluoro-1-methyl-ethyl)-2-methyl-phenol

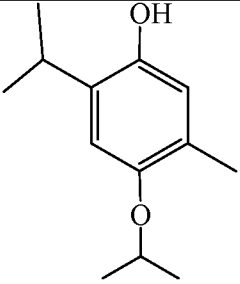
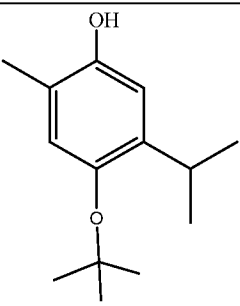
256	 5-(2,2-Difluoro-1-methyl-ethyl)-4-fluoro-2-methyl-phenol
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Family 1b Species

Example Number	Species Structure Species Name
4-trifluoromethyl Series (abbreviated) 257	 5-Isopropyl-2-methyl-4-trifluoromethoxy-phenol
258	 2-Isopropyl-5-methyl-4-trifluoromethoxy-phenol
259	 2-Cyclopropyl-5-isopropyl-4-trifluoromethoxy-phenol
260	 5-Cyclopropyl-2-methyl-4-trifluoromethoxy-phenol
261	 2,5-Dicyclopropyl-4-trifluoromethoxy-phenol

4-<i>tert</i>-butyl series 262	 <i>4-tert</i> -Butoxy-2-isopropyl-5-methyl-phenol
263	 <i>4-tert</i> -Butoxy-5-cyclopropyl-2-methyl-phenol
264	 <i>4-tert</i> -Butoxy-2-cyclopropyl-5-methyl-phenol
265	 <i>4-tert</i> -Butoxy-2,5-dicyclopropyl-phenol
4-isopropyl Series (abbreviated) 266	 5-Ethyl-4-isopropoxy-2-methyl-phenol

267	 4-Isopropoxy-5-isopropyl-2-methyl-phenol
268	 2-Ethyl-4-isopropoxy-5-isopropyl-phenol
269	 5-Cyclopropyl-4-isopropoxy-2-methyl-phenol
270	 5-Cyclopropyl-2-ethyl-4-isopropoxy-phenol

271	 4-Isopropoxy-2-isopropyl-5-methyl-phenol
272	 4-<i>tert</i>-Butoxy-5-isopropyl-2-methyl-phenol

C. Methods of Treatment

[0101] The present disclosure further provides methods for treating a condition in a subject having or susceptible to having such a condition, by administering to the subject a therapeutically-effective amount of one or more compounds as described above; such compounds may optionally include one or more deuterium or tritium atoms. In one embodiment, the treatment is preventative treatment. In another embodiment, the treatment is palliative treatment. In another embodiment, the treatment is restorative treatment.

10

1. Conditions

[0102] The conditions that can be treated in accordance with the present invention include, but are not limited to Alzheimer's Disease, anxiety, atherosclerosis, bipolar disorder, celiac sprue, convulsions, dementia, depression, epilepsy, fibromyalgia, glomerulonephritis, Huntington's Chorea, inflammation disorders, inflammatory bowel disease, mania, memory, migraine, multiple sclerosis, neuropathic pain, Parkinson's Disease, pelvic inflammatory disease, rheumatoid arthritis, seizures, tinnitus, Tourette's Syndrome, and tremors. In certain preferred embodiments, the compounds described herein can be administered prophylactically to prevent one or more of the above listed

15

conditions. In particularly preferred embodiments, the compounds described herein can be administered prophylactically to individuals such as soldiers, sailors, biohazard remediation professionals, and the like, who are particularly susceptible to one or more of the above listed conditions as a result of exposure to their work environments.

5 **[0103]** In certain embodiments, the compounds of the present invention may be administered as adjunctive therapy in the treatment of partial onset seizures in adults and children with epilepsy. In certain embodiments the compounds of the present invention may be administered as adjunctive therapy in the treatment of myoclonic seizures in adults and adolescents with juvenile myoclonic epilepsy. In certain embodiments the compounds
10 of the present invention may be administered as adjunctive therapy in the treatment of primary generalized tonic-clonic seizures in adults and children with idiopathic generalized epilepsy.

[0104] The present invention also relates to compounds having microbial-static and microbicidal effects in mammals or on inanimate objects. Compounds of the present
15 invention are useful for sanitizing objects, and therefore are useful for preventing the spread of microorganisms causing infectious disease. Compounds of the present invention are also useful for preserving food, beverage, pharmaceutical and cosmetic preparations at antimicrobial concentrations. They are furthermore useful to prevent and treat infections in mammals, such as the treatment of skin ulcers or periodontal disease, by causing
20 antimicrobial effects on mammalian tissue. In certain embodiments, the compounds of the present invention cause antimicrobial effects while not causing sedation in animals or humans, regardless of whether exposure is deliberate (such as during treatment of a mammalian subject), or inadvertant (such as exposure resulting from application of compounds of the present invention to inanimate objects in the environment of a
25 mammalian subject).

[0105] Specifically, the compounds of the present invention can be used to kill or prevent the growth of microorganisms, such as Enterobacteriaceae (such as *Escherichia coli*), Firmicutes (such as *Staphylococcus aureus*, *Listeria monocytogenes*, and *Bacillus spp.*), Archaeobacteria, Protozoans (such as *Giardia lamblia*) and Yeasts (such as *Candida spp.*).
30 Disclosed compounds may be used alone, in combination with other compounds of this invention, or in combination with other substances to cause antimicrobial effects.

2. Subjects

[0106] Suitable subjects to be treated according to the present invention include mammalian subjects. Mammals according to the present invention include, but are not limited to, human, canine, feline, bovine, caprine, equine, ovine, porcine, rodents, lagomorphs, primates, including humans, and the like, and encompass mammals *in utero*.
5 Subjects may be of either gender and at any stage of development, including infancy, childhood, adolescence, young adulthood, adulthood, and senescence.

3. Administration and Dosing

[0107] The compounds of the present invention are generally administered in a therapeutically effective amount. The compounds of the present invention may be
10 administered in amounts ranging from about 1 mg to about 100 mg per kilogram of body weight per day, for example about 10 mg/kg, about 20 mg/kg, about 30 mg/kg, about 40 mg/kg, about 50 mg/kg, about 60 mg/kg, about 70 mg/kg, about 80 mg/kg, or about 90 mg/kg per day. The total daily dosage may run from 10 to 1000 mg, such as from 30 to 500 mg, or even from 50 to 250 mg per day. The dosage regimen may be adjusted to
15 provide the optimum therapeutic response and is preferably administered one to three times a day. For example, several divided doses may be administered daily or the dose may be proportionally reduced as indicated by the exigencies of the therapeutic situation. A decided practical advantage is that the active compound may be administered in any convenient manner such as by oral, intravenous, intramuscular, or subcutaneous routes.

20 D. Pharmaceutical Compositions

[0108] For the treatment of the conditions referred to above, the compounds described herein can be administered as follows:

1. Oral Administration

[0109] Oral administration includes pills, tablets, capsules, syrups, powders, tonics,
25 and the like

2. Parenteral Administration

[0110] Parenteral administration includes enemas, suppositories, and the like.

3. Topical Administration

[0111] Topical administration includes lotions, creams, salves, ointments, patches,
30 and the like

E. Prodrugs

[0112] In yet another embodiment, the compounds of the present invention may be synthesized and/or administered as prodrugs. Propofol and certain other phenol containing

drugs can have short duration of action in vivo or poor oral absorption by virtue of their susceptibility to extensive first pass metabolism. Prodrugs of propofol have been prepared to increase aqueous solubility for intravenous administration. Methods of making prodrugs are well known in the art (see, e.g., US 6,362,234, US 2011/257587, US 2010/087536, US 5 2009/005352, US 2006/287525, US 2006/205969, US 2005/234050, US 2005/090431, US 2005/004381, and US 2003/176324, all incorporated by reference in their entireties herein). There are numerous approaches for protecting phenols, including but not limited to the formation of esters, carbonates, phosphates, carbamates, sulfamates, and acylmethylesters. The rate of esterase hydrolysis is known to be highly sensitive to the 10 steric environment about the ester carbonyl. Without being bound by theory, many prodrugs are designed to take advantage of this fact allowing the release kinetics to be adjusted. Other release mechanisms can be similarly affected by the steric environment.

F. Combinations and Combination Therapy

[0113] The compounds of the present invention can be used, alone or in combination 15 with other pharmaceutically active compounds, to treat conditions such as those previously described above. In certain embodiments, a compound according to Formula (I) can be administered simultaneously with a second agent (either in the same dosage form or in separate dosage forms) or sequentially with a second agent. Accordingly, in one embodiment, the present invention comprises methods for treating a condition by 20 administering to the subject a therapeutically-effective amount of one or more compounds according to Formula (I) and one or more additional pharmaceutically active compounds.

[0114] In certain non-limiting embodiments, the second agent can comprise one or more anticonvulsants, for example selected from acetylpheneturide, albutoin, aminogluthetamide, 4-amino-3-hydroxybutyric acid, atrolactamide, beclamide, buramate, 25 carbamazepine, cinromide, clomethiazole, clonazepam, decimemide, diethadione, dimethadione, doxenitoin, eterobarb, ethadione, ethosuximide, ethotoin, felbamate, fluoresone, fosphenytoin, gabapentin, ganaxolone, lamotrigine, levetiracetam, lorazepam, mephenytoin, mephobarbital, metharbital, methetoin, methsuximide, midazolam, narcobarbital, nitrazepam, oxcarbazepine, paramethadione, phenacemide, phenetharbital, 30 pheneturide, phenobarbital, phensuximide, phenylmethylbarbituric acid, phenytoin, phenethylate, pregabalin, primidone, progabide, remacemide, rufinamide, suclofenide, sulthiame, talampanel, tetrantoin, tiagabine, topiramate, trimethadione, valproic acid,

valpromide, vigabatrin, zonisamide, pharmaceutically acceptable salts thereof, and combinations thereof.

[0115] In other non-limiting embodiments, the second agent can comprise an analgesic or anti-inflammatory drug, for example selected from the group consisting of

5 acetaminophen, alfentanil, allylprodine, alphaprodine, anileridine, benzylmorphine, bezitramide, buprenorphine, butorphanol, clonitazene, codeine, cyclazocine, desomorphine, dextromoramide, dextropropoxyphene, dezocine, diampromide, diamorphine, dihydrocodeine, dihydromorphine, dimenoxadol, dimepheptanol, dimethylthiambutene, dioxaphetyl butyrate, dipipanone, dipyrone (metamizol), eptazocine,

10 ethoheptazine, ethylmethylthiambutene, ethylmorphine, etonitazene, fentanyl, heroin, hydrocodone, hydromorphine, hydroxypethidine, isomethadone, ketobemidone, levallorphan, levorphanol, levophenacyl-morphan, lofentanil, meperidine, meptazinol, metazocine, methadone, metopon, morphine, myrophine, nalbuphine, nalorphine, narceine, nicomorphine, norlevorphanol, normethadone, normorphine, norpipanone,

15 opium, oxycodone, oxymorphone, papavereturn, pentazocine, phenadoxone, phenazocine, phenomorphan, phenoperidine, piminodine, piritramide, proheptazine, promedol, properidine, propiram, propoxyphene, sufentanil, tilidine, tramadol, NO-naproxen, NCX-701, ALGRX-4975, alclometasone, amcinonide, betamethasone, betamethasone 17-valerate, clobetasol, clobetasol propionate, clocortolone, cortisone, dehydrotestosterone,

20 deoxycorticosterone, desonide, desoximetasone, dexamethasone, dexamethasone 21-isonicotinate, diflorasone, fluocinonide, fluocinolone, fluorometholone, flurandrenolide, fluticasone, halcinonide, halobetasol, hydrocortisone, hydrocortisone acetate, hydrocortisone cypionate, hydrocortisone hemisuccinate, hydrocortisone 21-lysinate, hydrocortisone sodium succinate, isoflupredone, isoflupredone acetate,

25 methylprednisolone, methylprednisolone acetate, methylprednisolone sodium succinate, methylprednisolone suleptanate, mometasone, prednicarbate, prednisolone, prednisolone acetate, prednisolone hemisuccinate, prednisolone sodium phosphate, prednisolone sodium succinate, prednisolone valerate-acetate, prednisone, triamcinolone, triamcinolone acetone, salicylic acid derivatives (such as salicylic acid, acetylsalicylic acid, methyl

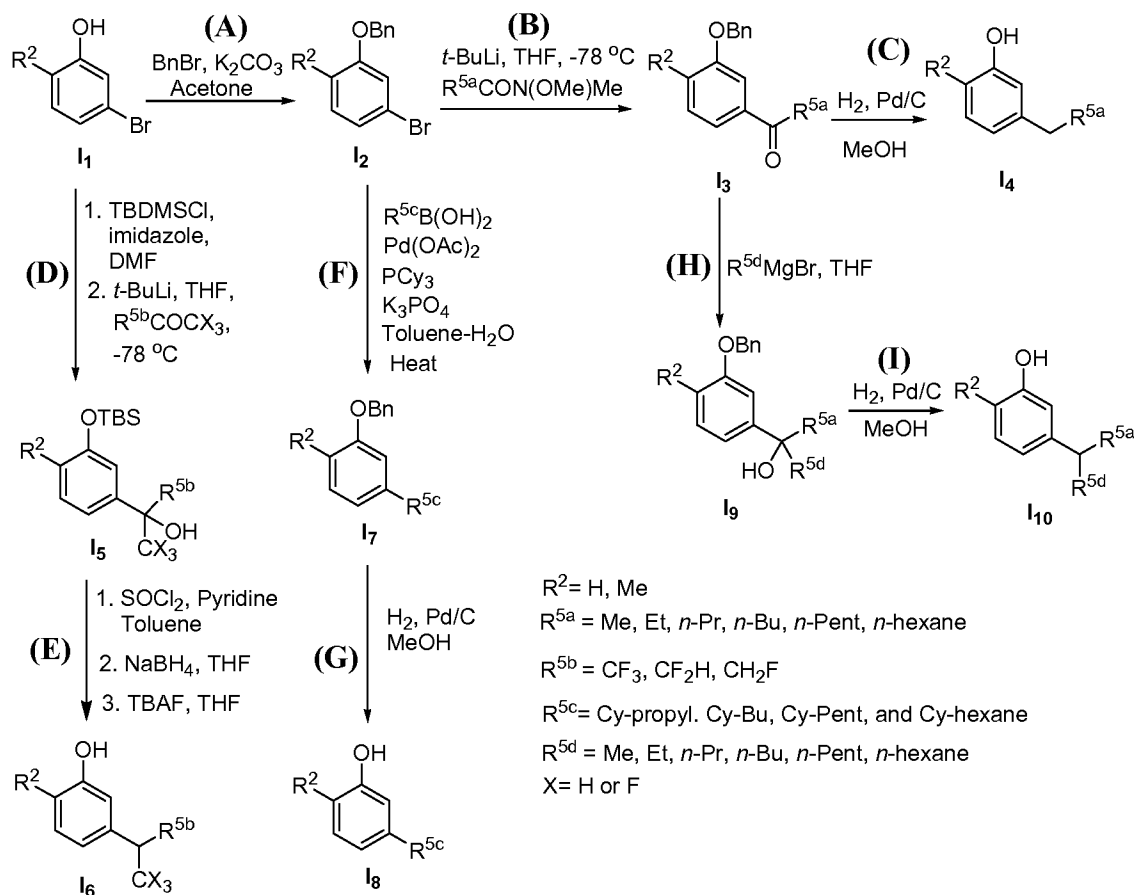
30 salicylate, diflunisal, olsalazine, salsalate and sulfasalazine), indole and indene acetic acids (such as indomethacin, etodolac and sulindac), fenamates (such as etofenamic, meclofenamic, mefenamic, flufenamic, niflumic and tolfenamic acids), heteroaryl acetic acids (such as acemetacin, alclofenac, clidanac, diclofenac, fenchlofenac, fentiazac,

furofenac, ibufenac, isoxepac, ketorolac, oxipinac, tiopinac, tolmetin, zidometacin and zomepirac), aryl acetic acid and propionic acid derivatives (such as alminoprofen, benoxaprofen, bucloxic acid, carprofen, fenbufen, fenoprofen, fluprofen, flurbiprofen, ibuprofen, indoprofen, ketoprofen, mioprofen, naproxen, oxaprozin, pirofen, 5 pranoprofen, suprofen, tiaprofenic acid and tioxaprofen), enolic acids (such as the oxicam derivatives ampiroxicam, cinnoxicam, droxicam, lornoxicam, meloxicam, piroxicam, sudoxicam and tenoxicam, and the pyrazolone derivatives aminopyrine, antipyrine, apazone, dipyrene, oxyphenbutazone and phenylbutazone), alkanones (such as nabumetone), nimesulide, proquazone, MX-1094, licofelone, celecoxib, deracoxib, 10 valdecoxib, parecoxib, rofecoxib, etoricoxib, lumiracoxib, PAC-10549, cimicoxib, GW-406381, LAS-34475, CS-502, and pharmaceutically acceptable salts thereof, and combinations thereof.

G. General Synthetic Schemes

[0116] The present invention also relates to methods of manufacturing the 15 compounds of the present invention for use in treatment of nervous conditions such as seizure or convulsion disorders. The compounds of the present invention can be prepared using the methods illustrated in the general synthetic schemes and experimental procedures detailed below. These general synthetic schemes and experimental procedures are presented for purposes of illustration and are not intended to be limiting. The starting 20 materials used to prepare the compounds of the present invention are commercially available or can be prepared using routine methods known in the art. Compounds embraced by Formula I may be prepared in accordance with Schemes I–IV, which follow, wherein the R substituent are as defined herein.

Scheme I



[0117] Conversion (A): The hydroxy group of 3-bromophenol I₁ is protected as a benzyl ether by treating I₁ with benzyl bromide (BnBr) and potassium carbonate (K₂CO₃) in acetone.

[0118] Conversion (B): The benzyl protected bromophenol I₂ is then treated with *t*-BuLi in THF at -78 °C and treated with R^{5a}CON(OMe)Me, yielding Scheme I intermediate I₃.

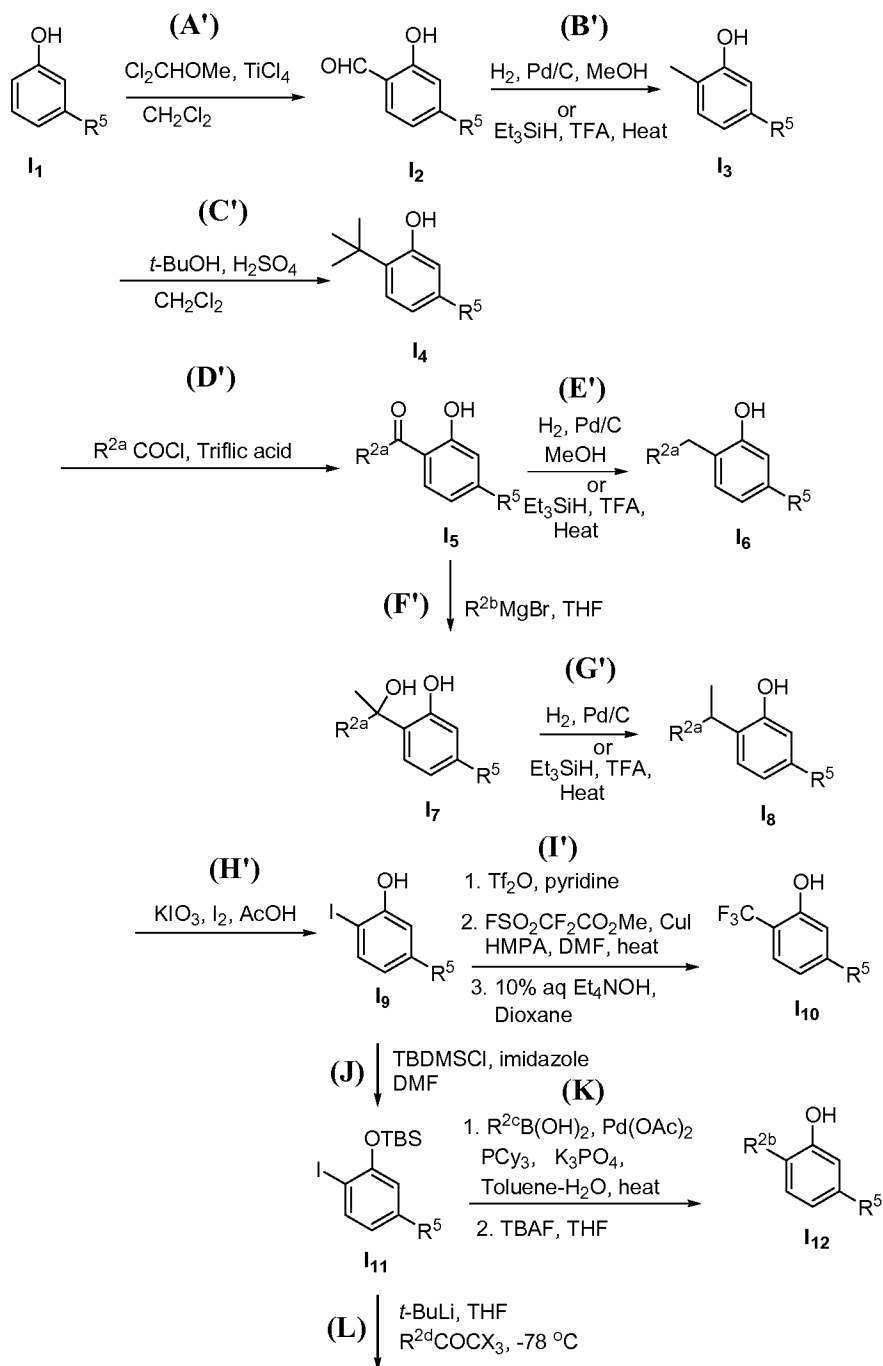
10 [0119] Conversion (C): The carbonyl functional group and benzyl ether of intermediate I₃ is reduced by subjecting it to hydrogenation conditions to yield Scheme I intermediate I₄.

[0120] Conversion (D): The hydroxy group of 3-bromophenol I₁ is protected as a *tert*-butyl di-methyl silyl ether by treating it with TBDMSCl and imidazole in DMF. The silyl ether is then treated with *t*-BuLi in THF at -78 °C and ketone R^{5a}COX₃ to afford the Scheme I intermediate I₅.

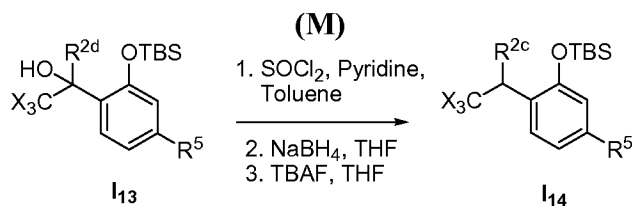
- [0121] Conversion (E): Intermediate **I**₅ is treated with thionyl chloride and pyridine to convert the *tert*-hydroxy group to chloride, which is reduced by treating it with sodium borohydride in THF. In the final step the silyl ether is cleaved by treating it with TBAF in THF to yield Scheme I intermediate **I**₆.
- 5 [0122] Conversion (F): The Intermediate **I**₂ is subjected to Suzuki coupling with boronic acid R^{5c}B(OH)₂, palladium acetate and potassium phosphate to afford the Scheme I intermediate **I**₇.
- [0123] Conversion (G): The benzyl ether of Intermediate **I**₇ is then cleaved under hydrogenation condition to yield the Scheme I intermediate **I**₈.
- 10 [0124] Conversion (H): The intermediate **I**₃ is treated with Grignard reagent R^{5d}MgX in THF to afford the Scheme I intermediate **I**₉.

[0125] Conversion (I): The *tert*-hydroxy group and benzyl ether of intermediate **I₉** is reduced under hydrogenation condition to give the Scheme I intermediate **I₁₀**.

Scheme II



Scheme II contd.



$R^5 =$ Me, Et, *n*-Pr, *n*-Bu, *n*-Pent, *n*-Hex, *sec*-Bu, CH(Me)*n*-Pr, CH(Et)₂, CH(Et)*n*-Bu, CH(*n*-Pr)₂, CH(*n*-Pr)*n*-Bu, CH(*n*-Bu)₂, *t*-Bu, C(CD₃)₃, CF₃, CF₂H, CFH₂, CHCH₃(CF₃), CHCH₃(CF₂H), CHCH₃(CFH₂), *cy*-Pr, *cy*-Bu, *cy*-Pent, *cy*-Hex

$R^{2a} =$ Me, Et, *n*-Pr, *n*-Bu, *n*-Pent, *n*-Hex

$R^{2b} =$ Me, Et, *n*-Pr, *n*-Bu, *n*-Pent, *n*-Hex

$R^{2c} =$ *cy*-Pr, *cy*-Bu, *cy*-Pent, *cy*-Hex

$R^{2d} =$ CF₃, CF₂H, CFH₂

[0126] Conversion (A'): Scheme II intermediate phenol **I**₁ is formylated at 2-position using TiCl₄ and dichloromethyl methyl ether in methylene chloride to afford Scheme II intermediate benzaldehyde **I**₂.

[0127] Conversion (B'): The formyl group of intermediate benzaldehyde **I**₂ is reduced with either Et₃SiH and TFA or under hydrogenation condition to afford the intermediate phenol **I**₃.

[0128] Conversion (C'): Scheme II intermediate phenol **I**₁ is treated with *tert*-butanol in sulfuric acid and acetic acid to give the intermediate phenol **I**₄.

[0129] Conversion (D'): Scheme II intermediate phenol **I**₁ is treated with acid chloride R^{2a}COCl in trifluoromethane sulfonic acid to afford the intermediate phenol **I**₅.

[0130] Conversion (E'): The carbonyl group of Scheme II intermediate **I**₅ is then reduced either with Et₃SiH and TFA or hydrogenation condition to yield the intermediate phenol **I**₆.

[0131] Conversion (F'): Scheme II intermediate **I**₅ is treated with Grignard reagent R^{2b}MgBr in THF to give the intermediate carbinol **I**₇.

[0132] Conversion (G'): The *tert*-hydroxy group of Scheme II intermediate carbinol **I**₇ is then reduced either with Et₃SiH and TFA or hydrogenation condition to yield the intermediate phenol **I**₈.

[0133] Conversion (H'): Scheme II intermediate phenol **I**₁ is iodinated with iodine and KIO₃ in acetic acid to afford the iodinated intermediate phenol **I**₉.

[0134] Conversion (I'): Treatment of iodo-phenol, Scheme II intermediate phenol **I**₉ with trifluoromethanesulfonic anhydride and pyridine gives aryl triflate. Reaction of the resultant aryl triflate with FSO₂CF₂CO₂Me and CuI in DMF-HMPA affords trifluoromethylated aryl triflate. The triflate ester is hydrolyzed with 10 % aqueous Et₄NOH in dioxane to afford Scheme II intermediate, 2-trifluoromethyl phenol **I**₁₀.

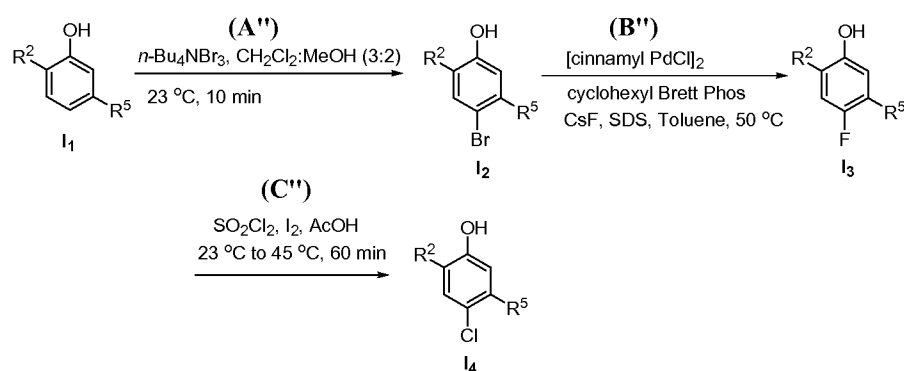
[0135] Conversion (J): Scheme II intermediate, iodo-phenol **I**₉ on treatment with TBDMSCl and imidazole in DMF protects the phenol hydroxy as *tert*-butyl dimethyl silyl ether, intermediate **I**₁₁.

[0136] Conversion (K): Scheme II intermediate **I**₁₁ under goes Suzuki coupling with R^{2c}B(OH)₂, palladium acetate, PCy₃, potassium phosphate in toluene and water at 100 °C. The silyl ether of the Suzuki coupled product is cleaved with TBAF in THF to give Scheme II intermediate phenol **I**₁₂.

[0137] Conversion (L): Intermediate **I**₁₁ on treatment with *t*-BuLi in THF at -78 °C and ketone R^{2d}COCX₃ gives the *tert*-carbinol intermediate **I**₁₃.

[0138] Conversion (M): The *tert*-hydroxy group of intermediate **I**₁₃ is transformed to its chloride on treatment with thionyl chloride and pyridine. The chloro derivative is then reduced on treatment with sodium borohydride. Finally, the silyl ether is cleaved with TBAF in THF to afford Scheme II intermediate phenol **I**₁₄.

Scheme III



R²= Me, Et, n-Pr, n-Bu, n-Pent, n-Hex, sec-Bu, CH(Me)n-Pr, CH(Et)₂, CH(Et)n-Bu, CH(n-Pr)₂, CH(n-Pr)n-Bu, CH(n-Bu)₂, t-Bu, C(CD₃)₃, CF₃, CHCH₃(CF₃), CHCH₃(CF₂H), CHCH₃(CFH₂), cy-Pr, cy-Bu, cy-Pent, cy-Hex

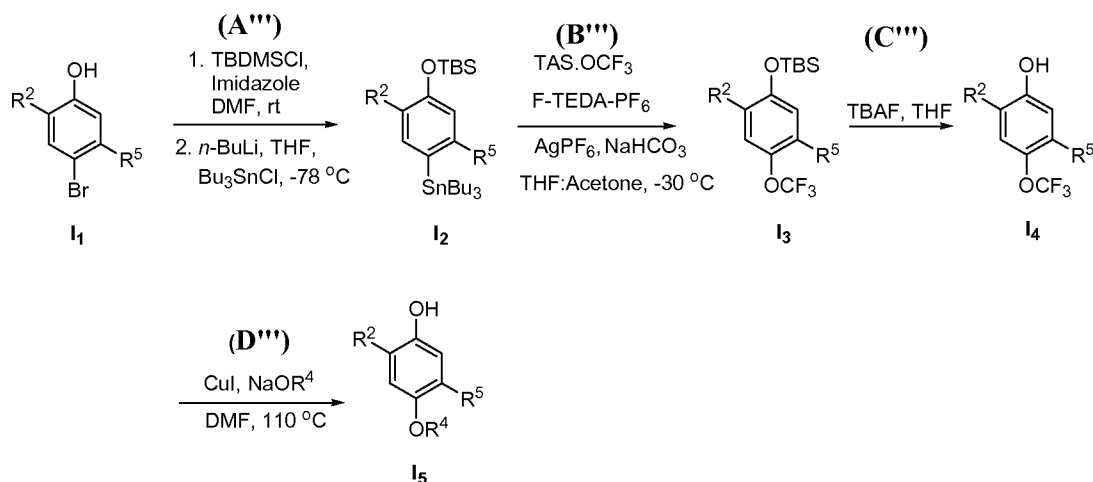
R⁵= Me, Et, n-Pr, n-Bu, n-Pent, n-Hex, sec-Bu, CH(Me)n-Pr, CH(Et)₂, CH(Et)n-Bu, CH(n-Pr)₂, CH(n-Pr)n-Bu, CH(n-Bu)₂, t-Bu, C(CD₃)₃, CF₃, CF₂H, CFH₂, CHCH₃(CF₃), CHCH₃(CF₂H), CHCH₃(CFH₂), cy-Pr, cy-Bu, cy-Pent, cy-Hex

[0139] Conversion (A''): Scheme III, intermediate phenol **I**₁ on treatment with *n*-Bu₄NBr₃ in a (3:2) mixture of methylene chloride and methanol affords the 4-bromo phenol **I**₂.

[0140] Conversion (B''): Scheme III intermediate phenol **I**₂ on palladium catalyzed transformation with [cinnamyl PdCl]₂, cyclohexyl Brett Phos, CsF, and sodium dodecyl sulfate (SDS) in toluene at 50 °C affords the 4-fluoro phenol **I**₃.

[0141] Conversion (C''): Scheme III intermediate phenol **I**₁ on treatment with sulfuryl chloride and catalytic amount of iodine in acetic acid at 45 °C affords the 4-chloro-phenol **I**₄.

Scheme IV



R²= Me, Et, *n*-Pr, *n*-Bu, *n*-Pent, *n*-Hex, *sec*-Bu, CH(Me)*n*-Pr, CH(Et)₂, CH(Et)*n*-Bu, CH(*n*-Pr)₂, CH(*n*-Pr)*n*-Bu, CH(*n*-Bu)₂, *t*-Bu, C(CD₃)₃, CF₃, CHCH₃(CF₃), CHCH₃(CF₂H), CHCH₃(CFH₂), *cy*-Pr, *cy*-Bu, *cy*-Pent, *cy*-Hex

R⁴= Me, Et, *n*-Pr, *sec*-Bu, *t*-Bu, *i*-Pr

R⁵= Me, Et, *n*-Pr, *n*-Bu, *n*-Pent, *n*-Hex, *sec*-Bu, CH(Me)*n*-Pr, CH(Et)₂, CH(Et)*n*-Bu, CH(*n*-Pr)₂, CH(*n*-Pr)*n*-Bu, CH(*n*-Bu)₂, *t*-Bu, C(CD₃)₃, CF₃, CF₂H, CFH₂, CHCH₃(CF₃), CHCH₃(CF₂H), CHCH₃(CFH₂), *cy*-Pr, *cy*-Bu, *cy*-Pent, *cy*-Hex

10

[0142] Conversion A''': The hydroxy group of Scheme IV intermediate phenol **I**₁ is protected as *tert*-butyl dimethyl silyl ether by treating it with TBDMSCl and imidazole in DMF. The intermediate silyl ether is treated with *n*BuLi in THF at -78 °C followed by Bu₃SnCl to afford 4-tributylstannane phenol, intermediate **I**₂.

[0143] Conversion B''': Silver mediated coupling of aryl tributylstannane **I**₂ with tris dimethyl ammonium sulfonium trifluoromethoxide (TAS.OCF₃) at -30 °C in THF:acetone to afford Scheme IV 4-trifluoromethoxy aryl silyl ether, intermediate **I**₃.

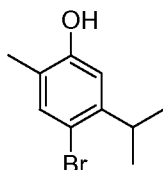
[0144] Conversion C''': The silyl ether of intermediate **I**₃ is cleaved by treating it with TBAF in THF to afford 4-trifluoromethoxy phenol, Scheme IV intermediate **I**₄.

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[0145] Conversion D": Scheme I intermediate 4-bromo phenol **I₁** on treatment with CuI and sodium alkoxide in DMF at 110 °C, affords the 4-alkoxy phenol **I₅**.

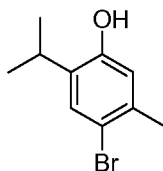
G. Compound Prep Examples

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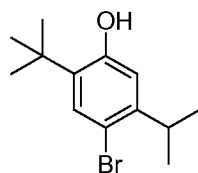
4-Bromo-5-isopropyl-2-methylphenol (9)

[0146] **4-Bromo-5-isopropyl-2-methylphenol (9)**: As outlined in Scheme III, conversion A", 4-bromo-5-isopropyl-2-methylphenol was obtained from commercially available 5-isopropyl-2-methylphenol (Carvacrol, Sigma Aldrich). Accordingly, 5-isopropyl-2-methylphenol (Carvacrol, Sigma Aldrich) (2 gm, 13.31 mmol) was dissolved in 80 mL of CH₂Cl₂:MeOH (3:2). To this solution was added drop wise a solution of *n*-Bu₄NBr₃ in 66 mL of CH₂Cl₂:MeOH (3:2). The reaction was stirred at room temperature for 10 minutes. The solvent was then removed under *vacuo* and the residue was dissolved in ether (100 mL), which was then washed with water (3 x 50 mL). It was dried over anhydrous sodium sulfate, filtered, concentrated and purified by column chromatography using hexanes and ethyl acetate to afford the title compound 2.8 g (93 %) as an light yellow oil, which crystallized on prolonged standing at room temperature. ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.25 (s, 1H), 6.68 (s, 1H), 4.62 (s, 1H), 3.24 (sep, *J* = 6.8 Hz, 1H), 2.17 (s, 3H), 1.18 (d, *J* = 7.2 Hz, 6H).



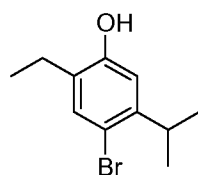
4-Bromo-2-isopropyl-5-methylphenol (132)

[0147] **4-Bromo-2-isopropyl-5-methylphenol (132)**: Compound **132** was synthesized from 2-isopropyl-5-methylphenol (Thymol, Sigma Aldrich), following the procedure used for the synthesis of compound **9**. ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.28 (s, 1H), 6.66 (s, 1H), 4.60 (s, 1H), 3.22 (sep, *J* = 6.8 Hz, 1H), 2.14 (s, 3H), 1.19 (d, *J* = 7.2 Hz, 6H).



4-Bromo-2-*tert*-butyl-5-isopropyl phenol (204)

[0148] **4-Bromo-2-*tert*-butyl-5-isopropylphenol (204):** Compound **204** was synthesized from 5-isopropyl phenol in accordance to (a) Scheme II conversion C', and (b) Scheme III conversion A". **Scheme II Conversion C'...Synthesis of 2-*tert*-Butyl-5-isopropyl phenol:** As outlined in Scheme II, conversion C', to a solution of 5-isopropyl phenol (2.5 g, 18.37 mmol, TCI US) in CH₂Cl₂ (25 mL) at 0° C was added *tert*-butanol (1.76 mL, 18.35 mmol) and concentrated sulfuric acid (0.98 mL, 18.35 mmol). The reaction was allowed to warm to room temperature and stirred for 24 hour. The mixture was poured on to ice-water (50 mL) and quenched with NaHCO₃. The organic layer was removed and the aqueous layer was extracted with CH₂Cl₂ (3 x 50 mL). The combine organic extract was dried over anhydrous sodium sulfate, filtered, and concentrated in *vacuo*. The residue was purified by column chromatography using hexanes and ethyl acetate, giving 3 g (86 %) of the desired phenol as an oil. ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.20 (d, *J* = 8.1 Hz, 1H), 6.76 (dd, *J* = 8.1, 1.8 Hz, 1H), 6.54 (d, *J* = 1.8 Hz, 1H), 4.71 (s, 1H), 2.83 (sept, *J* = 6.9 Hz, 1H), 1.41 (s, 9H), 1.24 (d, *J* = 6.9 Hz, 6H). **Scheme III Conversion A'...Synthesis of 4-Bromo-2-*tert*-butyl-5-isopropylphenol:** Compound **204** was synthesized from 2-*tert*-butyl-5-isopropyl phenol obtained above, following the procedure adopted for the synthesis of compound **9**. ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.39 (s, 1H), 6.60 (s, 1H), 4.41 (s, 1H), 3.26 (sep, *J* = 6.8 Hz, 1H), 1.35 (s, 9H), and 1.18 (d, *J* = 7.2 Hz, 6H).



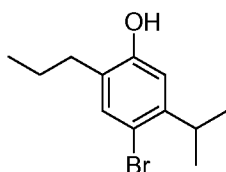
4-Bromo-2-ethyl-5-isopropyl phenol (64)

[0149] **4-Bromo-2-ethyl-5-isopropyl phenol (64):** Compound **64** was synthesized from 3-isopropyl phenol in accordance to (a) Scheme II Conversion D' and E', and (b) Scheme III Conversion A". **Scheme II Conversion D'...Synthesis of 1-(2-Hydroxy-4-**

isopropyl-phenyl) ethanone: A solution of 3-isopropyl phenol (2 g, 14.68 mmol) and acetyl chloride (1.05 mL, 14.68 mmol) in 10 mL of triflic acid was stirred at room temperature for 16 h. The reaction mixture was poured on to ice-cold water and extracted with EtOAc. The organic layer was washed with 1 N HCl, saturated NaHCO₃, and brine solution. The organic layer was dried over anhydrous Na₂SO₄, filtered, and concentrated under vacuo. The residue was purified by column chromatography using hexanes and ethyl acetate to afford 2 gm (77 %) of the title compound as a yellow oil. ¹H NMR (400 MHz, CDCl₃, ppm): δ 12.26 (s, 1H), 7.63 (d, *J*= 8.4 Hz, 1H), 6.82 (d, *J*=1.6 Hz, 1H), 6.75 (dd, *J*= 8.4 Hz, 1.6 Hz, 1H), 2.87 (sep, *J*= 7.2 Hz, 1H), 2.58 (s, 3H), and 1.23 (d, *J*= 6.8 Hz, 6H). **Scheme II Conversion E'...**

Synthesis of 2-Ethyl-5-isopropyl phenol: To a solution of 1-(2-Hydroxy-4-isopropyl-phenyl) ethanone (1.5 g, 8.41 mmol) in TFA (4mL) at 0 °C was added Et₃SiH (6.72 mL, 42.05 mmol) drop wise. The reaction mixture was heated at 55 °C for 36 h. The reaction mixture was allowed to cool to room temperature and water (50 mL) and CH₂Cl₂ (50 mL) were added. The aqueous layer was separated and extracted with CH₂Cl₂ (3 x 50 mL). The combined organic extracts were washed with brine and dried over anhydrous Na₂SO₄, filtered, and concentrated under *vacuo*. The residue was purified by column chromatography using hexanes and ethyl acetate to afford 1.2 g (87 %) the title phenol as a yellow oil. ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.03 (d, *J*= 7.6 Hz, 1H), 6.74 (dd, *J*= 7.6 Hz, 1.6 Hz), 6.64 (d, *J*= 1.6 Hz), 2.80 (sep, *J*= 7.2 Hz), 2.58 (q, *J*= 8.0 Hz, 2H), 1.21 (t, *J*= 8.0 Hz, 3H), and 1.20 (d, *J*= 6.8 Hz, 6H). **Scheme III Conversion A'...**

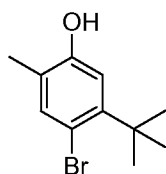
Synthesis of 4-Bromo-2-ethyl-5-isopropyl phenol (64): Compound **64** was synthesized from 2-ethyl-5-isopropyl phenol obtained above, following a procedure adopted for the synthesis of compound **9**. ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.27 (s, 1H), 6.69 (s, 1H), 4.65 (s, 1H), 3.25 (sep, *J*= 6.8 Hz, 1H), 3.37 (q, *J*= 7.2 Hz, 2H), 1.21 (t, *J*= 7.6 Hz, 3H), and 1.20 (d, *J*= 7.2 Hz, 6H).



4-Bromo-5-isopropyl-2-n-propyl phenol (92)

[0150] **4-Bromo-5-isopropyl-2-n-propyl phenol:** Compound **92** was synthesized from 3-isopropyl phenol following the procedure adopted for the synthesis of compound **64**. In the first step, propionyl chloride was used instead of acetyl chloride. **1-(2-Hydroxy-**

4-isopropyl-phenyl) propan-1-one: ^1H NMR (400 MHz, CDCl_3 , ppm): δ 12.37 (s, 1H), 7.68 (d, $J=8.0$ Hz, 1H), 6.84 (d, $J=2.0$ Hz, 1H), 6.76 (dd, $J=8.0$ Hz, 1.6 Hz, 1H), 3.00 (q, $J=7.6$ Hz, 2H), 2.88 (sep, $J=6.8$ Hz, 1H), and 1.23 (m, 9H). **2-n-Propyl-5-isopropyl phenol:** ^1H NMR (400 MHz, CDCl_3 , ppm): δ 7.03 (d, $J=7.6$ Hz, 1H), 6.74 (dd, $J=7.6$ Hz, 1.6 Hz, 1H), 6.64 (d, $J=1.6$ Hz, 1H), 2.83 (sep, $J=7.2$ Hz, 1H), 2.54 (t, $J=7.6$ Hz, 2H), 1.63 (m, 2H), 1.22 (d, $J=6.8$ Hz, 6H), and 0.98 (t, $J=7.2$ Hz, 3H). **4-Bromo-5-isopropyl-2-n-propyl phenol:** ^1H NMR (400 MHz, CDCl_3 , ppm): δ 7.25 (s, 1H), 6.68 (s, 1H), 4.60 (s, 1H), 3.25 (sep, $J=6.8$ Hz, 1H), 2.50 (t, $J=7.6$ Hz, 2H), 1.62 (m, 2H), 1.20 (d, $J=6.8$ Hz, 6H), and 0.97 (t, $J=7.2$ Hz, 3H).



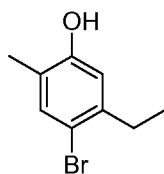
4-Bromo-5-tert-butyl-2-methyl phenol (25)

[0151] **4-Bromo-5-tert-butyl-2-methyl phenol (25):** Compound **25** was synthesized from commercially available 3-tert-butyl phenol in accordance to (a) Scheme II Conversion A' and B', and (b) Scheme III Conversion A". **Scheme II Conversion A'...Synthesis of 4-tert-Butyl-2-hydroxy benzaldehyde:** To a solution of 3-tert-butyl phenol (4 g, 26.62 mmol) in anhydrous CH_2Cl_2 (50 mL) at 0 °C was added TiCl_4 (5.85 mL, 53.24 mmol), followed by Cl_2CHOMe (4.82 mL, 53.23 mmol). The reaction mixture was allowed to warm to room temperature over 1 h, quenched cautiously with ice and water. It was then extracted with CH_2Cl_2 (3 x 50 mL). The organic extract was washed with water and brine, dried over anhydrous Na_2SO_4 , filtered, and concentrated in *vacuo*. The residue was purified by column chromatography using hexanes and ethyl acetate to afford 3.5 g (74 %) of the title compound as a yellow oil. ^1H NMR (400 MHz, CDCl_3 , ppm): δ 11.98 (s, 1H), 9.83 (s, 1H), 7.46 (d, $J=8.4$ Hz), 7.04 (dd, $J=8.4$ Hz, 2.0 Hz, 1H), 6.99 (d, $J=1.6$ Hz, 1H), and 1.30 (s, 9H). **Scheme II Conversion B'...Synthesis of 5-tert-Butyl-2-methyl phenol:** To a solution of 4-tert-butyl-2-hydroxy benzaldehyde (1.9 g, 10.66 mmol) in TFA (5mL) at 0 °C was added Et_3SiH (20.4 mL, 128.0 mmol) drop wise. The reaction mixture was stirred at room temperature for 8 h. Water (50 mL) and CH_2Cl_2 (50 mL) are added. The aqueous layer is separated and extracted with CH_2Cl_2 (3 x 50 mL). The combined organic extracts is washed with brine and dried over anhydrous Na_2SO_4 ,

filtered, and concentrated under *vacuo*. The residue was purified by column chromatography using hexanes and ethyl acetate to afford 1.5 g (85 %) the title phenol as an yellow oil. ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.03 (d, *J*=8.0 Hz, 1H), 6.86 (dd, *J*=7.6 Hz, 1.6 Hz, 1H), 6.80 (d, *J*=1.6 Hz, 1H), 4.56 (s, 1H), 2.20 (s, 1H), and 1.27 (s, 9H).

5 **Scheme III Conversion A'....Synthesis of 4-Bromo-5-*tert*-butyl-2-methyl phenol (25):**

Compound **25** was synthesized from 5-*tert*-butyl-2-methyl phenol, obtained above, following the procedure adopted for the synthesis of compound **9**. ¹H NMR (400 MHz, CDCl₃, ppm): δ 7.32 (s, 1H), 6.86 (s, 1H), 4.63 (s, 1H), 2.17 (s, 3H), and 1.47 (s, 9H).



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4-Bromo-5-ethyl-2-methyl phenol (5)

[0152] **4-Bromo-5-ethyl-2-methyl phenol (5):** Compound **5** is synthesized from commercially available 5-bromo-2-methyl phenol in accordance to (a) Scheme I Conversion A, B, and C, and Scheme III Conversion A". **Scheme I Conversion A:** As outlined in Scheme I, conversion A, benzyl bromide (1 equivalent) is added to a suspension of 5-bromo-2-methyl phenol (1 equivalent) and potassium carbonate (2 equivalents) in acetone. The reaction mixture is stirred at room temperature. After completion of the reaction, the mixture is filtered, concentrated, and the residue is purified by column chromatography to yield the phenol protected as its benzyl ether, Scheme I intermediate **I₂**. **Scheme I Conversion B:** Intermediate **I₂** (1 equivalent) is dissolved in anhydrous THF and cooled to -78 °C. To this cold solution *tert*-BuLi (1 equivalent) is added drop wise and the reaction is stirred for 30 minutes. *N*-methoxy-*N*-methylacetamide (1.2 equivalents) is then added drop wise and the reaction is allowed to warm to room temperature. After completion of reaction, the reaction mixture is quenched with dil HCl and extracted with ethylacetate. The organic extracts are dried over anhydrous sodium sulfate, and concentrated in *vacuo*. The residue is purified by column chromatography to give intermediate **I₃**. **Scheme I Conversion C:** A suspension Intermediate **I₃** and catalytic amount of 5% Pd/C in methanol under hydrogen atmosphere is stirred for 12 hours. The reaction mixture is carefully filtered over a plug of Celite and the solvent is removed in *vacuo*. The residue is purified by column chromatography to yield the 5-ethyl-2-methyl phenol, Scheme I intermediate **I₄**. **Scheme III conversion A'':** The intermediate **I₄**,

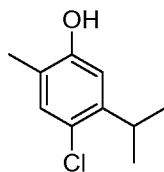
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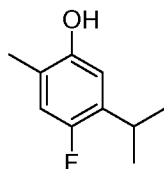
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obtained above is brominated at 4-position using *n*-BuNBr₃ in a mixture of CH₂Cl₂:MeOH (3:2), following the procedure described for the synthesis of compound **9** to obtain compound **5**.



5 **4-Chloro-5-isopropyl-2-methyl phenol (10)**

[0153] **4-Chloro-5-isopropyl-2-methyl phenol (10)**: Compound **10** is synthesized from Carvacrol in accordance to the method outlined in Scheme III, conversion C". Accordingly to a solution of Carvacrol (1 equivalent) in acetic acid is added few crystals of iodine. Sulfuryl chloride (1.5 equivalent) is then added drop wise to the reaction mixture and the mixture is then heated at 45 °C for 60 minutes. The reaction mixture is cooled to room temperature and partitioned between CH₂Cl₂ and water. The organic layer is washed with water until the aqueous pH is neutral. The organic layer is dried over anhydrous sodium sulfate, filtered, and concentrated in *vacuo*. The residue is purified by column chromatography to afford the compound **10**.

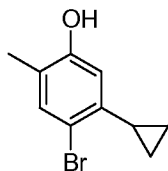


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4-Fluoro-5-isopropyl-2-methyl phenol (11)

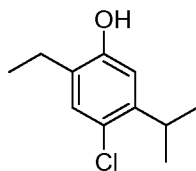
[0154] **4-Fluoro-5-isopropyl-2-methyl phenol (11)**: As outlined in Scheme III, conversion B", compound **11** is derived from compound **9**. Accordingly, compound **9** (1 equivalent), ligand cyclohexyl Brett Phos (0.1 equivalent), [cinnamylPdCl]₂ (0.02 equivalent), CsF (1.5 equivalent) is added to a suspension of sodium dodecyl sulfate (60 equivalent) in toluene. The reaction mixture is then agitated at 110 °C for 6 hour under argon atmosphere. The reaction mixture is cooled to room temperature. Cetyltrimethylammonium bromide (60 equivalent) and toluene are added to the reaction mixture. The reaction mixture is then agitated for another 10 minutes. The reaction mixture is filtered through a plug of Celite. Filtrate is concentrated under reduced pressure and purified by flash chromatography to give the fluorinated compound **11**.

25



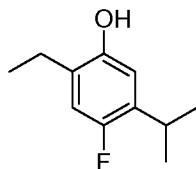
4-Bromo-2-cyclopropyl-5-methyl phenol (41)

[0155] **4-Bromo-2-cyclopropyl-5-methyl phenol (41):** Compound **41** is synthesized from 5-bromo-2-methyl phenol in accordance to (a) Scheme I, conversions A, F and G, and (b) Scheme III, conversion A". **Scheme I Conversion F:** Accordingly, the Scheme I intermediate **I₂** obtained during the synthesis of compound **5** is subjected to Suzuki coupling. A suspension of intermediate **I₂** (1 equivalent), cyclopropylboronic acid (1.5 equivalent), K₃PO₄ (3.5 equivalent), PCy₃ (0.1 equivalent), and Pd(OAc)₂ (0.05 equivalent) in toluene-water is stirred for 3 hours at 100 °C. The reaction mixture is cooled to room temperature and diluted with ether. The organic layer is washed with water, and brine, dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure. The residue is purified by column chromatography to yield cyclopropyl substituted Scheme I intermediate **I₇**. **Scheme I Conversion G:** A suspension of intermediate **I₇** and catalytic amount of 5% Pd/C in methanol is agitated under hydrogen atmosphere using a hydrogen balloon for 12 hours. The reaction mixture is filtered through a plug of Celite. The filtrate is concentrated under *vacuo* and the residue is purified by column chromatography to afford the intermediate phenol **I₈**. **Scheme III Conversion A":** The intermediate phenol **I₈** is brominated at 4-position with *n*Bu₄NBr₃ in CH₂Cl₂:MeOH using a procedure described for the synthesis of compound **9**, to afford the compound **41**.



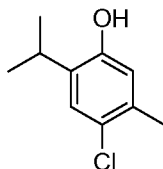
4-Chloro-2-ethyl-5-isopropyl phenol (65)

[0156] **4-Chloro-2-ethyl-5-isopropyl phenol (65):** Compound **65** is derived from intermediate phenol, 2-ethyl-5-isopropyl phenol obtained during the synthesis of compound **64**, according to the procedure described for the synthesis of compound **10**.

**2-Ethyl-4-fluoro-5-isopropyl phenol (66)**

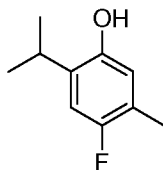
[0157] **2-Ethyl-4-fluoro-5-isopropyl phenol (66):** Compound **66** is derived from compound **64**, according to the procedure described for the synthesis of compound **11**.

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**4-Chloro-5-isopropyl-2-methyl phenol (133)**

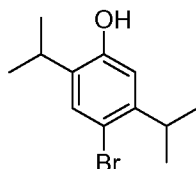
[0158] **4-Chloro-5-isopropyl-2-methyl phenol (133):** Compound **133** is derived from thymol, according to the procedure described for the synthesis of compound **10**.

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**4-Fluoro-2-isopropyl-5-methyl phenol (134)**

[0159] **4-Fluoro-2-isopropyl-5-methyl phenol (134):** Compound **134** is derived from compound **132**, according to the procedure described for the synthesis of compound **11**.

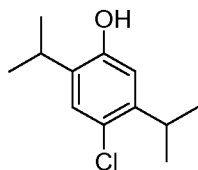
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**4-Bromo-2,5-diisopropyl phenol (148)**

[0160] **4-Bromo-2,5-diisopropyl phenol (148):** Compound **148** is synthesized from 3-isopropyl phenol in accordance to (a) Scheme II, conversion D', F' and G', and (b) Scheme III, conversion A". **Scheme II Conversion D':** Accordingly, a solution of 3-isopropyl phenol (1 equivalent) and acetyl chloride (1 equivalent) in trifluoromethane sulfonic acid is stirred at room temperature for 6 hours. The reaction mixture is then poured on to ice-water and extracted with ether. The organic layer is dried over sodium sulfate, filtered, and concentrated under vacuo. The residue is purified by column

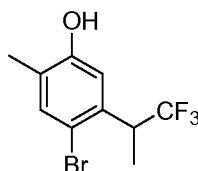
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chromatography to afford Scheme II intermediate phenol **I₅**. **Scheme II Conversion F'**: To a solution of phenol **I₅** (1 equivalent) in anhydrous THF at 0 °C is added a solution of methylmagnesium bromide in ether (5 equivalent). The reaction mixture is allowed to warm to room temperature and stirred till the completion of reaction. The reaction mixture is quenched slowly with aqueous NH₄Cl solution then extracted with ether. The organic layer is dried over sodium sulfate, filtered, and concentrated under *vacuo*. The residue is then purified by column chromatography to afford Scheme II intermediate phenol **I₇**. **Scheme II Conversion G'**: A suspension of phenol **I₇** and catalytic amount of 5% Pd/C in methanol under hydrogen atmosphere is stirred at room temperature for 12 hours, Scheme II, conversion G'. The reaction mixture is filtered through a plug of Celite and the filtrate concentrated under reduced pressure. The residue is purified by column chromatography to afford Scheme II intermediate phenol **I₈**. **Scheme III Conversion A''**: The intermediate phenol **I₈** is brominated at 4-position, according to the procedure described for the synthesis of compound **9**, to afford compound **148**.



4-Chloro-2,5-diisopropyl phenol (149)

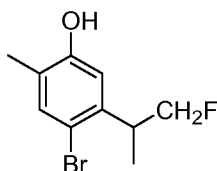
[0161] **4-Chloro-2,5-diisopropyl phenol (149)**: Compound **149** is derived from Scheme II intermediate phenol **I₈**, obtained during the synthesis of compound **148**, according to the procedure described for the synthesis of compound **10**.



4-Bromo-2-methyl-5-(2,2,2-trifluoro-1-methyl-ethyl)-phenol (216)

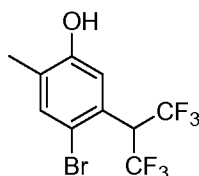
[0162] **4-Bromo-2-methyl-5-(2,2,2-trifluoro-1-methyl-ethyl)-phenol (216)**: Compound **216** is synthesized from commercially available 5-bromo-2-methyl phenol in accordance to (a) Scheme I, conversions D and E, and (b) Scheme III, conversion A". **Scheme I conversion D**: A solution of 5-bromo-2-methyl-phenol (1 equivalent), imidazole (2 equivalent), and TBDMSCl (1 equivalent) in anhydrous DMF is stirred at room temperature. After the completion of the reaction, the reaction mixture is partitioned between ether and water. The ether layer is washed ice-cold brine, dried over sodium

sulfate, filtered, and concentrated under *vacuo*. The residue is purified by column chromatography to afford the silyl ether. To a solution of silyl ether (1 equivalent) in anhydrous THF at -78 °C is added a solution of *t*-BuLi in hexane (1.5 equivalent) is added drop wise and the reaction mixture is stirred for 30 minutes at -78 °C. CF₃COCH₃ (1.5 equivalent) is then added drop wise at -78 °C and the reaction mixture is allowed to warm to room temperature. After the completion of reaction, the reaction is slowly quenched with aqueous ammonium chloride solution. The mixture is then extracted with ether. The ether layer is washed brine, dried over anhydrous sodium sulfate, filtered, and concentrated under *vacuo*. The residue is purified by column chromatography to afford the Scheme I intermediate phenol **I₅**. **Scheme I Conversion E:** Thionyl chloride (2 equivalent) is added drop wise to a solution of intermediate phenol **I₅** (1 equivalent) in toluene and pyridine (few drops) at 0 °C. The reaction mixture is allowed to warm to room temperature and stirred for 12 hours. The reaction mixture is poured on to water and extracted with ethyl acetate. The combined ethyl acetate extracts is washed with aqueous NaHCO₃ solution, dried over sodium sulfate, filtered, and concentrated under *vacuo*. The residue is purified by column chromatography to afford the *tert*-chloro derivative. A suspension of *tert*-chloro derivative (1 equivalent) and sodium borohydride (15 equivalent) in anhydrous THF is stirred at room temperature. After completion of reaction, the reaction is quenched with water and extracted with ethyl acetate. The combined ethyl acetate layers are dried over sodium sulfate, filtered, and concentrated under *vacuo*. The residue is purified by column chromatography to afford the de-chlorinated derivative. A solution of the de-chlorinated derivative (1 equivalent) and TBAF (5 equivalent) in THF is stirred at room temperature. After completion of reaction, the solvent is removed under *vacuo*. The residue is dissolved in water and extracted with ethyl acetate. The combine organic extract is dried over sodium sulfate, filtered, and concentrated. The residue is purified by column chromatography to yield the Scheme I intermediate phenol **I₆**. **Scheme III, Conversion A'':** The intermediate phenol **I₆** is brominated at 4-position according to the procedure described for the synthesis of compound **9**, to afford compound **216**.



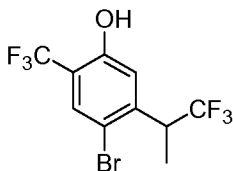
4-Bromo-5-(2-fluoro-1-methyl-ethyl)-2-methyl phenol (220)

[0163] **4-Bromo-5-(2-fluoro-1-methyl-ethyl)-2-methyl phenol (220):** Compound **220** is derived from 5-bromo-2-methyl phenol according to the procedure described for the synthesis of compound **216**, using $\text{CH}_2\text{FCOCH}_3$ instead of CH_3COCF_3 in the second step of the synthesis.



4-Bromo-2-methyl-5-(2,2,2-trifluoro-1-trifluoromethyl-ethyl)-phenol (224)

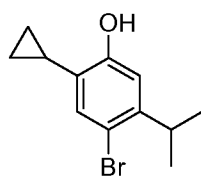
[0164] **4-Bromo-2-methyl-5-(2,2,2-trifluoro-1-trifluoromethyl-ethyl)-phenol (224):** Compound **224** is derived from 5-bromo-2-methyl phenol according to the procedure described for the synthesis of compound **216**, using CF_3COCF_3 instead of CH_3COCF_3 in the second step of the synthesis.



4-Bromo-2-trifluoromethyl-5-(2,2,2-trifluoro-1-methyl-ethyl)-phenol (228)

[0165] **4-Bromo-2-trifluoromethyl-5-(2,2,2-trifluoro-1-trifluoromethyl-ethyl)-phenol (228):** Compound **228** is synthesized from commercially available 3-bromo-phenol in accordance to (a) Scheme I, conversion D and E, (b) Scheme II, conversion H' and I', (c) Scheme III, conversion A". **Scheme I Conversions D and E:** Scheme I intermediate phenol **I₆** is synthesized from 3-bromo phenol, according to the procedure described for the synthesis of an analogous intermediate, used for the synthesis of compound **216**. **Scheme II conversion H':** A mixture of intermediate phenol **I₆** (1 equivalent), KIO_3 (0.2 equivalent), iodine (0.5 equivalent) in acetic acid is stirred at room temperature for 3 days. The solvent is removed under *vacuo*. The residue is dissolved in ether and washed with aqueous NaHCO_3 , $\text{Na}_2\text{S}_2\text{O}_3$, and brine. The organic layer is dried over anhydrous sodium sulfate, filtered, and concentrated under *vacuo*. The residue is purified by column

chromatography to yield the Scheme II intermediate iodinated phenol **I₉**. **Scheme II conversion I'**: Triflic anhydride (1 equivalent) is added drop wise to an ice cooled solution of 3-iodo phenol derivative (1 equivalent) and Et₃N (2 equivalent) in CH₂Cl₂. The reaction mixture is allowed to warm to room temperature. After completion of reaction, the reaction mixture is diluted with CH₂Cl₂ and washed with water. The organic layer is dried over anhydrous sodium sulfate, filtered, and concentrated under *vacuo*. The residue is purified by flash column chromatography to yield the triflate. A solution of aryl triflate (1 equivalent), FSO₂CF₂CO₂Me (5 equivalent), HMPA (5 equivalent), and CuI (1.2 equivalent) in DMF is stirred at 70 °C. After completion of reaction, the reaction mixture is cooled to room temperature. A saturated aqueous solution of NH₄Cl is added and the reaction mixture is extracted with ether. The organic layer is washed with aqueous NaHCO₃ and brine, and dried over sodium sulfate. The solvent is removed under *vacuo*. The residue was purified by column chromatography to afford the 3-trifluoromethyl substituted intermediate aryl triflate. To a solution of aryl triflate (1 equivalent) in dioxane is added 10 % aqueous Et₄NOH solution (2 equivalent) at room temperature and the reaction is stirred till completion of reaction. The reaction mixture is diluted with CHCl₃, washed with 1M HCl, water, and brine. The organic layer is dried over anhydrous sodium sulfate and concentrated under *vacuo*. The residue is purified by column chromatography to afford Scheme II intermediate phenol **I₁₀**. **Scheme III conversion A"**: Phenol **I₁₀** is brominated at 4-position according to the procedure described for the synthesis of compound **9**, to afford compound **228**.



4-Bromo-2-cyclopropyl-5-isopropyl phenol (240)

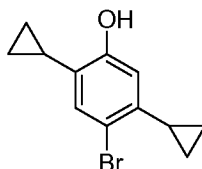
[0166] **4-Bromo-2-cyclopropyl-5-isopropyl phenol (240)**: Compound **240** is synthesized from commercially available 3-isopropyl phenol in accordance to (a) Scheme II, conversion H', J, and K, and (b) Scheme III, conversion A". **Scheme II Conversion H'**: 3-Isopropyl phenol is iodinated according to the procedure described for the synthesis of an analogous intermediate phenol **I₉**, used in the synthesis of compound **228**. **Scheme II Conversion J**: A solution of 3-iodo-5-isopropyl phenol (1 equivalent), imidazole (2 equivalent), and TBDMSCl (1 equivalent) in anhydrous DMF is stirred at room

temperature. After the completion of the reaction, the reaction mixture is partitioned between ether and water. The ether layer is washed ice-cold brine, dried over sodium sulfate, filtered, and concentrated under *vacuo*. The residue is purified by column chromatography to afford the silyl ether, Scheme II intermediate **I**₁₁. **Scheme II**

5 **Conversion K**: A suspension of intermediate **I**₁₁ (1 equivalent), cyclopropylboronic acid (1.5 equivalent), K₃PO₄ (3.5 equivalent), PCy₃ (0.1 equivalent), and Pd(OAc)₂ (0.05 equivalent) in toluene-water is stirred for 3 hours at 100 °C. The reaction mixture is cooled to room temperature and diluted with ether. The organic layer is washed with water, and brine, dried over sodium sulfate, filtered, and concentrated under reduced pressure. The

10 residue is purified by column chromatography to yield 3-cyclopropyl substituted intermediate. A solution of above intermediate (1 equivalent) and TBAF (5 equivalent) in THF is stirred at room temperature. After completion of reaction, the solvent is removed under *vacuo*. The residue is dissolved in water and extracted with ethyl acetate. The combine organic extract is dried over anhydrous sodium sulfate, filtered, and concentrated

15 in *vacuo*. The residue is purified by column chromatography to yield the Scheme II intermediate phenol **I**₁₂. **Scheme III Conversion A''**: Phenol **I**₁₂ is brominated at 4-position according to the procedure described for the synthesis of compound **9**, to afford compound **240**.



20 **4-Bromo-2,5-dicyclopropyl phenol (247)**

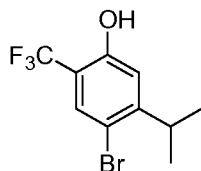
[0167] **4-Bromo-2,5-dicyclopropyl phenol (247)**: Compound **247** is synthesized from commercially available 3-bromo phenol in accordance to (a) Scheme I Conversion A, F and G, (b) Scheme II, conversion H', J, and K, and (c) Scheme III, conversion A".

Scheme I Conversion A, F, and G: The intermediate 3-cyclopropyl phenol is synthesized

25 according to the procedure described for the synthesis of Scheme I intermediate, 5-cyclopropyl-2-methyl phenol **I**₈, obtained during the synthesis of compound **41**. **Scheme II, conversion H', J, and K**: The intermediate 2,5-dicyclopropyl phenol is synthesized from 3-cyclopropyl phenol according to the procedure described for the synthesis of Scheme II intermediate phenol **I**₁₂, obtained during the synthesis of compound **240**.

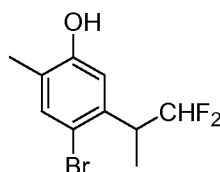
30 **Scheme III conversion A''**: 2,5-dicyclopropyl phenol is brominated at 4-position

according to the procedure described for the synthesis of compound **9**, to afford compound **247**.



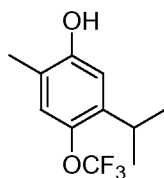
4-Bromo-5-isopropyl-2-trifluoromethyl phenol (266)

- 5 [0168] **4-Bromo-5-isopropyl-2-trifluoromethyl phenol (266)**: Compound **266** is synthesized from commercially available 3-isopropyl phenol according to the procedure described for the synthesis of compound **228**, starting from Scheme II conversion H'.



4-Bromo-5-(2,2-difluoro-1-methyl-ethyl)-2-methyl phenol (269)

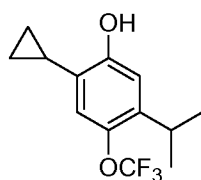
- 10 [0169] **4-Bromo-5-(2,2-difluoro-1-methyl-ethyl)-2-methyl phenol (269)**: Compound **269** is derived from 5-bromo-2-methyl phenol according to the procedure described for the synthesis of compound **216**, using $\text{CHF}_2\text{COCH}_3$ instead of CH_3COCF_3 in the second step of the synthesis.



5-Isopropyl-2-methyl-4-trifluoromethoxy phenol (251)

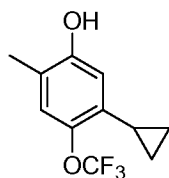
- [0170] **5-Isopropyl-2-methyl-4-trifluoromethoxy phenol (251)**: Compound **251** is synthesized from compound **9** in accordance to Scheme IV, conversion A''', B''', and C'''.
- Scheme IV Conversion A'''**: A solution compound **9** (1 equivalent), imidazole (2 equivalent), and TBDMSCl (1 equivalent) in anhydrous DMF is stirred at room temperature. After the completion of the reaction, the reaction mixture is partitioned between ether and water. The ether layer is washed ice-cold brine, dried over anhydrous sodium sulfate, filtered, and concentrated under *vacuo*. The residue is purified by column chromatography to afford the silyl ether. To a solution of silyl ether of compound **9** (1 equivalent) in THF at -78°C is added *n*BuLi (1 equivalent). The reaction mixture is stirred

at -78 °C for 30 minutes before the addition of Bu₃SnCl (1 equivalent). After stirring for 1 hour at -78 °C, the reaction mixture is warmed to room temperature and the solvent is removed in *vacuo*. The residue is dissolved in ether and filtered through a plug of neutral alumina. The filtrate is concentrated in *vacuo* and the residue is purified via column chromatography to afford Scheme IV, intermediate **I₁**. **Scheme IV Conversion B'''**: To a suspension of tris(dimethylamino)sulfonium difluorotrimethylsilicate (2.00 equivalent), sodium bicarbonate (2.00 equiv), and Scheme IV intermediate **I₁** (1.00 equivalent) in anhydrous THF at -30 °C is added trifluoromethyl trifluoromethanesulfonate (4.1 equivalent), and the suspension is stirred vigorously. The reaction mixture is stirred at -30 °C for 30 minutes, then a solution cooled to -30 °C of 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(hexafluorophosphate) (1.20 equivalent) and silver hexafluorophosphate (2.00 equivalent) in dry acetone is added by cannula. The reaction mixture is stirred for 2.5 hours in the dark, then warmed to 23 °C. The reaction mixture is filtered through a pad of celite eluting with CH₂Cl₂ and the filtrate concentrated in *vacuo* at 5 °C. The residue is purified via column chromatography on silica gel to afford Scheme IV intermediate **I₂**. **Scheme IV Conversion C'''**: A solution of intermediate **I₂** (1 equivalent) and TBAF (5 equivalent) in THF is stirred at room temperature. After completion of reaction, the solvent is removed under *vacuo*. The residue is dissolved in water and extracted with ethyl acetate. The combine organic extract is dried over anhydrous sodium sulfate, filtered, and concentrated in *vacuo*. The residue is purified by column chromatography to afford the compound **251**.



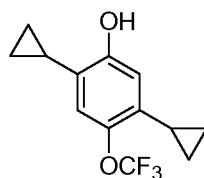
2-Cyclopropyl-5-isopropyl-4-trifluoromethoxy phenol (253)

[0171] **2-Cyclopropyl-5-isopropyl-4-trifluoromethoxy phenol (253)**: Compound **253** is synthesized from compound **240**, according to the procedure described for the synthesis of compound **251**.



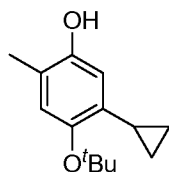
5-Cyclopropyl-2-methyl-4-trifluoromethoxy phenol (254)

[0172] **5-Cyclopropyl-2-methyl-4-trifluoromethoxy phenol (254):** Compound **254** is synthesized from compound **41**, according to the procedure described for the synthesis of compound **251**.



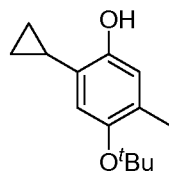
2,5-Dicyclopropyl-4-trifluoromethoxy phenol (255)

[0173] **2,5-Dicyclopropyl-4-trifluoromethoxy phenol (255):** Compound **255** is synthesized from compound **247**, according to the procedure described for the synthesis of compound **251**.



4-tert-Butoxy-5-cyclopropyl-2-methyl phenol (257)

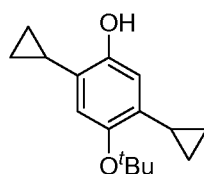
[0174] **4-tert-Butoxy-5-cyclopropyl-2-methyl phenol (257):** Compound **257** is synthesized from compound **41** in accordance to Scheme IV conversion D". A suspension of compound **41** (1.0 equivalent), sodium *tert*-butoxide (11.0 equivalent), CuI (3.0 equivalent) in DMF is stirred at 110 °C for 48 hours. The reaction mixture is cooled to room temperature followed by addition of ether and aqueous NH₄Cl solution. The aqueous phase is extracted with ether, and the combine organic phase is washed with saturated aqueous NaHCO₃ solution and brine. The organic phase is dried over anhydrous sodium sulfate, filtered, and concentrated under *vacuo*. The residue is purified by column chromatography to afford the compound **257**.



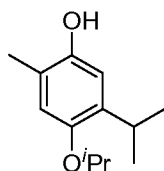
4-*tert*-Butoxy-2-cyclopropyl-5-methyl phenol (258)

[0175] **4-*tert*-Butoxy-2-cyclopropyl-5-methyl phenol (258):** Compound **258** is synthesized from commercially available 3-methyl phenol in accordance to (a) Scheme II conversion H', J, and K, (b) Scheme III conversion A", and (c) Scheme IV conversion D'''.

- 5 **Scheme II Conversion H', J, and K:** The intermediate 2-cyclopropyl-5-methyl phenol is synthesized from 3-methyl phenol according to the procedure described for the synthesis of Scheme II intermediate phenol **I**₁₂, obtained during the synthesis of compound **240**. **Scheme III conversion A":** 2-cyclopropyl-5-methyl phenol is brominated at 4-position according to the procedure described for the synthesis of compound **9**, to afford Scheme
- 10 III intermediate phenol **I**₂. **Scheme IV Conversion D''':** Compound **258** is synthesized from Scheme intermediate phenol **I**₂, by the procedure described for the synthesis of compound **257**.

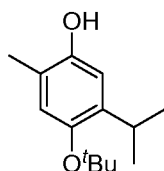
**4-*tert*-Butoxy-2,5-dicyclopropyl phenol (259)**

- 15 [0176] **4-*tert*-Butoxy-2,5-dicyclopropyl phenol (259):** Compound **259** is synthesized from compound **247**, according to the procedure described for the synthesis of compound **257**.



- 20 **4-Isopropoxy-5-isopropyl-5-methyl phenol (261)**

[0177] **4-Isopropoxy-5-isopropyl-5-methyl phenol (261):** Compound **261** is synthesized from compound **9**, according to the procedure described for the synthesis of compound **257**, using sodium isopropoxide instead of sodium *tert*-butoxide.



4-*tert*-Butoxy-5-isopropyl-2-methyl phenol (272)

[0178] 4-*tert*-Butoxy-5-isopropyl-2-methyl phenol (272): Compound 272 is synthesized from compound 9, according to the procedure described for the synthesis of compound 251.

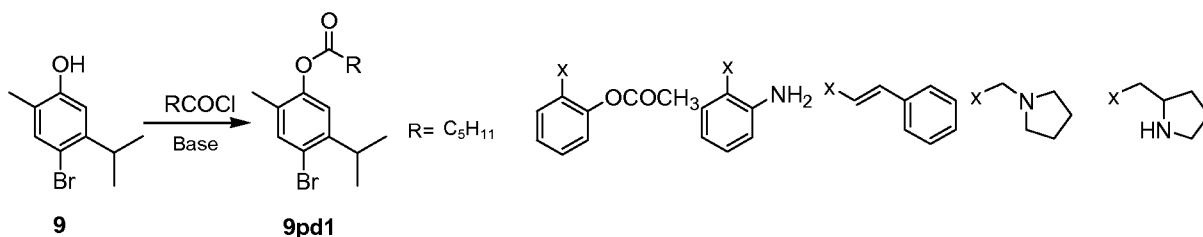
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Pro-Drugs

Alkyl/Aryl ester pro-drugs

[0179] Phenols are excellent nucleophiles known to condense with a wide variety of acid chlorides. For example, compound 9 can be treated with acid chloride in the presence of base to provide the 4-bromo-5-isopropyl-2-methyl phenol alkyl/aryl esters (**Scheme V**).

10 Given that there are a number of commercially available acid chlorides, a wide variety of this class of pro-drug with a wide variety of oral bioavailability and pharmacokinetic parameters can be synthesized. Those of skill in the art will understand that the exemplary scheme set forth in **Scheme V** shows one reaction among many, and should not be construed to limit the invention.



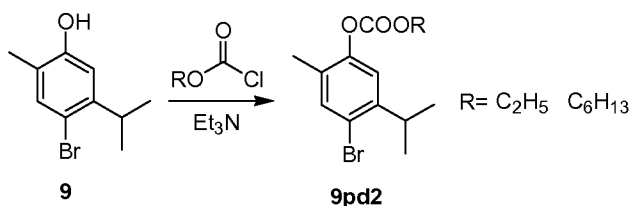
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Scheme V. Synthesis of Alkyl and aryl esters of Compound 9

Carbonate and Carbamate prodrugs

[0180] Numerous chloroformate derivatives are commercially available. Reaction of a phenol with a chloroformate (**Scheme VI**) can yield excellent prodrugs with improved oral absorption and desirable PK properties.

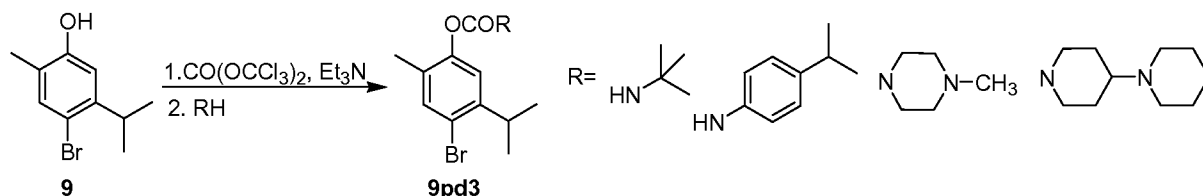
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Scheme VI. Synthesis of Carbonate Pro-drugs of 9

[0181] Carbamates prodrugs can protect the parent phenol drug against first-pass metabolism following oral administration or can serve as substrates for specific enzymes. The use of carbamate prodrugs also helps in increasing the lipophilicity of the prodrug at neutral pH and to increase the aqueous solubility at an acidic pH. Several amines are commercially available and they can be coupled with 4-bromo-5-isopropyl-2-methyl

5 phenyl chloroformate to give the carbamates of **Scheme VII**.

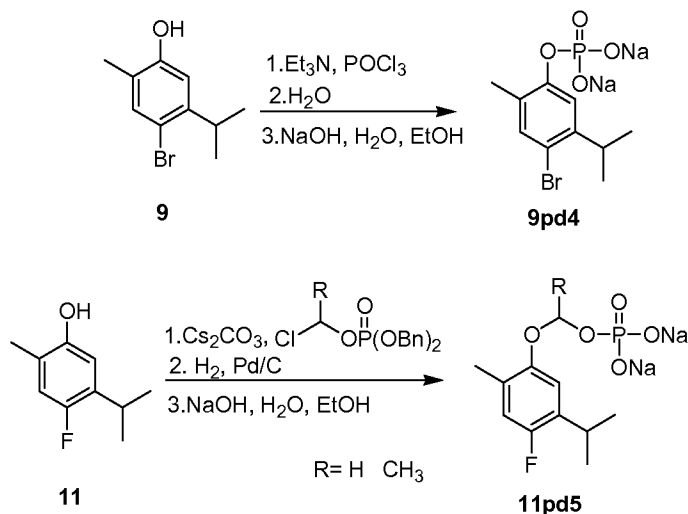


Scheme VII. Synthesis of Carbamate Pro-Drugs of Compound 9

10

Phosphate prodrugs

[0182] Prodrugs containing a phosphate moiety have been successfully employed for increasing oral absorption and modulation of duration of action *in vivo*. Shown below are potential phosphate containing analogs of compound **9** and **11** (**Scheme VIII**).



Scheme VIII. Synthesis of Phosphate esters Pro-Drug of Compound 9 and 11

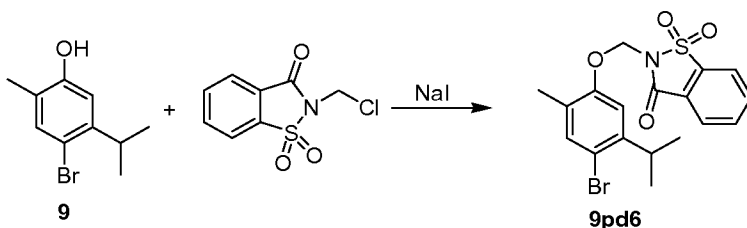
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Ether Prodrugs

[0183] Ether prodrug approach has been used to enhance lipophilicity, favoring the permeation into cellular membranes and the blood brain barrier, and/or to improve the pharmacokinetic properties of the parent drug. Many phenolic group-containing drugs

cannot be administrated orally due to their rapid metabolism by the enzymes in the intestinal tract and liver. Ether prodrugs undergo chemical hydrolysis and are not always enzyme dependent for their cleavage. *O*-(saccharinylmethyl) prodrug can protect the drug from first pass metabolism and increase the drugs oral potency. It can be synthesized by

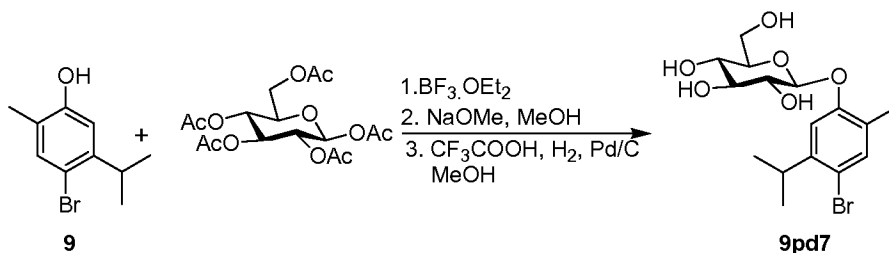
5 treating the phenol with saccharinyl methyl chloride (**Scheme IX**).



Scheme IX. Synthesis of Ether Prodrugs: *O*-(Saccharinylmethyl) derivative of Compound 9

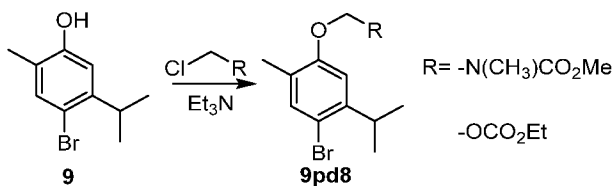
[0184] Glycosides derivatives of dopamine have shown high stability in plasma and a sustained release of dopamine in brain extract through an activation mechanism catalyzed by glycosidase. A glycosyl derivative can be prepared by coupling the phenol

10 with glucose penta acetate (**Scheme X**).



Scheme X: Ether Prodrugs: Synthesis of Glycosyl derivative of Compound 9

[0185] The *N*-alkyloxycarbonylaminomethyl and alkylcarbonyloxymethyl prodrugs have been used for the topical delivery of the phenol drug and increase its biphasic stability. The synthesis can be achieved as described in **Scheme XI**.

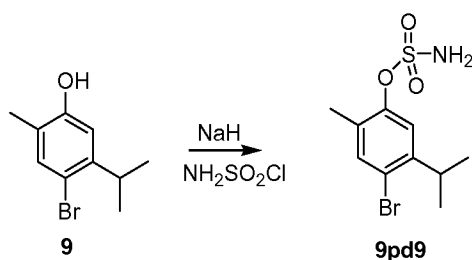


15 **Scheme XI. Ether Prodrugs: Synthesis of *N*-alkyloxycarbonylaminomethyl and Alkylcarbonyloxymethyl derivatives of compound 9**

Sulfamate prodrugs:

[0186] Sulfamate ester pro-drugs have been employed to mitigate hepatic first-pass metabolism of selected phenol drugs. Once these molecules reach systemic circulation

they are converted by hydrolysis to the corresponding phenols by esterases and amidases. Shown in Scheme XII is a sulfamate ester of compound 9. A variety of substituents can be incorporated into the sulfamate moiety to modulate kinetics of parent molecule release.



Scheme XII. Synthesis of Sulfamate Prodrug of compound 9

5

H. Biological Assays

1. Minimal Clonic Seizure (6Hz, 32mA or 44 mA) Test

[0187] The minimal clonic seizure (6Hz) test is used to assess a compound's efficacy against electrically induced seizures but uses a lower frequency (6Hz) and longer duration of stimulation (3s) than the MES test (Barton ME KB, Wolf HH, White HS: Pharmacological characterization of a 6 HZ psychomotor seizure model of partial epilepsy. *Epilepsy Res* 2001; 47:217–27). Test compounds are pre-administered to mice via i.p. injection. At varying times, individual mice (four per time point) are challenged with sufficient current delivered through corneal electrodes to elicit a psychomotor seizure in 97% of animals (32 mA or 44 mA for 3s) (Toman JEP, Everett GM, Richards RK: The Search for New Drugs against Epilepsy. *Texas Reports on Biology and Medicine* 1952; 10:96–104). Untreated mice will display seizures characterized by a minimal clonic phase followed by stereotyped, automatistic behaviors described originally as being similar to the aura of human patients with partial seizures. Animals not displaying this behavior are considered protected. The test compounds are evaluated quantitatively by measuring the responses at varying doses at a determined time of peak effect (TPE).

6Hz 32mA Epilepsy Model (Qualitative Screen) - Test 7-1								
	Species	Route	Efficacy			Toxicity		
			Dose (mg/kg)	Time (TPE)	animals protected/animals tested	Dose (mg/kg)	Time (TPT)	Toxicity Ratio

				(hrs)			(hrs)	
Ex. 9	Mouse	IP	100	0.5	3/4	100	N/A	0/4
	Mouse	Oral	100	N/A	0/4	100	N/A	0/4
Ex. 132	Mouse	IP	100	0.5	3/4	100	N/A	0/4
Ex. 204	Mouse	IP	100	0.5	2/4	100	N/A	0/4
Ex. 64	Mouse	IP	30	0.5	1/4	30	NA	0/8
	Mouse	IP	100	0.5	3/4	100	NA	0/8
	Mouse	IP	300	0.5	4/4	300	0.5	6/8
Ex. 25	Mouse	IP	30	0.5	2/4	30	NA	0/8
	Mouse	IP	100	0.5	2/4	100	NA	0/8
	Mouse	IP	300	2	4/4	300	0.5	4/8
Ex. 95	Mouse	IP	30	0.5	0/4	30	0.5	0/8
	Mouse	IP	10	0.5	3/4	10	0.5	1/8
	Mouse	IP	300	0.5	3/4	300	0.5	3/8

6Hz 32mA Model (Dose Response) - Test 7-2					
	Efficacy		Toxicity		Protective Index (PI)
	Time (TPE) (hrs)	ED ₅₀ (mg/kg)	Time (TPT) (hrs)	TD ₅₀ (mg/kg)	
Ex. 9	0.5	19	6	398	21.5
Ex. 132	0.5	28	4	>200	>7.3

Ex. 204					
Ex, 64					
Ex. 25					
Ex. 95					

6Hz 44mA Epilepsy Model (Qualitative Screen) - Test 7-3								
	Species	Route	Efficacy			Toxicity		
			Dose (mg/kg)	Time (TPE) (hrs)	animals protected/animals tested	Dose (mg/kg)	Time (TPT) (hrs)	Toxicity Ratio
Ex. 9								
Ex. 132	Mouse	IP	100	2	2/4	100	NA	0/4
Ex. 204								
Ex, 64	Mouse	IP	100	0.25	1/4	100	N/A	0/4
Ex. 25								
Ex. 95								

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2. Corneal Kindling (focal seizures)

[0188] Mice are kindled electrically with 3 sec stimulation, 8 mA, 60 Hz, and corneal electrodes to a criterion of 10 consecutive Stage 5 seizures (facial clonus and head nodding progressing to forelimb clonus, and finally rearing and falling accompanied by a generalized clonic seizure as described by Racine (Racine RJ: Modification of Seizure Activity by Electrical Stimulation. II. Motor Seizure. *Electroen Clin Neuro* 1972; 32:281–94). Stage 5 is generally reached after twice daily stimulation for 8 days. With continued stimulation once a day, animals usually progress to a reproducible Stage 5 after 10–14 additional days. At least 72 hours after the mice have been kindled, the test substance is administered either intraperitoneal (i.p.) or *per os* (p.o.) and, at the previously determined TPE, each animal is given the electrical stimulus indicated above. Following stimulation, the animals are observed for the presence or absence of the rearing and falling criteria of a Stage 5 seizure. Treated animals not displaying a Stage 3, 4, or 5 seizure are considered protected.

15 The dose of the test substance is varied between the limits of 0 and 100% efficacy, and the ED₅₀ and 95% confidence intervals calculated by probit analysis. Mean values and the S.E.M. are calculated for the length of clonus and seizure duration and p values are determined by the Student's t-test.

Corneal Kindled Mouse - Test 26						
	Species	Route	Dose (mg/kg)	Time (TPE) (hrs)	Seizure Ratio	Average Seizure Score
Ex. 9	Mouse	IP	19	0.5	1/4	3.75
Ex. 132	Mouse	IP	28	0.5	1/4	4.5
Ex. 204						

Ex, 64						
Ex. 25						
Ex. 95						

3. Maximal Electroshock Seizure (MES) Test

[0189] MES test is performed as in the Minimal Clonic Seizure (6 Hz) test, but the MES test utilizes a current of 50 mA (mice) or 150 mA (rats), frequency of 50–60 Hz, and a stimulation time of 0.2 seconds. Upon stimulation, untreated test subjects display immediate severe tonic seizure (including maximal extension of legs) and the body becomes stiffened for roughly 10–15 seconds. Next, clonic seizures start (including shaking of body and paddling movements of the hind limbs) and may last 20–30 seconds (Castel-Branco MM, Alves GL, Figueiredo IV, Falcao AC, Caramona MM: The Maximal Electroshock Seizure (MES) Model in the Preclinical Assessment of Potential New Antiepileptic Drugs. Methods and Findings in Experimental and Clinical Pharmacology 2009; 31:101–06). Test subjects that display reduced or eliminated symptoms of MES-type seizures during and/or after stimulation are considered protected.

	MES Model (Screen) - Test 1, 2, 8						
	Species	Route	Dose (mg/kg)	Time (TPE) (hrs)	animals protected/animals tested	Time (TPT) (hrs)	Toxicity Ratio
Ex. 9	Mouse	IP	100	0.25	1/4	N/A	0/8
Ex. 132	Mouse	IP	100	1	2/4	0.5	1/8

Ex. 204	Mouse	IP	100	0.25	1/4	N/A	0/8
	Mouse	IP	30	NA	0/4	NA	0/8
Ex. 64	Mouse	IP	100	0.5	1/4	NA	0/8
	Mouse	IP	300	0.5	2/4	0.5	6/8
	Mouse	IP	30	NA			
Ex. 25	Mouse	IP	100	NA			
	Mouse	IP	300	NA			
	Mouse	IP	30	0.5	0/4		
Ex. 95	Mouse	IP	100	0.5	0/4		
	Mouse	IP	300	0.5	1/4		

4. Acute Toxicity-Minimal Motor Impairment

[0190] To assess a compound's undesirable side effects (toxicity), animals are monitored for overt signs of impaired neurological or muscular function. In mice, the rotorod (Dunham NW, Miya TS: A Note on a Simple Apparatus for Detecting Neurological Deficit in Rats and Mice. Journal of the American Pharmaceutical Association 1957; 46:208–09), procedure is used to disclose minimal muscular or neurological impairment. When a mouse is placed on a rod that rotates at a speed of 6 rpm, the animal can maintain its equilibrium for long periods of time. The animal is considered toxic if it falls off this rotating rod three times during a 1-min period. In rats, minimal motor deficit is indicated by ataxia, which is manifested by an abnormal, uncoordinated gait. Rats used for evaluating toxicity are examined before the test drug is administered, since individual animals may have peculiarities in gait, equilibrium, placing response, *etc.*, which might be attributed erroneously to the test substance. In addition to minimum motor impairment, animals may exhibit a circular or zigzag gait, abnormal body posture and spread of the legs, tremors, hyperactivity, lack of exploratory behavior, somnolence, stupor, catalepsy, loss of placing response, and changes in muscle tone.

[0191] The above examples are strictly exemplary, and should not be construed to limit the scope or understanding of the present invention. It should be understood by those skilled in the art that various changes may be made and equivalents may be substituted without departing from the true spirit and scope of the Invention. In particular, paragraphs [00157]–[00164] disclose syntheses of exemplary prodrugs, but the teachings provided could be applied to any chemically analogous drug. In addition, many modifications may

be made to adapt a particular situation, material, composition of matter, process, process step or steps, to the objective, spirit and scope of the described invention. All such modifications are intended to be within the scope of the claims appended hereto. It must also be noted that as used herein and in the appended claims, the singular forms “a,” “an,”
5 and “the” include plural referents unless the context clearly dictates otherwise. Each technical and scientific term used herein has the same meaning each time it is used. The use of “or” in a listing of two or more items indicates that any combination of the items is contemplated, for example, “A or B” indicates that A alone, B alone, or both A and B are intended. The publications discussed herein are provided solely for their disclosure prior to
10 the filing date of the present application. Nothing herein is to be construed as an admission that the described invention is not entitled to antedate such publication by virtue of prior invention. Further, the dates of publication provided may be different from the actual publication dates which may need to be confirmed independently.

2,4,5-ALKYL-HALOALKYL-PHENOL COMPOUNDS

Description of the Related Art

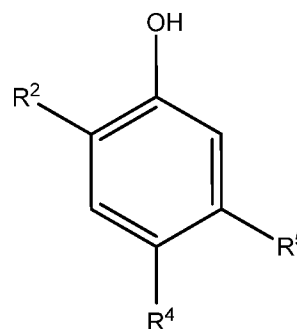
[0192] Compounds useful as voltage-gated sodium channel inhibitors are described by Hadidah-Ruah et al., in WO 2011/140425 published 10 November 2008. The compounds described therein include 4-iodo-2,5-dimethyl-phenol used as an intermediate to make 4-isopropoxy-2,5-dimethylbenzoic acid. 4-isopropoxy-2,5-dimethylbenzoic acid is used as an intermediate in a multi-step process to make compounds useful as voltage-gated sodium channel inhibitors.

[0193] Amine containing compounds useful for mainly excitatory CNS effects are described in Ermili *et al.*, *Edizione Scientifica*, 32(10):713–24 (1977). 4-chloro-2-isopropyl-5-methylphenol is used as an intermediate to make compounds which had mainly excitatory CNS effects. Two end product compounds, Ve (2-dimethylamino-6-methylchromone) and Vs (2-(dimethylamino)-4H-benzo[h]chromen-4-one), have weak anti-convulsant activity. 4-chloro-2-isopropyl-5-methylphenol is not used as an intermediate in the synthesis of these two compounds.

[0194] Phenol derivatives with known GABAergic activity and structurally similar phenol derivatives were tested for lipophilic parameters because GABA receptors are present in cell membranes in Reiner et al., *Colloids and Surfaces, B: Biointerfaces*, 101:61–67 (2013). Reiner et al. considered 4-chloro-2-isopropyl-5-methylphenol to be structurally related to the compound thymol, which has known GABAergic activity, so 4-chloro-2-isopropyl-5-methylphenol was tested for membrane interaction. All five phenol derivatives tested were shown to interact with membranes.

SUMMARY OF THE INVENTION

[0195] In a first embodiment (Embodiment 1), a method is provided for treating a neurological or an inflammatory condition, the method comprising administering a therapeutically effective amount of a compound or pharmaceutically acceptable salt of the compound, wherein the compound has the structure of Formula (I):



(I)

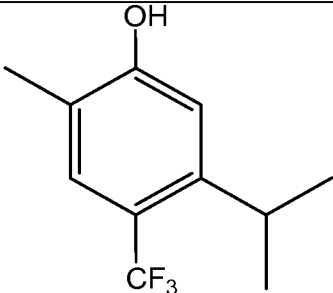
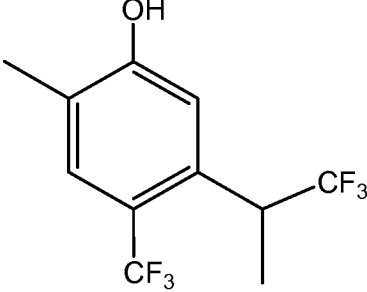
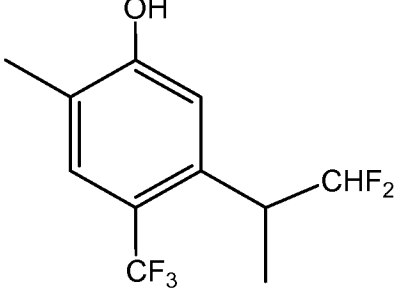
wherein:

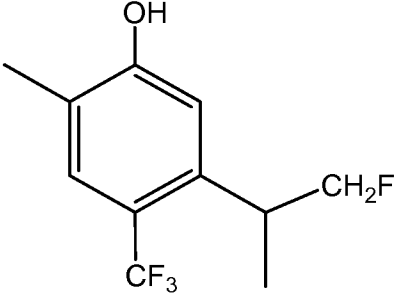
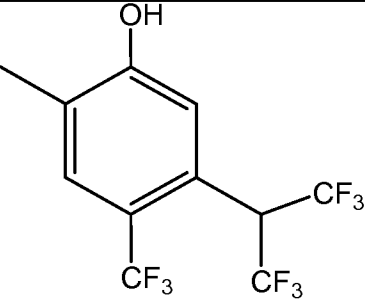
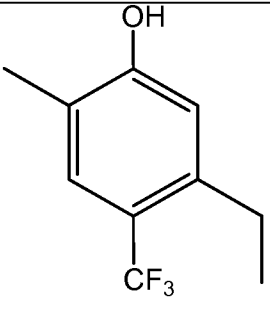
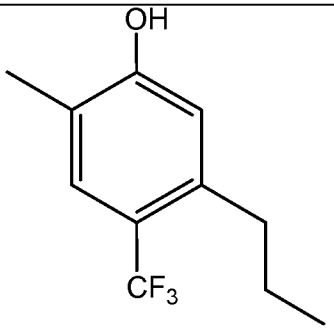
R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl, wherein the alkyl or haloalkyl is optionally substituted with one or more cycloalkyl substituents;

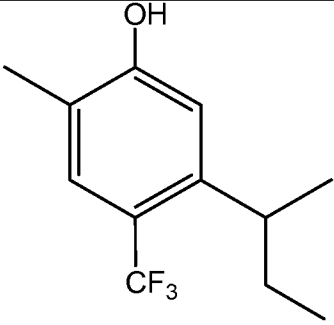
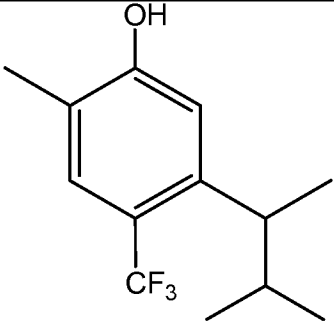
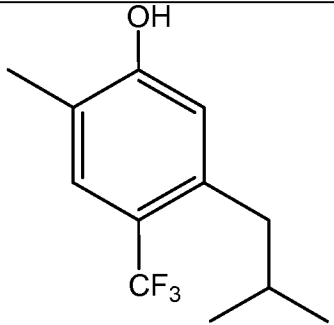
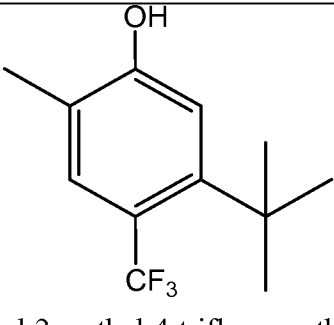
R^4 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl, wherein the alkyl or haloalkyl is optionally substituted with one or more cycloalkyl substituents,
5 and wherein R^4 is not methyl; and

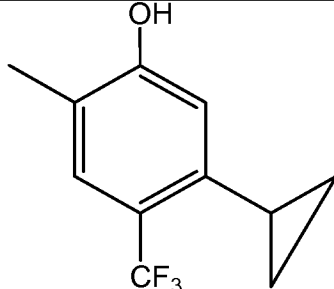
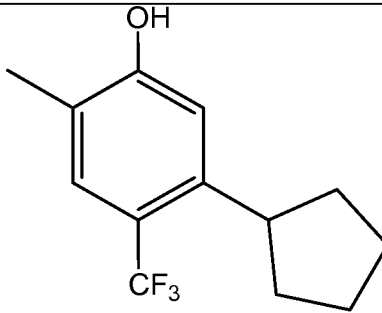
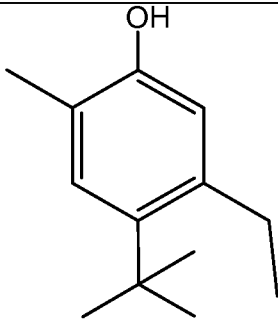
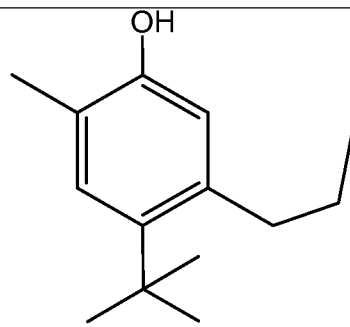
R^5 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl.

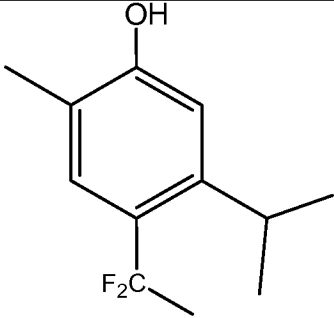
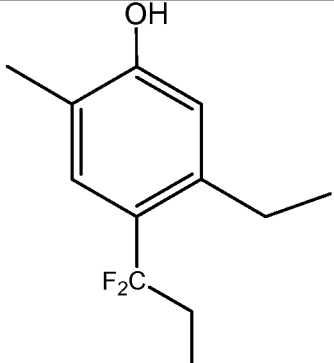
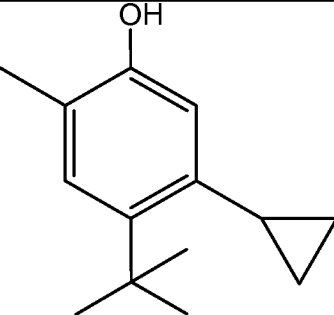
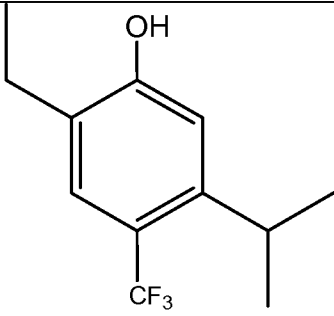
Table 2. Exemplary species

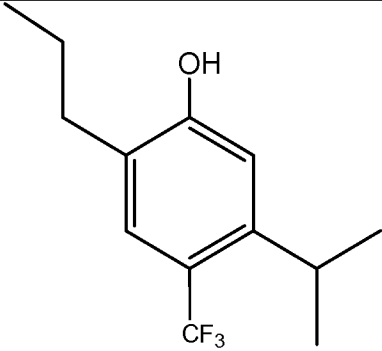
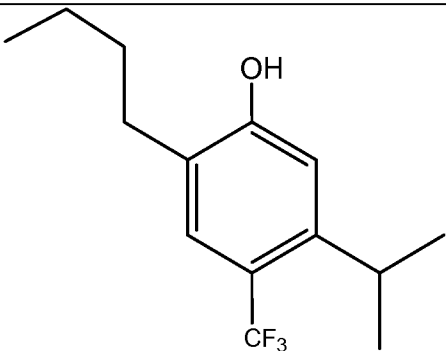
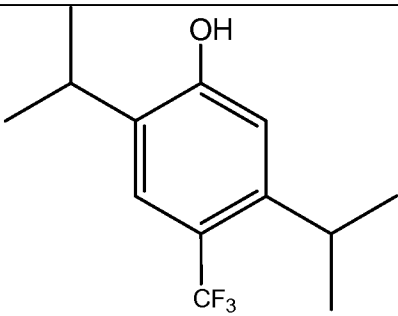
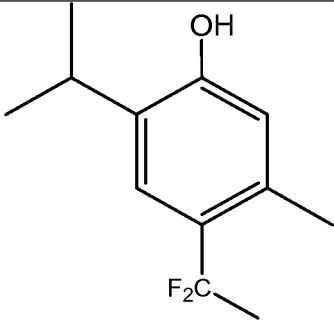
Example Number	Species Structure Species Name
Methyl series 1	 5-Isopropyl-2-methyl-4-trifluoromethyl-phenol
2	 2-Methyl-4-trifluoromethyl-5-(2,2,2-trifluoro-1-methyl-ethyl)-phenol
3	 5-(2,2-Difluoro-1-methyl-ethyl)-2-methyl-4-trifluoromethyl-phenol

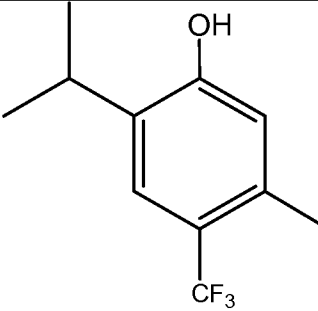
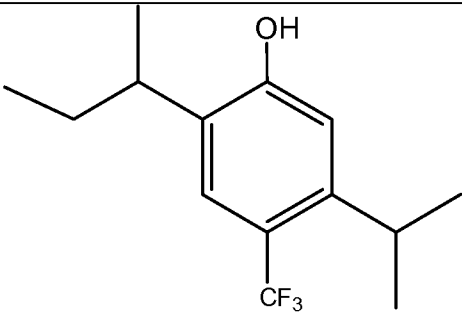
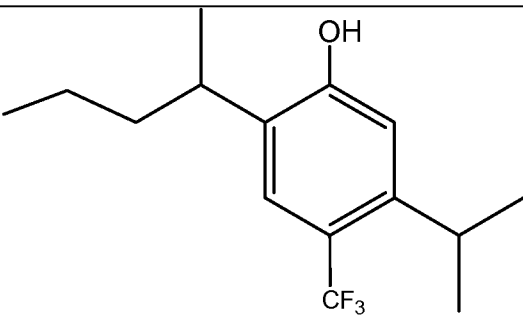
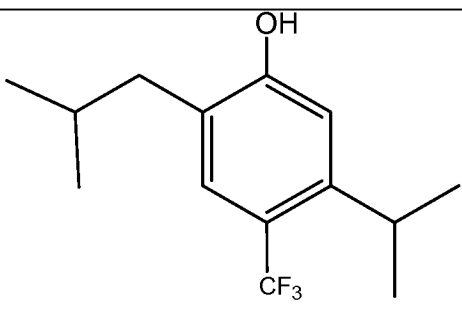
4	 5-(2-Fluoro-1-methyl-ethyl)-2-methyl-4-trifluoromethyl-phenol
5	 2-Methyl-4-trifluoromethyl-5-(2,2,2-trifluoro-1-trifluoromethyl-ethyl)-phenol
6	 5-Ethyl-2-methyl-4-trifluoromethyl-phenol
7	 2-Methyl-5-propyl-4-trifluoromethyl-phenol

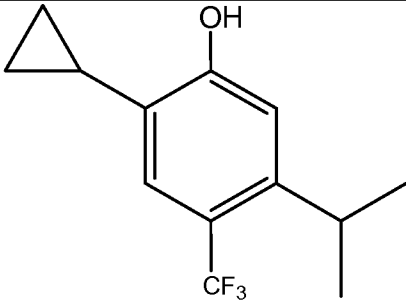
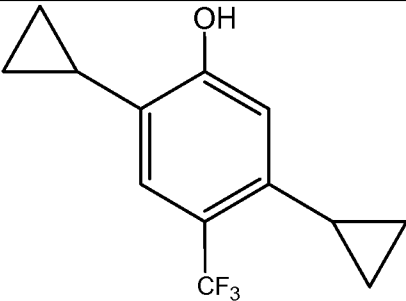
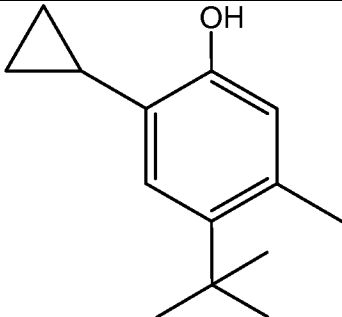
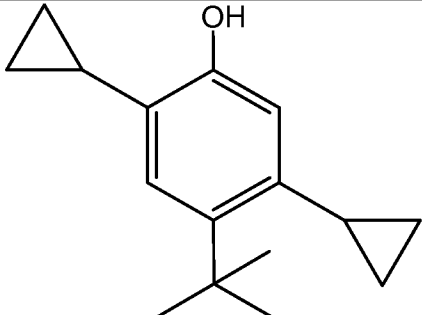
8	 5-<i>sec</i>-Butyl-2-methyl-4-trifluoromethyl-phenol
9	 5-(1,2-Dimethyl-propyl)-2-methyl-4-trifluoromethyl-phenol
10	 5-Isobutyl-2-methyl-4-trifluoromethyl-phenol
11	 5-<i>tert</i>-Butyl-2-methyl-4-trifluoromethyl-phenol

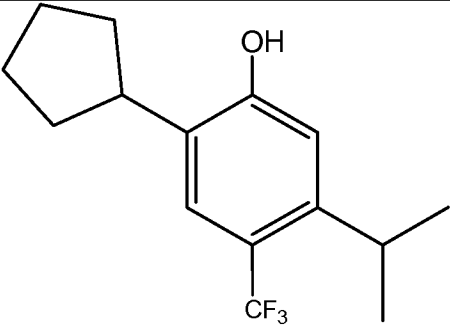
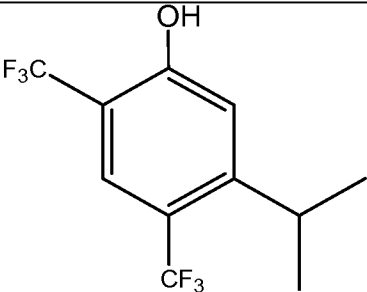
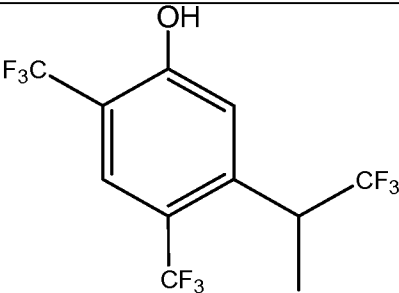
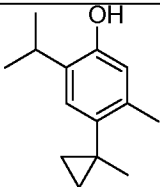
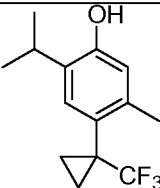
12	 5-Cyclopropyl-2-methyl-4-trifluoromethyl-phenol
13	 5-Cyclopentyl-2-methyl-4-trifluoromethyl-phenol
14	 4-<i>tert</i>-Butyl-5-ethyl-2-methyl-phenol
15	 4-<i>tert</i>-Butyl-2-methyl-5-propyl-phenol

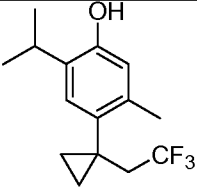
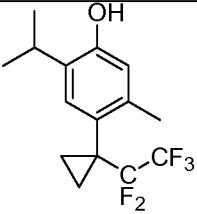
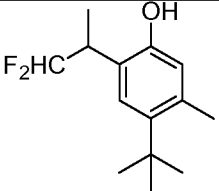
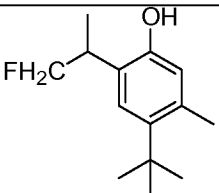
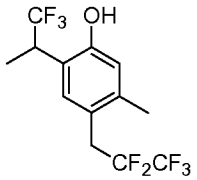
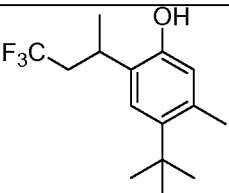
16	 4-(1,1-Difluoro-ethyl)-5-isopropyl-2-methyl-phenol
17	 4-(1,1-Difluoro-propyl)-5-ethyl-2-methyl-phenol
18	 4-<i>tert</i>-Butyl-5-cyclopropyl-2-methyl-phenol
19 Ethyl	 2-Ethyl-5-isopropyl-4-trifluoromethyl-phenol

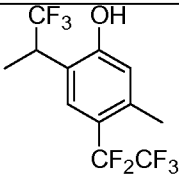
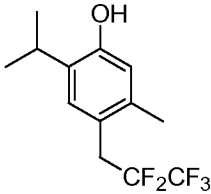
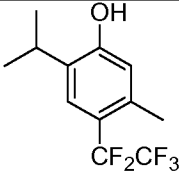
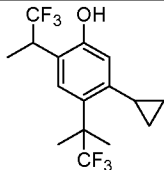
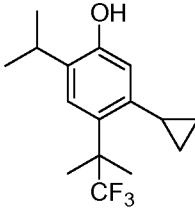
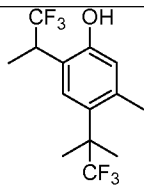
20 n-Propyl series	 5-Isopropyl-2-propyl-4-trifluoromethyl-phenol
21	 2-Butyl-5-isopropyl-4-trifluoromethyl-phenol
22 Isopropyl	 2,5-Diisopropyl-4-trifluoromethyl-phenol
23	 4-(1,1-Difluoro-ethyl)-2-isopropyl-5-methyl-phenol

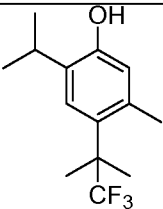
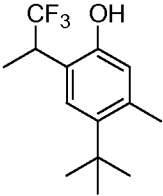
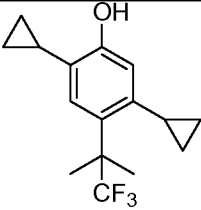
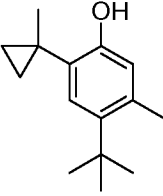
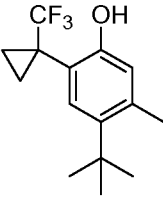
24	 2-Isopropyl-5-methyl-4-trifluoromethyl-phenol
25 Sec-butyl	 2-sec-Butyl-5-isopropyl-4-trifluoromethyl-phenol
26 Sec-pentyl	 5-Isopropyl-2-(1-methyl-butyl)-4-trifluoromethyl-phenol
27 Isobutyl	 2-Isobutyl-5-isopropyl-4-trifluoromethyl-phenol

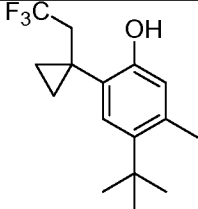
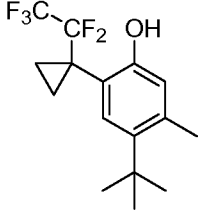
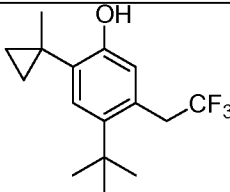
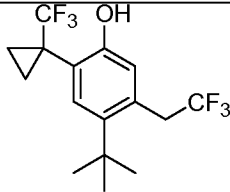
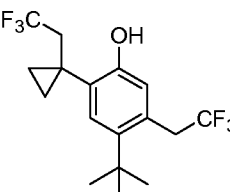
28 Cyclopropyl	 2-Cyclopropyl-5-isopropyl-4-trifluoromethyl-phenol
29	 2,5-Dicyclopropyl-4-trifluoromethyl-phenol
30	 4-<i>tert</i>-Butyl-2-cyclopropyl-5-methyl-phenol
31	 4-<i>tert</i>-Butyl-2,5-dicyclopropyl-phenol

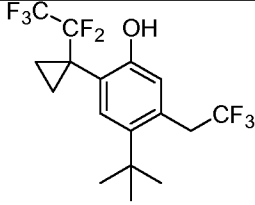
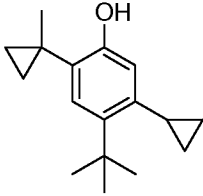
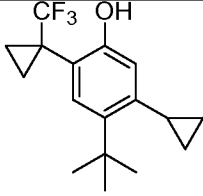
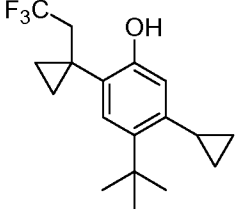
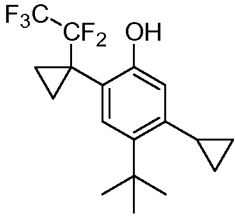
32 cyclopentyl	 2-Cyclopentyl-5-isopropyl-4-trifluoromethyl-phenol
33 Trifluoro- methyl	 5-Isopropyl-2,4-bis-trifluoromethyl-phenol
34	 2,4-Bis-trifluoromethyl-5-(2,2,2-trifluoro-1-methyl-ethyl)-phenol
35	 2-Isopropyl-5-methyl-4-(1-methyl-cyclopropyl)-phenol
36	 2-Isopropyl-5-methyl-4-(1-trifluoromethyl-cyclopropyl)-phenol

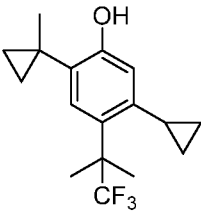
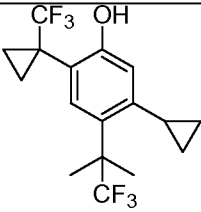
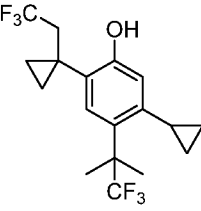
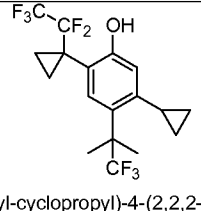
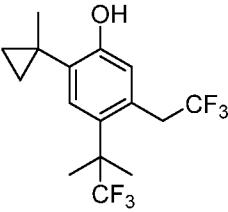
37	 2-Isopropyl-5-methyl-4-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol
38	 2-Isopropyl-5-methyl-4-(1-pentafluoroethyl-cyclopropyl)-phenol
39	 4-<i>tert</i>-Butyl-2-(2,2-difluoro-1-methyl-ethyl)-5-methyl-phenol
40	 4-<i>tert</i>-Butyl-2-(2-fluoro-1-methyl-ethyl)-5-methyl-phenol
41	 5-Methyl-4-(2,2,3,3,3-pentafluoro-propyl)-2-(2,2,2-trifluoro-1-methyl-ethyl)-phenol
42	 4-<i>tert</i>-Butyl-5-methyl-2-(3,3,3-trifluoro-1-methyl-propyl)-phenol
43	

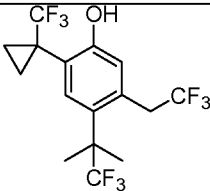
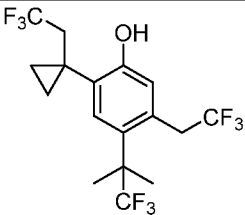
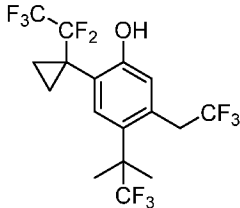
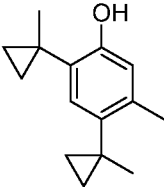
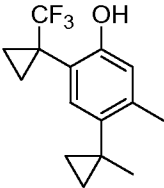
	 5-Methyl-4-pentafluoroethyl-2-(2,2,2-trifluoro-1-methyl-ethyl)-phenol
44	 2-Isopropyl-5-methyl-4-(2,2,3,3,3-pentafluoro-propyl)-phenol
46	 2-Isopropyl-5-methyl-4-pentafluoroethyl-phenol
47	 5-Cyclopropyl-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-2-(2,2,2-trifluoro-1-methyl-ethyl)-phenol
48	 5-Cyclopropyl-2-isopropyl-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol
49	 5-Methyl-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-2-(2,2,2-trifluoro-1-methyl-ethyl)-phenol
50	

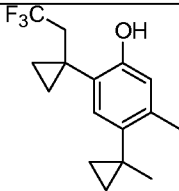
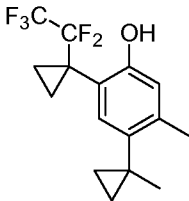
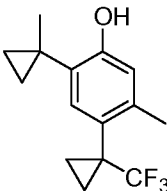
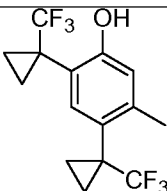
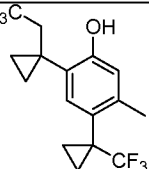
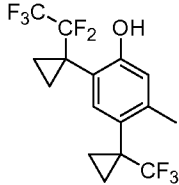
	 2-Isopropyl-5-methyl-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol
51	 4-<i>tert</i>-Butyl-5-methyl-2-(2,2,2-trifluoro-1-methyl-ethyl)-phenol
52	 2,5-Dicyclopropyl-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol
53	 4-<i>tert</i>-Butyl-5-methyl-2-(1-methyl-cyclopropyl)-phenol
54	 4-<i>tert</i>-Butyl-5-methyl-2-(1-trifluoromethyl-cyclopropyl)-phenol

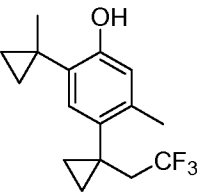
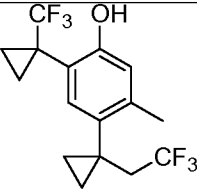
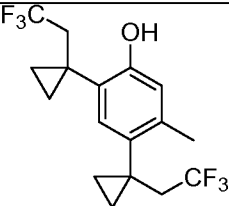
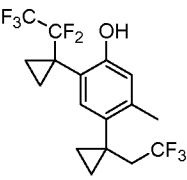
55	 4-<i>tert</i>-Butyl-5-methyl-2-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol
56	 4-<i>tert</i>-Butyl-5-methyl-2-(1-pentafluoroethyl-cyclopropyl)-phenol
57	 4-<i>tert</i>-Butyl-2-(1-methyl-cyclopropyl)-5-(2,2,2-trifluoro-ethyl)-phenol
58	 4-<i>tert</i>-Butyl-5-(2,2,2-trifluoro-ethyl)-2-(1-trifluoromethyl-cyclopropyl)-phenol
59	 4-<i>tert</i>-Butyl-5-(2,2,2-trifluoro-ethyl)-2-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol

60	 4-<i>tert</i>-Butyl-2-(1-pentafluoroethyl-cyclopropyl)-5-(2,2,2-trifluoro-ethyl)-phenol
61	 4-<i>tert</i>-Butyl-5-cyclopropyl-2-(1-methyl-cyclopropyl)-phenol
62	 4-<i>tert</i>-Butyl-5-cyclopropyl-2-(1-trifluoromethyl-cyclopropyl)-phenol
63	 4-<i>tert</i>-Butyl-5-cyclopropyl-2-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol
64	 4-<i>tert</i>-Butyl-5-cyclopropyl-2-(1-pentafluoroethyl-cyclopropyl)-phenol
65	

	 5-Cyclopropyl-2-(1-methyl-cyclopropyl)-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol
66	 5-Cyclopropyl-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-2-(1-trifluoromethyl-cyclopropyl)-phenol
67	 5-Cyclopropyl-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-2-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol
68	 5-Cyclopropyl-2-(1-pentafluoroethyl-cyclopropyl)-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol
69	 2-(1-Methyl-cyclopropyl)-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-5-(2,2,2-trifluoro-ethyl)-phenol
70	

	 4-(2,2,2-Trifluoro-1,1-dimethyl-ethyl)-5-(2,2,2-trifluoro-ethyl)-2-(1-trifluoromethyl-cyclopropyl)-phenol
71	 4-(2,2,2-Trifluoro-1,1-dimethyl-ethyl)-5-(2,2,2-trifluoro-ethyl)-2-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol
72	 2-(1-Pentafluoroethyl-cyclopropyl)-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-5-(2,2,2-trifluoro-ethyl)-phenol
73	 5-Methyl-2,4-bis-(1-methyl-cyclopropyl)-phenol
74	 5-Methyl-4-(1-methyl-cyclopropyl)-2-(1-trifluoromethyl-cyclopropyl)-phenol
75	

	 5-Methyl-4-(1-methyl-cyclopropyl)-2-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol
76	 5-Methyl-4-(1-methyl-cyclopropyl)-2-(1-pentafluoroethyl-cyclopropyl)-phenol
77	 5-Methyl-2-(1-methyl-cyclopropyl)-4-(1-trifluoromethyl-cyclopropyl)-phenol
78	 5-Methyl-2,4-bis-(1-trifluoromethyl-cyclopropyl)-phenol
79	 5-Methyl-2-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-4-(1-trifluoromethyl-cyclopropyl)-phenol
80	 5-Methyl-2-(1-pentafluoroethyl-cyclopropyl)-4-(1-trifluoromethyl-cyclopropyl)-phenol

81	 5-Methyl-2-(1-methyl-cyclopropyl)-4-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol
82	 5-Methyl-4-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-2-(1-trifluoromethyl-cyclopropyl)-phenol
83	 5-Methyl-2,4-bis-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol
84	 5-Methyl-2-(1-pentafluoroethyl-cyclopropyl)-4-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol

2,4-ALKYL/HALOALKYL-5-HALO/ETHER-PHENOL COMPOUNDS

Description of the Related Art

[0196] Compounds useful as voltage-gated sodium channel inhibitors are described by Hadidah-Ruah et al., in WO 2011/140425 published 10 November 2008. The compounds described therein include 4-iodo-2,5-dimethyl-phenol used as an intermediate to make 4-isopropoxy-2,5-dimethylbenzoic acid. 4-isopropoxy-2,5-dimethylbenzoic acid is used as an intermediate in a multi-step process to make compounds useful as voltage-gated sodium channel inhibitors.

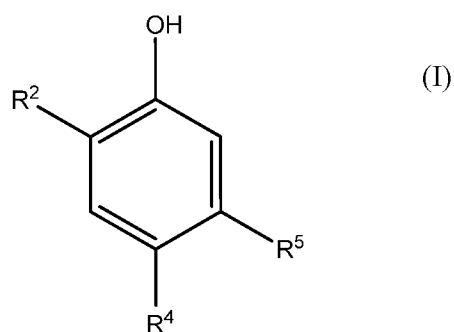
[0197] Amine containing compounds useful for mainly excitatory CNS effects are described in Ermili *et al.*, *Edizione Scientifica*, 32(10):713–24 (1977). 4-chloro-2-isopropyl-5-methylphenol is used as an intermediate to make compounds which had mainly excitatory CNS effects. Two end product compounds, Ve (2-dimethylamino-6-methylchromone) and Vs (2-(dimethylamino)-4H-benzo[h]chromen-4-one), have weak anti-convulsant activity. 4-chloro-2-isopropyl-5-methylphenol is not used as an intermediate in the synthesis of these two compounds.

[0198] Phenol derivatives with known GABAnergic activity and structurally similar phenol derivatives were tested for lipophilic parameters because GABA receptors are present in cell membranes in Reiner et al., *Colloids and Surfaces, B: Biointerfaces*, 101:61–67 (2013). Reiner et al. considered 4-chloro-2-isopropyl-5-methylphenol to be structurally related to the compound thymol, which has known GABAnergic activity, so 4-chloro-2-isopropyl-5-methylphenol was tested for membrane interaction. All five phenol derivatives tested were shown to interact with membranes.

[0199] Compounds useful as inhibitory glycine receptor agonists, including 3,5-di-*tert*-butyl-2-chloro-6-hydroxybenzoic acid, are reported in U.S. 2009/0192190 (Gyback *et al.*, published 30 July 2009). Gyback *et al.* report using 2,4-di-*tert*-butyl-5-chlorophenol as a reagent to synthesize 3,5-di-*tert*-butyl-2-chloro-6-hydroxybenzoic acid.

SUMMARY OF THE INVENTION

[0200] In a first embodiment (Embodiment 1), a method is provided for treating a neurological or an inflammatory condition, the method comprising administering a therapeutically effective amount of a compound or pharmaceutically acceptable salt of the compound, wherein the compound has the structure of Formula (I):



5

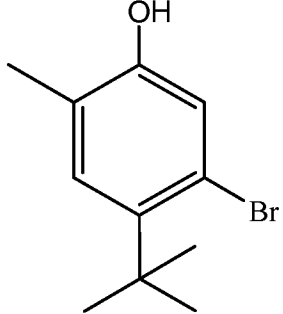
wherein:

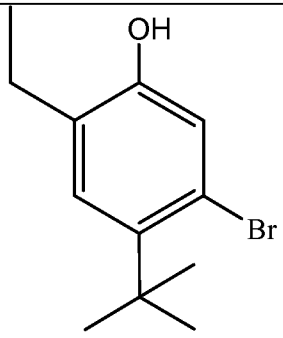
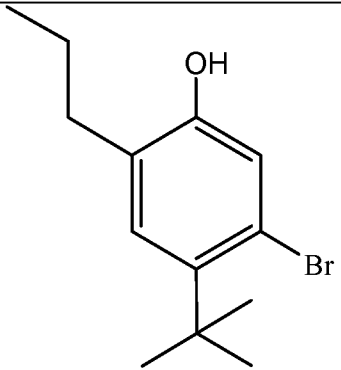
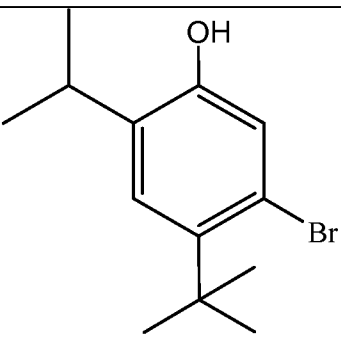
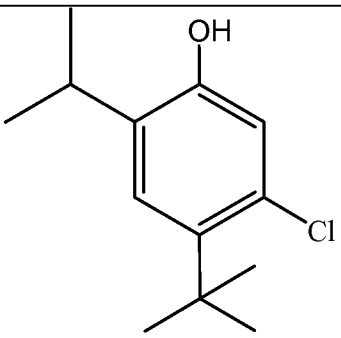
R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl, wherein the alkyl or haloalkyl is optionally substituted with one or more cycloalkyl substituents;

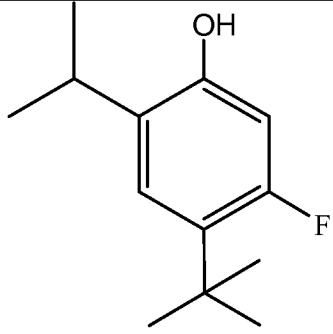
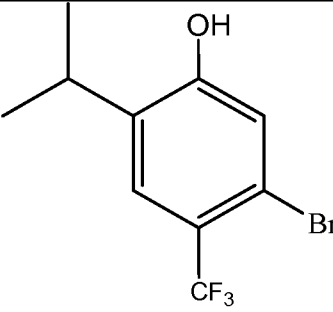
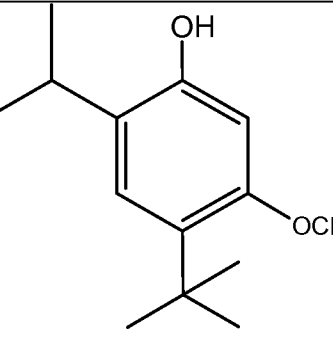
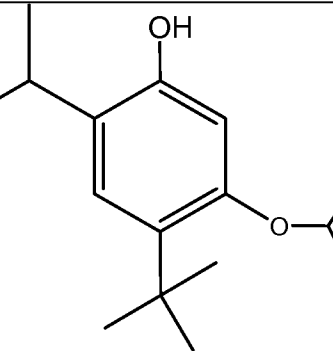
10 R^4 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl, wherein the alkyl or haloalkyl is optionally substituted with one or more cycloalkyl substituents, and wherein R^4 is not methyl; and

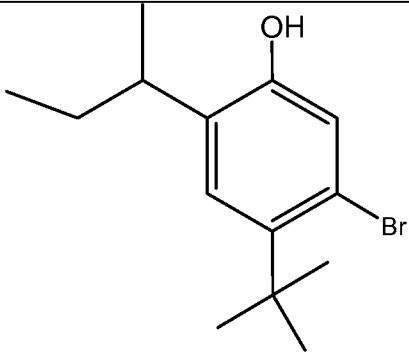
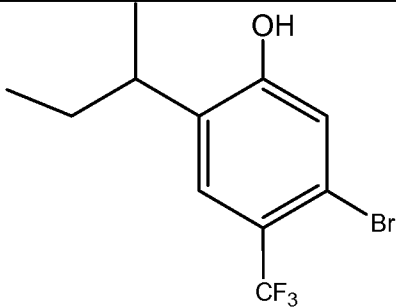
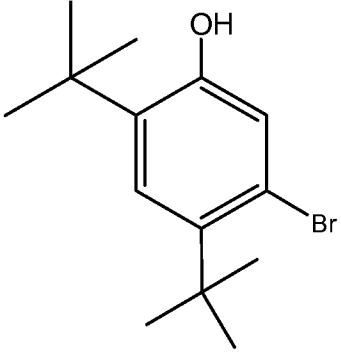
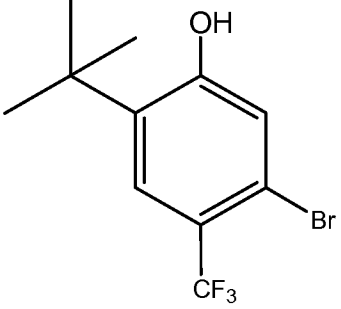
15 R^5 is selected from the group consisting of halo, and alkoxy, wherein the alkoxy may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl and halo.

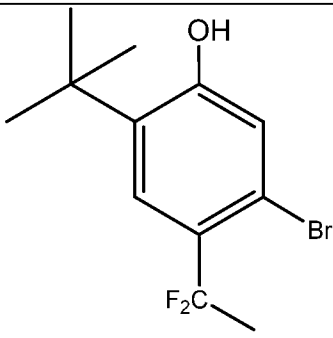
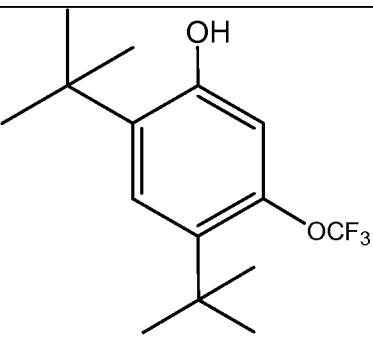
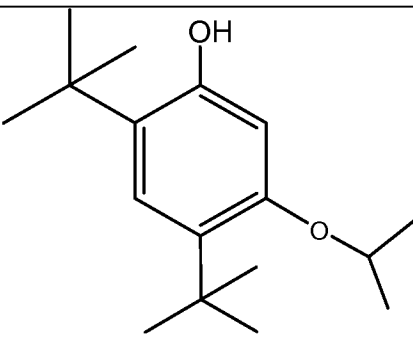
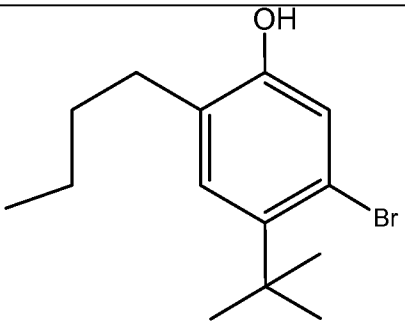
Table 3. Exemplary species

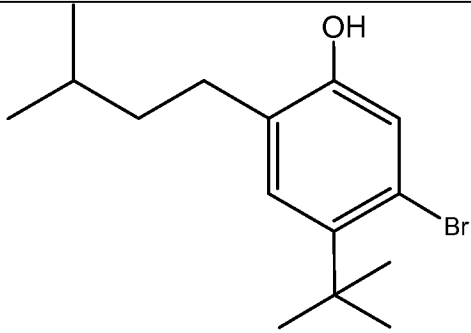
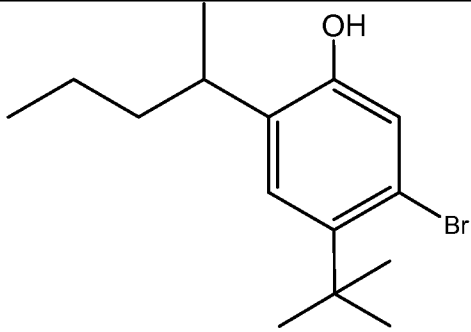
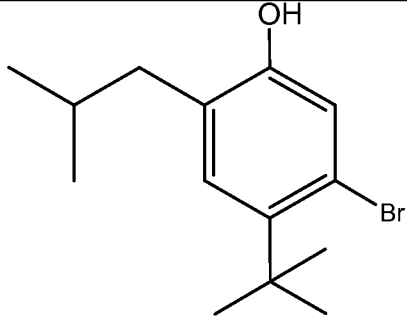
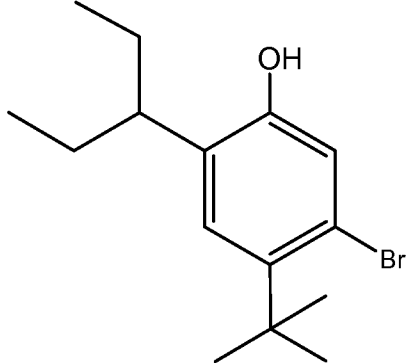
Example Number	Species Structure Species Name
1 methyl	 5-Bromo-4-<i>tert</i>-butyl-2-methyl-phenol

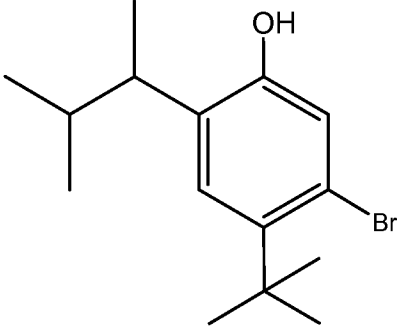
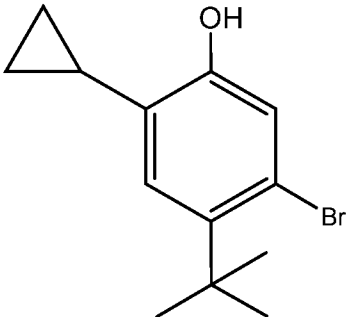
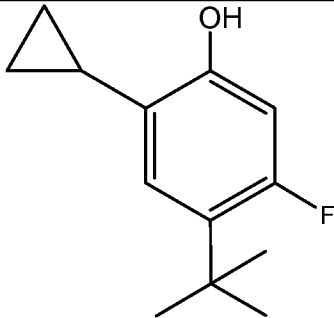
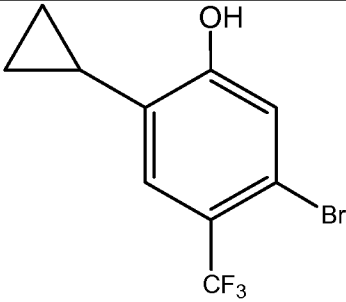
2 Ethyl	 5-Bromo-4-<i>tert</i>-butyl-2-ethyl-phenol
3 <i>n</i>-propyl	 5-Bromo-4-<i>tert</i>-butyl-2-propyl-phenol
4 Isopropyl	 5-Bromo-4-<i>tert</i>-butyl-2-isopropyl-phenol
5	 4-<i>tert</i>-Butyl-5-chloro-2-isopropyl-phenol

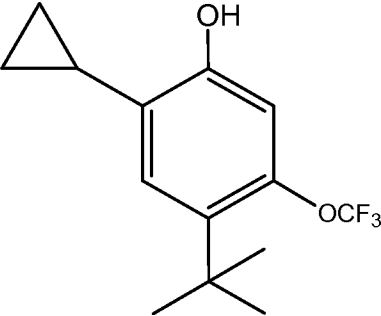
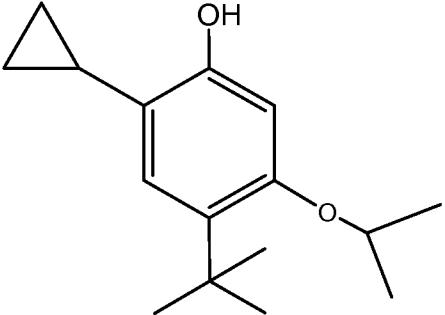
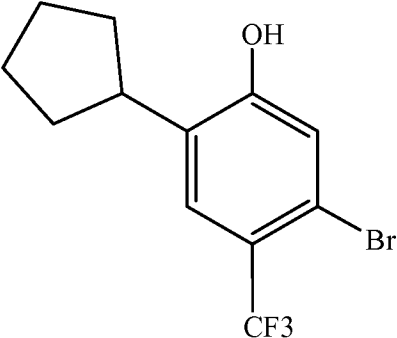
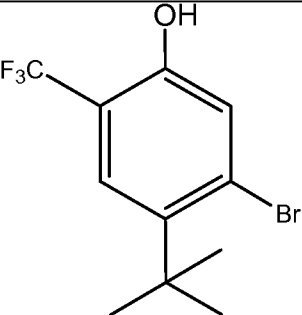
6	 4-<i>tert</i>-Butyl-5-fluoro-2-isopropyl-phenol
7	 5-Bromo-2-isopropyl-4-trifluoromethyl-phenol
8	 4-<i>tert</i>-Butyl-2-isopropyl-5-trifluoromethoxy-phenol
9	 4-<i>tert</i>-Butyl-5-isopropoxy-2-isopropyl-phenol

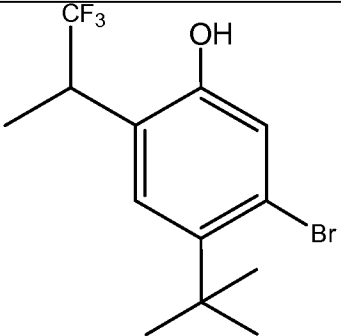
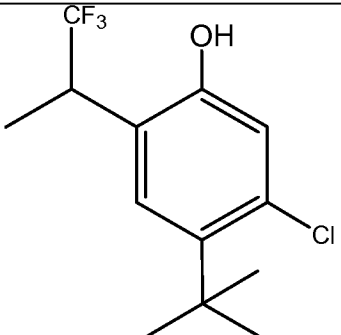
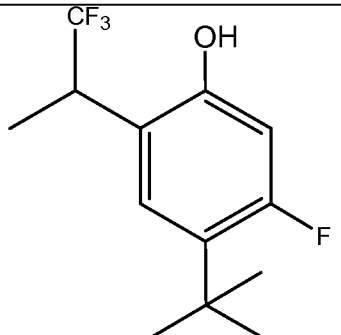
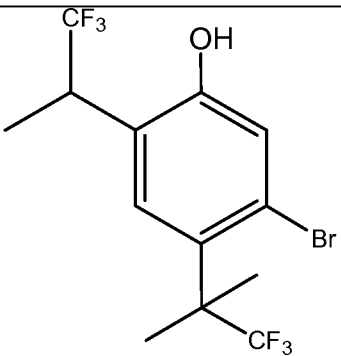
10	 5-Bromo-2-<i>sec</i>-butyl-4-<i>tert</i>-butyl-phenol
11	 5-Bromo-2-<i>sec</i>-butyl-4-trifluoromethyl-phenol
12 <i>tert</i> -butyl	 5-Bromo-2,4-di-<i>tert</i>-butyl-phenol
13	 5-Bromo-2-<i>tert</i>-butyl-4-trifluoromethyl-phenol

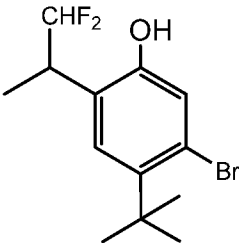
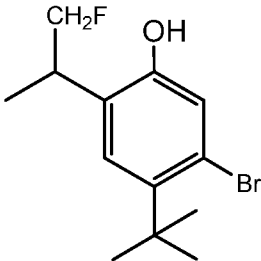
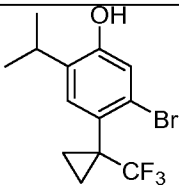
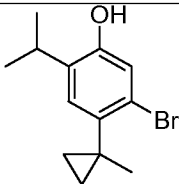
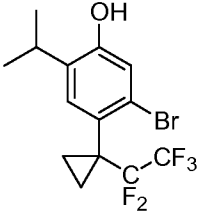
14	 5-bromo-2-(<i>tert</i>-butyl)-4-(1,1-difluoroethyl)phenol
15	 2,4-Di-<i>tert</i>-butyl-5-trifluoromethoxy-phenol
16	 2,4-Di-<i>tert</i>-butyl-5-isopropoxy-phenol
17 <i>n</i> -butyl	 5-Bromo-2-butyl-4-<i>tert</i>-butyl-phenol

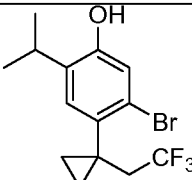
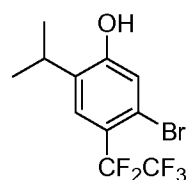
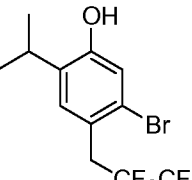
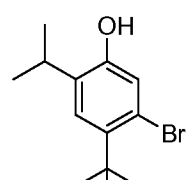
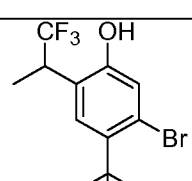
18 Isopentyl	 5-Bromo-4-<i>tert</i>-butyl-2-(3-methyl-butyl)-phenol
19 <i>Sec</i>-pentyl	 5-Bromo-4-<i>tert</i>-butyl-2-(1-methyl-butyl)-phenol
20 Isobutyl	 5-Bromo-4-<i>tert</i>-butyl-2-isobutyl-phenol
21	 5-Bromo-4-<i>tert</i>-butyl-2-(1-ethyl-propyl)-phenol

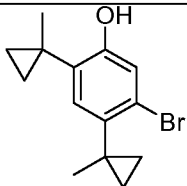
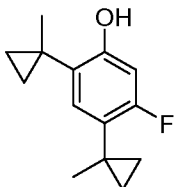
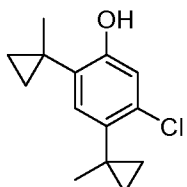
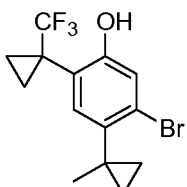
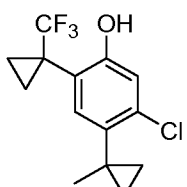
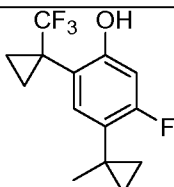
22	 5-Bromo-4-<i>tert</i>-butyl-2-(1,2-dimethyl-propyl)-phenol
23	 5-Bromo-4-<i>tert</i>-butyl-2-cyclopropyl-phenol
24	 4-<i>tert</i>-Butyl-2-cyclopropyl-5-fluoro-phenol
25	 5-Bromo-2-cyclopropyl-4-trifluoromethyl-phenol

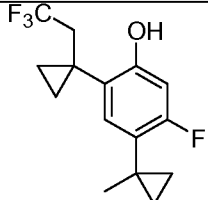
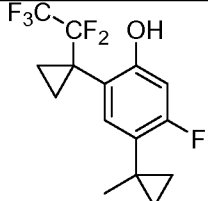
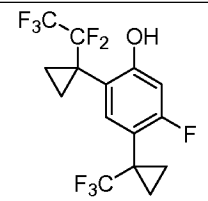
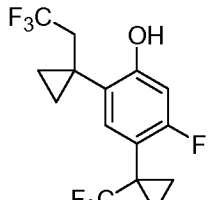
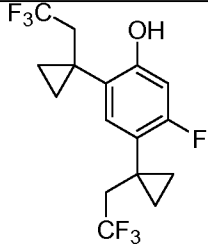
26	 4-<i>tert</i>-Butyl-2-cyclopropyl-5-trifluoromethoxy-phenol
28	 4-<i>tert</i>-Butyl-2-cyclopropyl-5-isopropoxy-phenol
29	 5-Bromo-2-cyclopentyl-4-trifluoromethyl-phenol
30 Trifluoromethyl	 5-Bromo-4-<i>tert</i>-butyl-2-trifluoromethyl-phenol

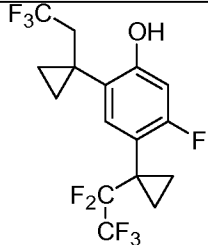
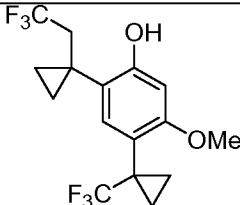
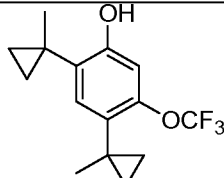
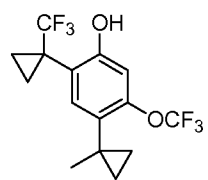
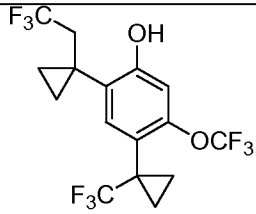
31 Trifluoroiso Propyl	 5-Bromo-4-<i>tert</i>-butyl-2-(2,2,2-trifluoro-1-methyl-ethyl)-phenol
32	 4-<i>tert</i>-Butyl-5-chloro-2-(2,2,2-trifluoro-1-methyl-ethyl)-phenol
33	 4-<i>tert</i>-Butyl-5-fluoro-2-(2,2,2-trifluoro-1-methyl-ethyl)-phenol
34	 5-Bromo-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-2-(2,2,2-trifluoro-1-methyl-ethyl)-phenol

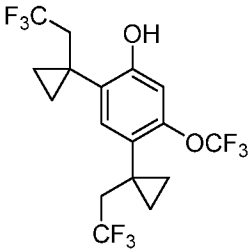
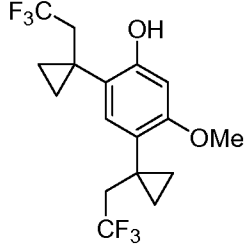
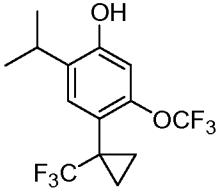
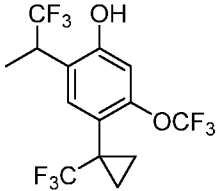
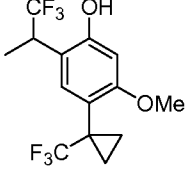
35	 5-Bromo-4-<i>tert</i>-butyl-2-(2,2-difluoro-1-methyl-ethyl)-phenol
36	 5-Bromo-4-<i>tert</i>-butyl-2-(2-fluoro-1-methyl-ethyl)-phenol
37	 5-Bromo-2-isopropyl-4-(1-trifluoromethyl-cyclopropyl)-phenol
38	 5-Bromo-2-isopropyl-4-(1-methyl-cyclopropyl)-phenol
39	 5-Bromo-2-isopropyl-4-(1-pentafluoroethyl-cyclopropyl)-phenol
40	

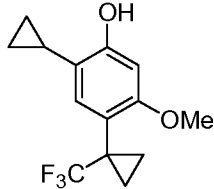
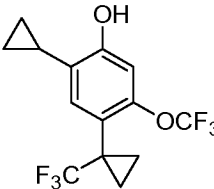
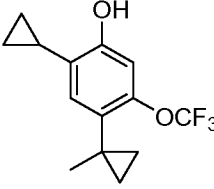
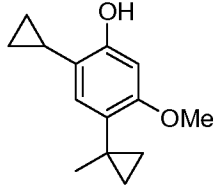
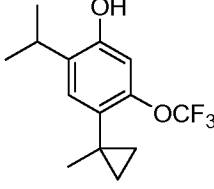
	 5-Bromo-2-isopropyl-4-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol
41	 5-Bromo-2-isopropyl-4-pentafluoroethyl-phenol
42	 5-Bromo-2-isopropyl-4-(2,2,3,3,3-pentafluoro-propyl)-phenol
43	 5-Bromo-2-isopropyl-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol
44	 5-Bromo-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-2-(2,2,2-trifluoro-1-methyl-ethyl)-phenol
45	

	 5-Bromo-2,4-bis-(1-methyl-cyclopropyl)-phenol
46	 5-Fluoro-2,4-bis-(1-methyl-cyclopropyl)-phenol
47	 5-Chloro-2,4-bis-(1-methyl-cyclopropyl)-phenol
49	 5-Bromo-4-(1-methyl-cyclopropyl)-2-(1-trifluoromethyl-cyclopropyl)-phenol
50	 5-Chloro-4-(1-methyl-cyclopropyl)-2-(1-trifluoromethyl-cyclopropyl)-phenol
51	 5-Fluoro-4-(1-methyl-cyclopropyl)-2-(1-trifluoromethyl-cyclopropyl)-phenol

52	 5-Fluoro-4-(1-methyl-cyclopropyl)-2-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol
53	 5-Fluoro-4-(1-methyl-cyclopropyl)-2-(1-pentafluoroethyl-cyclopropyl)-phenol
54	 5-Fluoro-2-(1-pentafluoroethyl-cyclopropyl)-4-(1-trifluoromethyl-cyclopropyl)-phenol
55	 5-Fluoro-2-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-4-(1-trifluoromethyl-cyclopropyl)-phenol
56	 5-Fluoro-2,4-bis-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol

57	 5-Fluoro-4-(1-pentafluoroethyl-cyclopropyl)-2-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol
58	 5-Methoxy-2-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-4-(1-trifluoromethyl-cyclopropyl)-phenol
59	 2,4-Bis-(1-methyl-cyclopropyl)-5-trifluoromethoxy-phenol
60	 4-(1-Methyl-cyclopropyl)-5-trifluoromethoxy-2-(1-trifluoromethyl-cyclopropyl)-phenol
61	 2-[1-(2,2,2-Trifluoro-ethyl)-cyclopropyl]-5-trifluoromethoxy-4-(1-trifluoromethyl-cyclopropyl)-phenol

62	 2,4-Bis-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-5-trifluoromethoxy-phenol
63	 5-Methoxy-2,4-bis-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol
64	 2-Isopropyl-5-trifluoromethoxy-4-(1-trifluoromethyl-cyclopropyl)-phenol
65	 5-Trifluoromethoxy-4-(1-trifluoromethyl-cyclopropyl)-2-(2,2,2-trifluoro-1-methyl-ethyl)-phenol
66	 5-Methoxy-4-(1-trifluoromethyl-cyclopropyl)-2-(2,2,2-trifluoro-1-methyl-ethyl)-phenol

67	 2-Cyclopropyl-5-methoxy-4-(1-trifluoromethyl-cyclopropyl)-phenol
68	 2-Cyclopropyl-5-trifluoromethoxy-4-(1-trifluoromethyl-cyclopropyl)-phenol
69	 2-Cyclopropyl-4-(1-methyl-cyclopropyl)-5-trifluoromethoxy-phenol
70	 2-Cyclopropyl-5-methoxy-4-(1-methyl-cyclopropyl)-phenol
71	 2-Isopropyl-4-(1-methyl-cyclopropyl)-5-trifluoromethoxy-phenol

2,4,5-SUBSTITUTED-6-HALO-PHENOL COMPOUNDS**Description of the Related Art**

[0201] Compounds useful as voltage-gated sodium channel inhibitors are described by Hadidah-Ruah et al., in WO 2011/140425 published 10 November 2008. The compounds described therein include 4-iodo-2,5-dimethyl-phenol used as an intermediate to make 4-isopropoxy-2,5-dimethylbenzoic acid. 4-isopropoxy-2,5-dimethylbenzoic acid is used as an intermediate in a multi-step process to make compounds useful as voltage-gated sodium channel inhibitors.

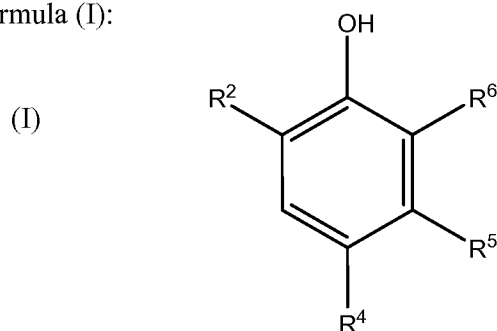
[0202] Amine containing compounds useful for mainly excitatory CNS effects are described in Ermili *et al.*, *Edizione Scientifica*, 32(10):713–24 (1977). 4-chloro-2-isopropyl-5-methylphenol is used as an intermediate to make compounds which had mainly excitatory CNS effects. Two end product compounds, Ve (2-dimethylamino-6-methylchromone) and Vs (2-(dimethylamino)-4H-benzo[h]chromen-4-one), have weak anti-convulsant activity. 4-chloro-2-isopropyl-5-methylphenol is not used as an intermediate in the synthesis of these two compounds.

[0203] Phenol derivatives with known GABAnergic activity and structurally similar phenol derivatives were tested for lipophilic parameters because GABA receptors are present in cell membranes in Reiner et al., *Colloids and Surfaces, B: Biointerfaces*, 101:61–67 (2013). Reiner et al. considered 4-chloro-2-isopropyl-5-methylphenol to be structurally related to the compound thymol, which has known GABAnergic activity, so 4-chloro-2-isopropyl-5-methylphenol was tested for membrane interaction. All five phenol derivatives tested were shown to interact with membranes.

[0204] Compounds useful as inhibitory glycine receptor agonists, including 3,5-di-*tert*-butyl-2-chloro-6-hydroxybenzoic acid, are reported in U.S. 2009/0192190 (Gyback *et al.*, published 30 July 2009). Gyback *et al.* report using 2,4-di-*tert*-butyl-5-chlorophenol as a reagent to synthesize 3,5-di-*tert*-butyl-2-chloro-6-hydroxybenzoic acid.

SUMMARY OF THE INVENTION

[0205] In a first embodiment (Embodiment 1), a method is provided for treating a neurological or an inflammatory condition comprising administering a therapeutically effective amount of a compound or pharmaceutically acceptable salt of the compound, wherein the compound has a structure of Formula (I):



wherein:

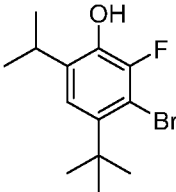
R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl, wherein the alkyl or haloalkyl is optionally substituted with one or more cycloalkyl substituents;

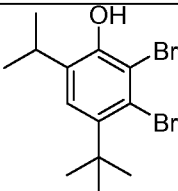
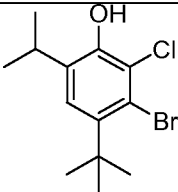
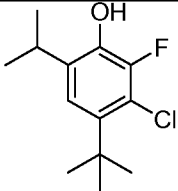
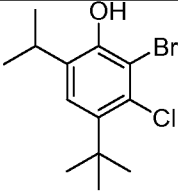
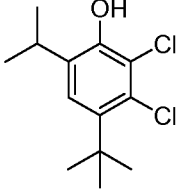
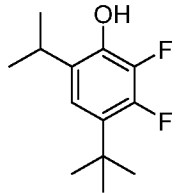
R^4 is selected from the group consisting of H, halo, alkyl, alkoxy, haloalkyl, haloalkoxy and cycloalkyl, wherein alkyl or haloalkyl is optionally substituted with one or more cycloalkyl substituents, wherein the alkyl portion of the alkoxy may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl and halo, and wherein R^4 is not methyl;

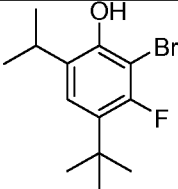
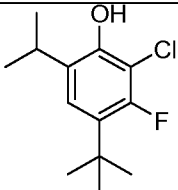
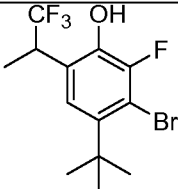
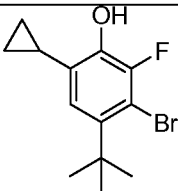
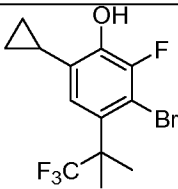
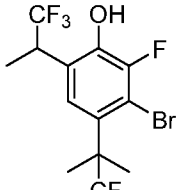
R^5 is selected from the group consisting of alkyl, haloalkyl, cycloalkyl, halo, and alkoxy, wherein the alkoxy may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl and haloalkyl; and

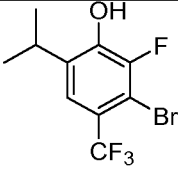
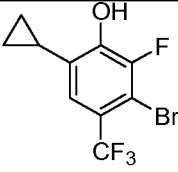
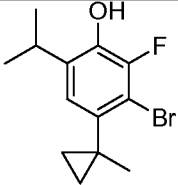
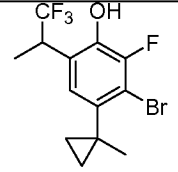
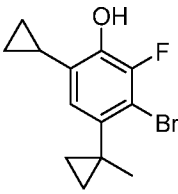
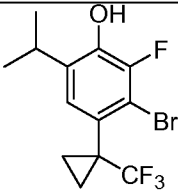
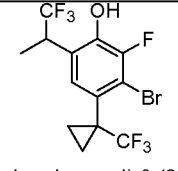
R^6 is halo.

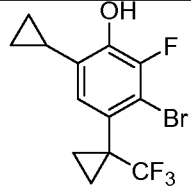
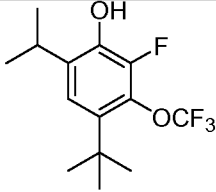
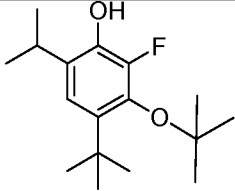
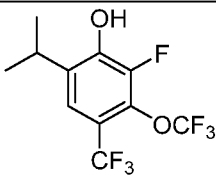
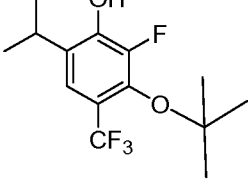
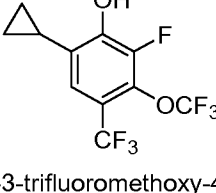
Table 4. Exemplary species

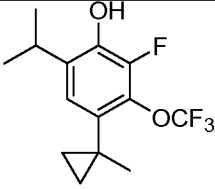
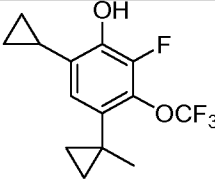
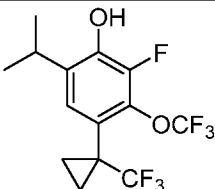
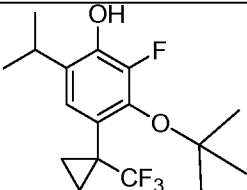
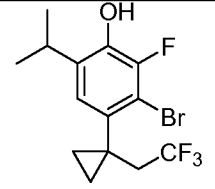
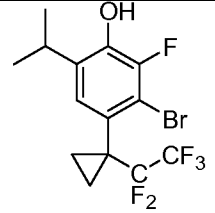
Example Number	Species Structure Species Name
1	 3-Bromo-4-<i>tert</i>-butyl-2-fluoro-6-isopropyl-phenol

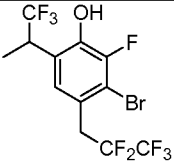
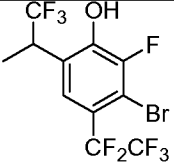
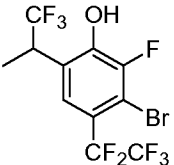
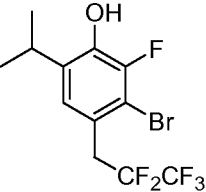
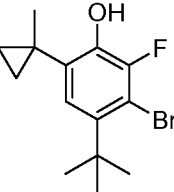
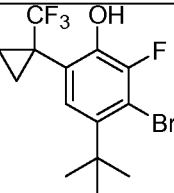
2	 2,3-Dibromo-4- <i>tert</i> -butyl-6-isopropyl-phenol
3	 3-Bromo-4- <i>tert</i> -butyl-2-chloro-6-isopropyl-phenol
4	 4- <i>tert</i> -Butyl-3-chloro-2-fluoro-6-isopropyl-phenol
5	 2-Bromo-4- <i>tert</i> -butyl-3-chloro-6-isopropyl-phenol
6	 4- <i>tert</i> -Butyl-2,3-dichloro-6-isopropyl-phenol
7	 4- <i>tert</i> -Butyl-2,3-difluoro-6-isopropyl-phenol

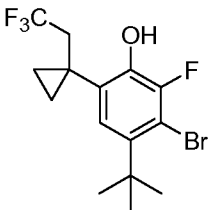
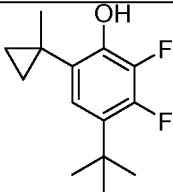
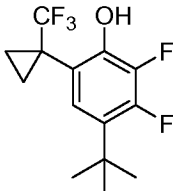
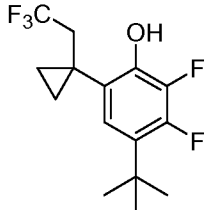
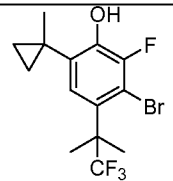
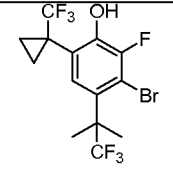
8	 2-Bromo-4-<i>tert</i>-butyl-3-fluoro-6-isopropyl-phenol
9	 4-<i>tert</i>-Butyl-2-chloro-3-fluoro-6-isopropyl-phenol
10	 3-Bromo-4-<i>tert</i>-butyl-2-fluoro-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol
11	 3-Bromo-4-<i>tert</i>-butyl-6-cyclopropyl-2-fluoro-phenol
12	 3-Bromo-6-cyclopropyl-2-fluoro-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol
13	 3-Bromo-2-fluoro-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol

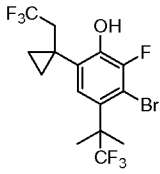
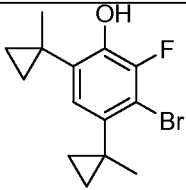
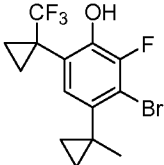
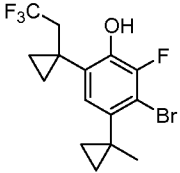
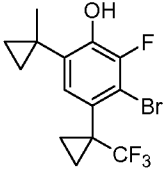
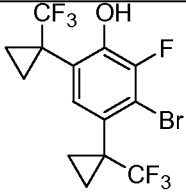
14	 3-Bromo-2-fluoro-6-isopropyl-4-trifluoromethyl-phenol
15	 3-Bromo-6-cyclopropyl-2-fluoro-4-trifluoromethyl-phenol
16	 3-Bromo-2-fluoro-6-isopropyl-4-(1-methyl-cyclopropyl)-phenol
17	 3-Bromo-2-fluoro-4-(1-methyl-cyclopropyl)-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol
18	 3-Bromo-6-cyclopropyl-2-fluoro-4-(1-methyl-cyclopropyl)-phenol
19	 3-Bromo-2-fluoro-6-isopropyl-4-(1-trifluoromethyl-cyclopropyl)-phenol
20	 3-Bromo-2-fluoro-4-(1-trifluoromethyl-cyclopropyl)-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol

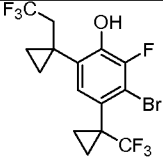
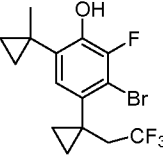
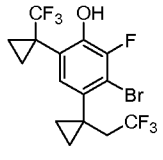
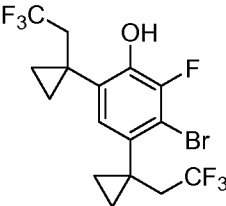
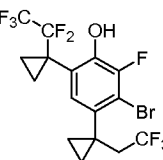
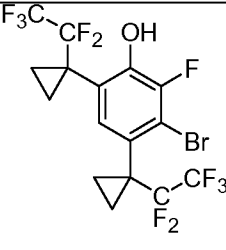
21	 3-Bromo-6-cyclopropyl-2-fluoro-4-(1-trifluoromethyl-cyclopropyl)-phenol
22	 4-<i>tert</i>-Butyl-2-fluoro-6-isopropyl-3-trifluoromethoxy-phenol
23	 3-<i>tert</i>-Butoxy-4-<i>tert</i>-butyl-2-fluoro-6-isopropyl-phenol
24	 2-Fluoro-6-isopropyl-3-trifluoromethoxy-4-trifluoromethyl-phenol
25	 3-<i>tert</i>-Butoxy-2-fluoro-6-isopropyl-4-trifluoromethyl-phenol
26	 6-Cyclopropyl-2-fluoro-3-trifluoromethoxy-4-trifluoromethyl-phenol

27	 2-Fluoro-6-isopropyl-4-(1-methyl-cyclopropyl)-3-trifluoromethoxy-phenol
28	 6-Cyclopropyl-2-fluoro-4-(1-methyl-cyclopropyl)-3-trifluoromethoxy-phenol
29	 2-Fluoro-6-isopropyl-3-trifluoromethoxy-4-(1-trifluoromethyl-cyclopropyl)-phenol
30	 3-<i>tert</i>-Butoxy-2-fluoro-6-isopropyl-4-(1-trifluoromethyl-cyclopropyl)-phenol
31	 3-Bromo-2-fluoro-6-isopropyl-4-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol
32	 3-Bromo-2-fluoro-6-isopropyl-4-(1-pentafluoroethyl-cyclopropyl)-phenol

33	 3-Bromo-2-fluoro-4-(2,2,3,3,3-pentafluoro-propyl)-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol
34	 3-Bromo-2-fluoro-4-pentafluoroethyl-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol
35	 3-Bromo-2-fluoro-4-pentafluoroethyl-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol
36	 3-Bromo-2-fluoro-6-isopropyl-4-(2,2,3,3,3-pentafluoro-propyl)-phenol
37	 3-Bromo-4-<i>tert</i>-butyl-2-fluoro-6-(1-methyl-cyclopropyl)-phenol
38	 3-Bromo-4-<i>tert</i>-butyl-2-fluoro-6-(1-trifluoromethyl-cyclopropyl)-phenol

39	 3-Bromo-4-<i>tert</i>-butyl-2-fluoro-6-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol
40	 4-<i>tert</i>-Butyl-2,3-difluoro-6-(1-methyl-cyclopropyl)-phenol
41	 4-<i>tert</i>-Butyl-2,3-difluoro-6-(1-trifluoromethyl-cyclopropyl)-phenol
42	 4-<i>tert</i>-Butyl-2,3-difluoro-6-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol
43	 3-Bromo-2-fluoro-6-(1-methyl-cyclopropyl)-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol
44	 3-Bromo-2-fluoro-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-6-(1-trifluoromethyl-cyclopropyl)-phenol

45	 3-Bromo-2-fluoro-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-6-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol
46	 3-Bromo-2-fluoro-4,6-bis-(1-methyl-cyclopropyl)-phenol
47	 3-Bromo-2-fluoro-4-(1-methyl-cyclopropyl)-6-(1-trifluoromethyl-cyclopropyl)-phenol
48	 3-Bromo-2-fluoro-4-(1-methyl-cyclopropyl)-6-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol
49	 3-Bromo-2-fluoro-6-(1-methyl-cyclopropyl)-4-(1-trifluoromethyl-cyclopropyl)-phenol
50	 3-Bromo-2-fluoro-4,6-bis-(1-trifluoromethyl-cyclopropyl)-phenol

51	 3-Bromo-2-fluoro-6-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-4-(1-trifluoromethyl-cyclopropyl)-phenol
52	 3-Bromo-2-fluoro-6-(1-methyl-cyclopropyl)-4-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol
53	 3-Bromo-2-fluoro-4-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-6-(1-trifluoromethyl-cyclopropyl)-phenol
54	 3-Bromo-2-fluoro-4,6-bis-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol
55	 3-Bromo-2-fluoro-6-(1-pentafluoroethyl-cyclopropyl)-4-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol
56	 3-Bromo-2-fluoro-4,6-bis-(1-pentafluoroethyl-cyclopropyl)-phenol

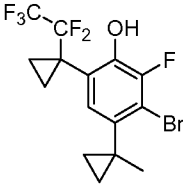
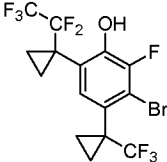
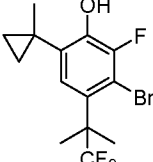
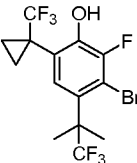
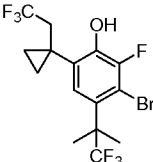
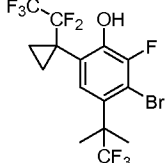
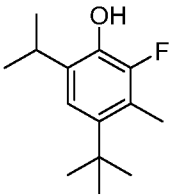
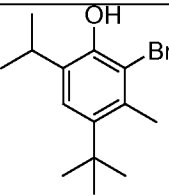
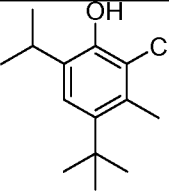
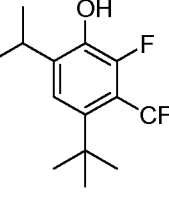
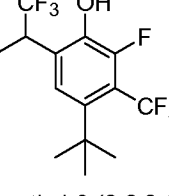
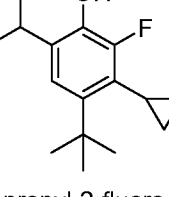
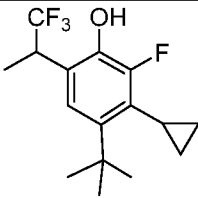
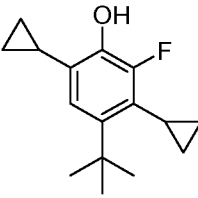
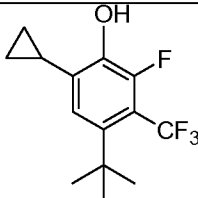
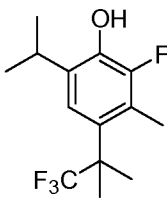
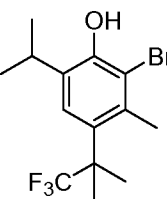
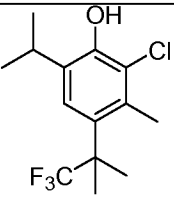
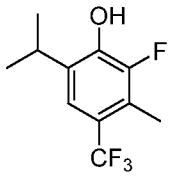
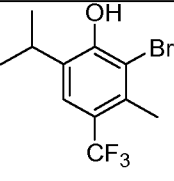
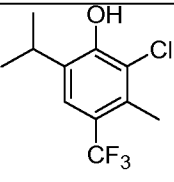
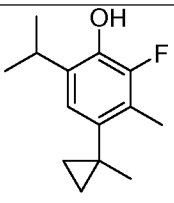
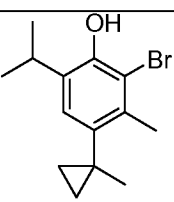
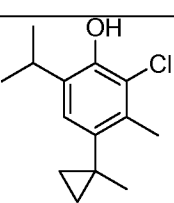
57	 3-Bromo-2-fluoro-4-(1-methyl-cyclopropyl)-6-(1-pentafluoroethyl-cyclopropyl)-phenol
58	 3-Bromo-2-fluoro-6-(1-pentafluoroethyl-cyclopropyl)-4-(1-trifluoromethyl-cyclopropyl)-phenol
59	 3-Bromo-2-fluoro-6-(1-methyl-cyclopropyl)-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol
60	 3-Bromo-2-fluoro-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-6-(1-trifluoromethyl-cyclopropyl)-phenol
61	 3-Bromo-2-fluoro-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-6-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol
62	 3-Bromo-2-fluoro-6-(1-pentafluoroethyl-cyclopropyl)-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol

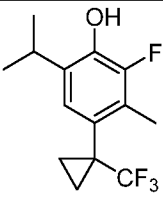
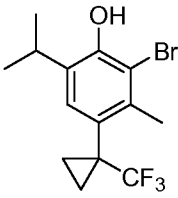
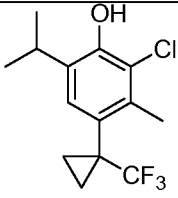
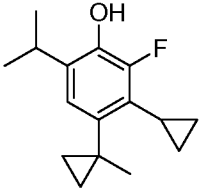
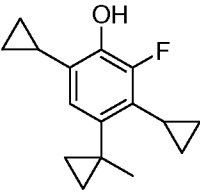
Table 5. Exemplary species

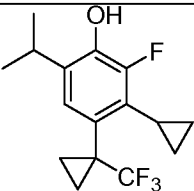
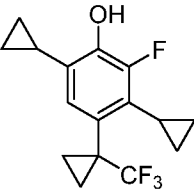
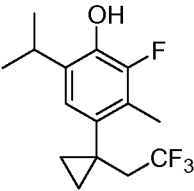
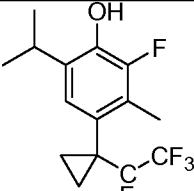
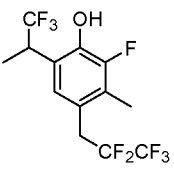
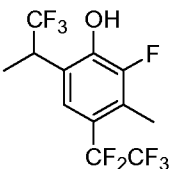
Example Number	Species Structure Species Name
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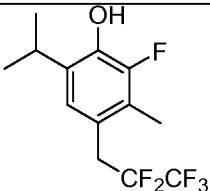
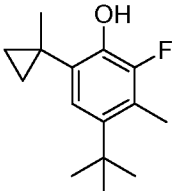
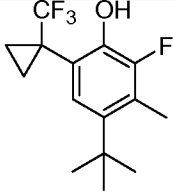
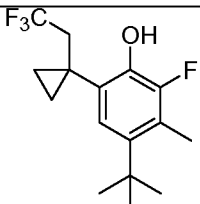
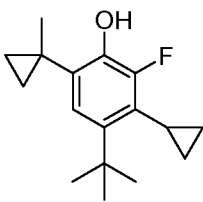
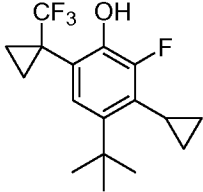
63	 4- <i>tert</i> -Butyl-2-fluoro-6-isopropyl-3-methyl-phenol
64	 2-Bromo-4- <i>tert</i> -butyl-6-isopropyl-3-methyl-phenol
65	 4- <i>tert</i> -Butyl-2-chloro-6-isopropyl-3-methyl-phenol
66	 4- <i>tert</i> -Butyl-2-fluoro-6-isopropyl-3-trifluoromethyl-phenol
67	 4- <i>tert</i> -Butyl-2-fluoro-3-trifluoromethyl-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol
68	 4- <i>tert</i> -Butyl-3-cyclopropyl-2-fluoro-6-isopropyl-phenol

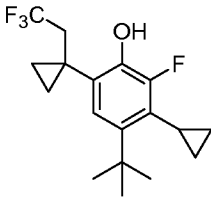
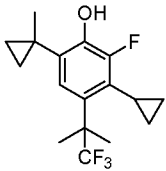
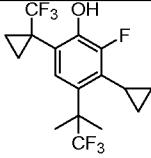
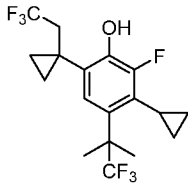
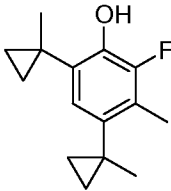
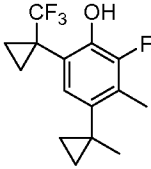
69	 4-<i>tert</i>-Butyl-3-cyclopropyl-2-fluoro-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol
70	 4-<i>tert</i>-Butyl-3,6-dicyclopropyl-2-fluoro-phenol
71	 4-<i>tert</i>-Butyl-6-cyclopropyl-2-fluoro-3-trifluoromethyl-phenol
72	 2-Fluoro-6-isopropyl-3-methyl-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol
73	 2-Bromo-6-isopropyl-3-methyl-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol
74	

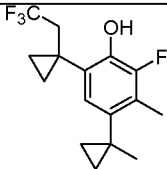
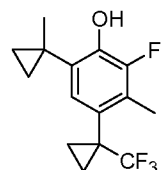
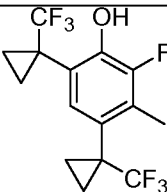
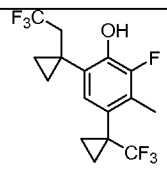
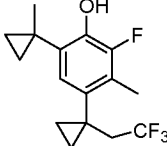
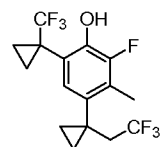
	 2-Chloro-6-isopropyl-3-methyl-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol
75	 2-Fluoro-6-isopropyl-3-methyl-4-trifluoromethyl-phenol
76	 2-Bromo-6-isopropyl-3-methyl-4-trifluoromethyl-phenol
77	 2-Chloro-6-isopropyl-3-methyl-4-trifluoromethyl-phenol
78	 2-Fluoro-6-isopropyl-3-methyl-4-(1-methyl-cyclopropyl)-phenol
79	 2-Bromo-6-isopropyl-3-methyl-4-(1-methyl-cyclopropyl)-phenol
80	 2-Chloro-6-isopropyl-3-methyl-4-(1-methyl-cyclopropyl)-phenol

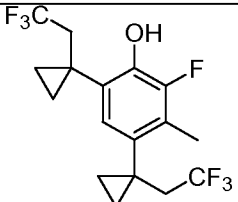
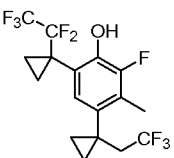
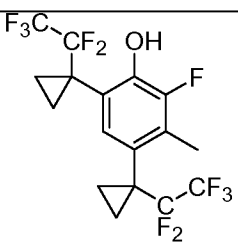
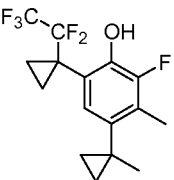
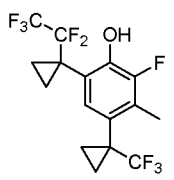
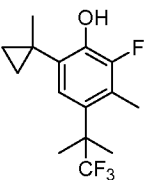
81	 2-Fluoro-6-isopropyl-3-methyl-4-(1-trifluoromethyl-cyclopropyl)-phenol
82	 2-Bromo-6-isopropyl-3-methyl-4-(1-trifluoromethyl-cyclopropyl)-phenol
83	 2-Chloro-6-isopropyl-3-methyl-4-(1-trifluoromethyl-cyclopropyl)-phenol
84	 3-Cyclopropyl-2-fluoro-6-isopropyl-4-(1-methyl-cyclopropyl)-phenol
85	 3,6-Dicyclopropyl-2-fluoro-4-(1-methyl-cyclopropyl)-phenol
86	

	 3-Cyclopropyl-2-fluoro-6-isopropyl-4-(1-trifluoromethyl-cyclopropyl)-phenol
87	 3,6-Dicyclopropyl-2-fluoro-4-(1-trifluoromethyl-cyclopropyl)-phenol
88	 2-Fluoro-6-isopropyl-3-methyl-4-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol
89	 2-Fluoro-6-isopropyl-3-methyl-4-(1-pentafluoroethyl-cyclopropyl)-phenol
90	 2-Fluoro-3-methyl-4-(2,2,3,3,3-pentafluoro-propyl)-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol
91	 2-Fluoro-3-methyl-4-pentafluoroethyl-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol
92	

	 2-Fluoro-6-isopropyl-3-methyl-4-(2,2,3,3,3-pentafluoro-propyl)-phenol
93	 4-<i>tert</i>-Butyl-2-fluoro-3-methyl-6-(1-methyl-cyclopropyl)-phenol
94	 4-<i>tert</i>-Butyl-2-fluoro-3-methyl-6-(1-trifluoromethyl-cyclopropyl)-phenol
95	 4-<i>tert</i>-Butyl-2-fluoro-3-methyl-6-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol
96	 4-<i>tert</i>-Butyl-3-cyclopropyl-2-fluoro-6-(1-methyl-cyclopropyl)-phenol
97	 4-<i>tert</i>-Butyl-3-cyclopropyl-2-fluoro-6-(1-trifluoromethyl-cyclopropyl)-phenol

98	 4-<i>tert</i>-Butyl-3-cyclopropyl-2-fluoro-6-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol
99	 3-Cyclopropyl-2-fluoro-6-(1-methyl-cyclopropyl)-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol
100	 3-Cyclopropyl-2-fluoro-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-6-(1-trifluoromethyl-cyclopropyl)-phenol
101	 3-Cyclopropyl-2-fluoro-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-6-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol
102	 2-Fluoro-3-methyl-4,6-bis-(1-methyl-cyclopropyl)-phenol
103	 2-Fluoro-3-methyl-4-(1-methyl-cyclopropyl)-6-(1-trifluoromethyl-cyclopropyl)-phenol
104	

	 2-Fluoro-3-methyl-4-(1-methyl-cyclopropyl)-6-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol
105	 2-Fluoro-3-methyl-6-(1-methyl-cyclopropyl)-4-(1-trifluoromethyl-cyclopropyl)-phenol
106	 2-Fluoro-3-methyl-4,6-bis-(1-trifluoromethyl-cyclopropyl)-phenol
107	 2-Fluoro-3-methyl-6-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-4-(1-trifluoromethyl-cyclopropyl)-phenol
108	 2-Fluoro-3-methyl-6-(1-methyl-cyclopropyl)-4-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol
109	 2-Fluoro-3-methyl-4-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-6-(1-trifluoromethyl-cyclopropyl)-phenol
110	

	 2-Fluoro-3-methyl-4,6-bis-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol
111	 2-Fluoro-3-methyl-6-(1-pentafluoroethyl-cyclopropyl)-4-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol
112	 2-Fluoro-3-methyl-4,6-bis-(1-pentafluoroethyl-cyclopropyl)-phenol
113	 2-Fluoro-3-methyl-4-(1-methyl-cyclopropyl)-6-(1-pentafluoroethyl-cyclopropyl)-phenol
114	 2-Fluoro-3-methyl-6-(1-pentafluoroethyl-cyclopropyl)-4-(1-trifluoromethyl-cyclopropyl)-phenol
115	 2-Fluoro-3-methyl-6-(1-methyl-cyclopropyl)-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol
116	

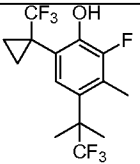
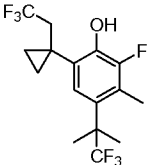
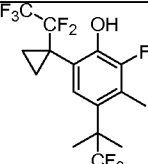
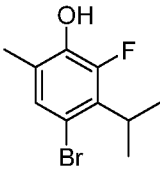
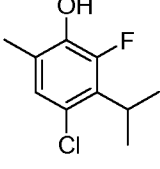
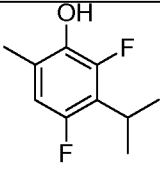
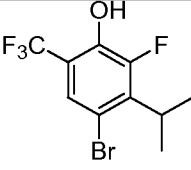
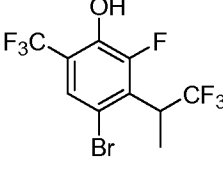
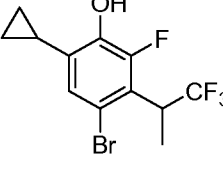
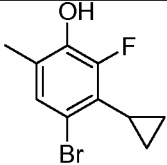
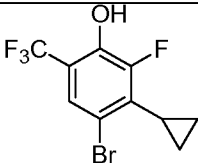
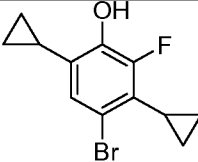
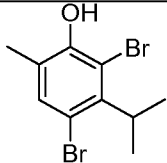
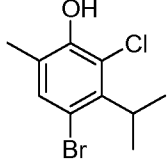
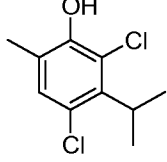
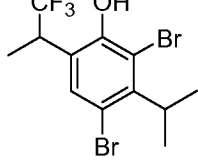
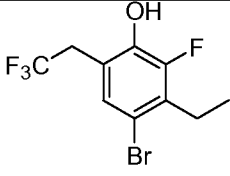
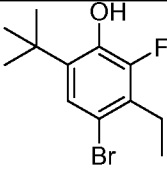
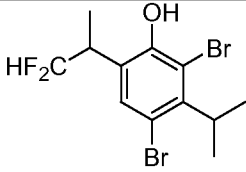
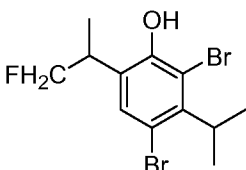
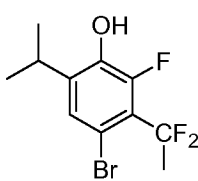
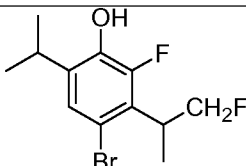
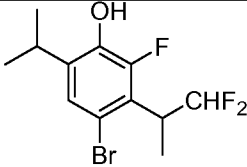
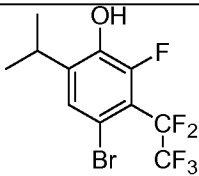
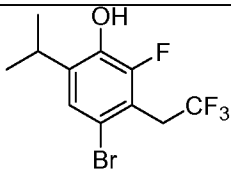
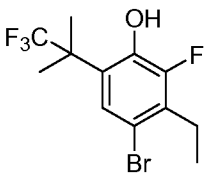
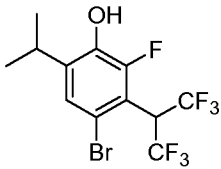
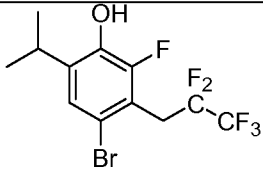
	 2-Fluoro-3-methyl-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-6-(1-trifluoromethyl-cyclopropyl)-phenol
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118	 2-Fluoro-3-methyl-6-(1-pentafluoroethyl-cyclopropyl)-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol

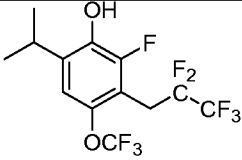
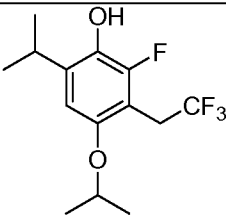
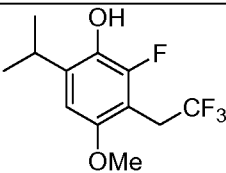
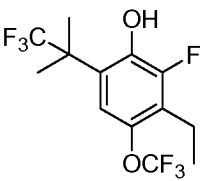
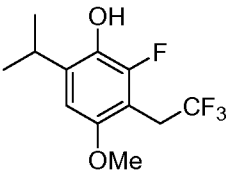
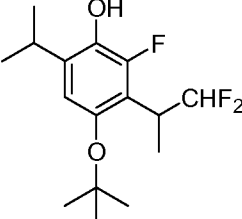
Table 6. Exemplary species

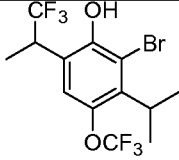
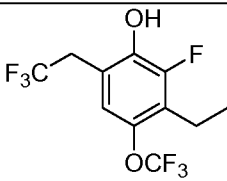
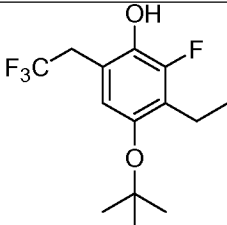
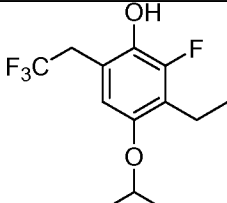
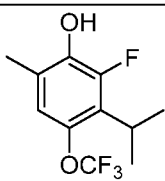
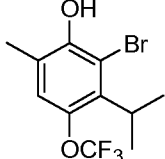
Example Number	Species Structure Species Name
119	 4-Bromo-2-fluoro-3-isopropyl-6-methyl-phenol
120	 4-Chloro-2-fluoro-3-isopropyl-6-methyl-phenol
121	 2,4-Difluoro-3-isopropyl-6-methyl-phenol
122	 4-Bromo-2-fluoro-3-isopropyl-6-trifluoromethyl-phenol
123	 4-Bromo-2-fluoro-6-trifluoromethyl-3-(2,2,2-trifluoro-1-methyl-ethyl)-phenol
124	 4-Bromo-6-cyclopropyl-2-fluoro-3-(2,2,2-trifluoro-1-methyl-ethyl)-phenol

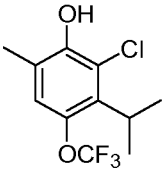
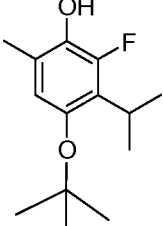
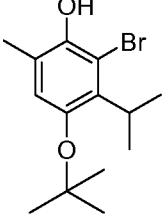
125	 4-Bromo-3-cyclopropyl-2-fluoro-6-methyl-phenol
126	 4-Bromo-3-cyclopropyl-2-fluoro-6-trifluoromethyl-phenol
127	 4-Bromo-3,6-dicyclopropyl-2-fluoro-phenol
128	 2,4-Dibromo-3-isopropyl-6-methyl-phenol
129	 4-Bromo-2-chloro-3-isopropyl-6-methyl-phenol
130	 2,4-Dichloro-3-isopropyl-6-methyl-phenol
131	 2,4-Dibromo-3-isopropyl-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol

132	 4-Bromo-3-ethyl-2-fluoro-6-(2,2,2-trifluoro-ethyl)-phenol
133	 4-Bromo-6-<i>tert</i>-butyl-3-ethyl-2-fluoro-phenol
134	 2,4-Dibromo-6-(2,2-difluoro-1-methyl-ethyl)-3-isopropyl-phenol
135	 2,4-Dibromo-6-(2-fluoro-1-methyl-ethyl)-3-isopropyl-phenol
136	 4-Bromo-3-(1,1-difluoro-ethyl)-2-fluoro-6-isopropyl-phenol
137	 4-Bromo-2-fluoro-3-(2-fluoro-1-methyl-ethyl)-6-isopropyl-phenol

138	 4-Bromo-3-(2,2-difluoro-1-methyl-ethyl)-2-fluoro-6-isopropyl-phenol
139	 4-Bromo-2-fluoro-6-isopropyl-3-pentafluoroethyl-phenol
140	 4-Bromo-2-fluoro-6-isopropyl-3-(2,2,2-trifluoro-ethyl)-phenol
141	 4-Bromo-3-ethyl-2-fluoro-6-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol
142	 4-Bromo-2-fluoro-6-isopropyl-3-(2,2,2-trifluoro-1-trifluoromethyl-ethyl)-phenol
143	 4-Bromo-2-fluoro-6-isopropyl-3-(2,2,3,3,3-pentafluoro-propyl)-phenol

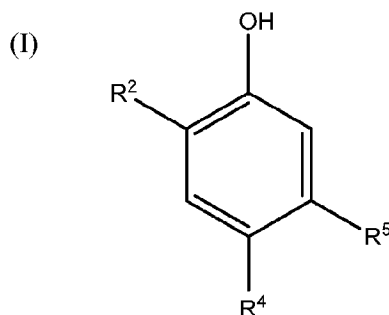
144	 2-Fluoro-6-isopropyl-3-(2,2,3,3,3-pentafluoro-propyl)-4-trifluoromethoxy-phenol
145	 2-Fluoro-4-isopropoxy-6-isopropyl-3-(2,2,2-trifluoro-ethyl)-phenol
146	 2-Fluoro-6-isopropyl-4-methoxy-3-(2,2,2-trifluoro-ethyl)-phenol
147	 3-Ethyl-2-fluoro-6-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-4-trifluoromethoxy-phenol
148	 2-Fluoro-6-isopropyl-4-methoxy-3-(2,2,2-trifluoro-ethyl)-phenol
149	 4-<i>tert</i>-Butoxy-3-(2,2-difluoro-1-methyl-ethyl)-2-fluoro-6-isopropyl-phenol

150	 2-Bromo-3-isopropyl-4-trifluoromethoxy-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol
151	 3-Ethyl-2-fluoro-6-(2,2,2-trifluoro-ethyl)-4-trifluoromethoxy-phenol
152	 4-<i>tert</i>-Butoxy-3-ethyl-2-fluoro-6-(2,2,2-trifluoro-ethyl)-phenol
153	 3-Ethyl-2-fluoro-4-isopropoxy-6-(2,2,2-trifluoro-ethyl)-phenol
154	 2-Fluoro-3-isopropyl-6-methyl-4-trifluoromethoxy-phenol
155	 2-Bromo-3-isopropyl-6-methyl-4-trifluoromethoxy-phenol

156	 2-Chloro-3-isopropyl-6-methyl-4-trifluoromethoxy-phenol
157	 4-<i>tert</i>-Butoxy-2-fluoro-3-isopropyl-6-methyl-phenol
158	 2-Bromo-4-<i>tert</i>-butoxy-3-isopropyl-6-methyl-phenol

WHAT IS CLAIMED IS:

1. A method of treating a neurological or an inflammatory condition comprising administering a therapeutically effective amount of a compound or pharmaceutically acceptable salt of the compound, wherein the compound has the structure of Formula (I):



wherein:

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

R^4 is selected from the group consisting of H, halo, and alkoxy, wherein the alkoxy may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl and halo, and wherein R^4 is not methyl; and

R^5 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl.

2. The method of claim 1 wherein each of R^2 and R^5 has between one and five carbons.

3. The method of claim 1 wherein the condition is epilepsy, seizures, or convulsions.

4. The method of claim 1 wherein the condition is neuropathic pain or fibromyalgia.

5. The method of claim 1 wherein the condition is a psychological disorder.

6. The method of claim 5 wherein the psychological disorder is anxiety, mania, bipolar disorder, or depression.

7. The method of claim 1, wherein the condition is Alzheimer's Disease, Huntington's Disease, Multiple Sclerosis, Parkinson's disease, Tourette's Syndrome, tinnitus, and tremors.

8. The method of Claims 1 or 3, wherein:

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

R^4 is halo.

5

9. The method of Claim 8, wherein:

R^4 is selected from the group consisting of Br, Cl, and F.

10. The method of Claim 9, wherein:

10 R^2 is alkyl; and

R^5 is alkyl having two or more carbons.

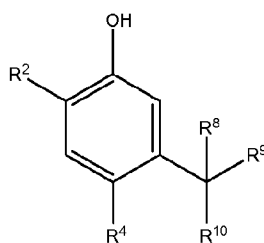
11. The method of Claim 10, wherein the compound is selected from a group consisting of: 4-chloro-5-*tert*-butyl-2-methyl-phenol; 4-chloro-2-isopropyl-5-methyl-phenol; 4-fluoro-2-isopropyl-5-methyl-phenol; 4-chloro-2,5-diisopropyl-phenol; 4-bromo-5-isopropyl-2-methylphenol; 4-bromo-2-isopropyl-5-methyl-phenol; 4-bromo-2-*tert*-butyl-5-isopropyl-phenol; 4-bromo-5-*tert*-butyl-2-methyl-phenol; and 4-fluoro-5-*tert*-butyl-2-methyl-phenol.

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12. The method of Claim 1, wherein the compound has the structure of Formula (II):

20

(II)



25

wherein:

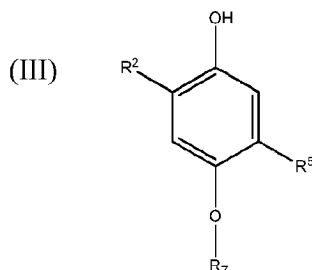
R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

R^4 is selected from the group consisting of Br, Cl, and F; and

R^8 , R^9 and R^{10} are each independently selected from the group consisting of H, alkyl, and haloalkyl.

30

13. The method of Claim 1, wherein the compound has the structure of Formula (III):



wherein:

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

R^5 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl; and

R_7 is selected from the group consisting of alkyl and haloalkyl.

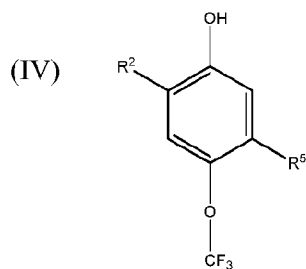
14. The method of Claim 13, wherein:

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

R^5 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl; and

R_7 is alkyl.

15. The method of Claim 14, wherein the compound has the structure of Formula (IV):



wherein:

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl; and

R^5 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl.

16. The method of Claim 15, wherein:

R^2 is selected from the group consisting of alkyl and cycloalkyl; and

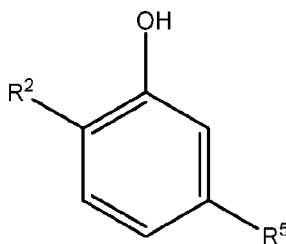
R^5 is selected from the group consisting of alkyl and cycloalkyl.

17. A compound selected from the group consisting of: 4-bromo-5-ethyl-2-methyl-phenol; 4-fluoro-5-isopropyl-2-methyl-phenol; 4-bromo-5-*tert*-butyl-2-methyl-phenol; 4-bromo-5-cyclopropyl-2-methyl-phenol; 4-bromo-2-ethyl-5-isopropyl-phenol; 4-chloro-2-ethyl-5-isopropyl-phenol; 2-ethyl-4-fluoro-5-isopropyl phenol; 4-bromo-5-isopropyl-2-propyl-phenol, 5-isopropyl-2-propyl-phenol; and 4-bromo-2,5-isopropyl-phenol.

18. A compound selected from the group consisting of: 4-bromo-2-methyl-5-(2,2,2-trifluoro-1-methyl-ethyl)-phenol; 4-bromo-5-(2-fluoro-1-methyl-ethyl)-2-methyl-phenol; 4-bromo-2-methyl-5-(2,2,2-trifluoro-1-trifluoromethyl-ethyl)-phenol; 4-bromo-2-trifluoromethyl-5-(2,2,2-trifluoro-1-methyl-ethyl)-phenol; 4-bromo-2-cyclopropyl-5-isopropyl-phenol; 4-bromo-2,5-dicyclopropyl-phenol; 5-isopropyl-2-methyl-4-trifluoromethoxy-phenol; 2-cyclopropyl-5-isopropyl-4-trifluoromethoxy-phenol; 5-cyclopropyl-2-methyl-4-trifluoromethoxy-phenol; 2,5-dicyclopropyl-4-trifluoromethoxy-phenol; 4-*tert*-butoxy-5-cyclopropyl-2-methyl-phenol; 4-*tert*-butoxy-2-cyclopropyl-5-methyl-phenol; 4-*tert*-butoxy-2,5-dicyclopropyl-phenol; 4-isopropoxy-5-isopropyl-2-methyl-phenol; 4-bromo-5-isopropyl-2-trifluoromethyl-phenol; 4-bromo-5-(2-fluoro-1-methyl-ethyl)-2-methyl-phenol; and 4-*tert*-butoxy-5-isopropyl-2-methyl-phenol.

19. A compound or pharmaceutically acceptable salt of the compound, wherein the compound has the structure of Formula (V):

20 (V)



25 wherein:

R² is selected from the group consisting of haloalkyl and cycloalkyl; and

R⁵ is selected from the group consisting of haloalkyl and cycloalkyl.

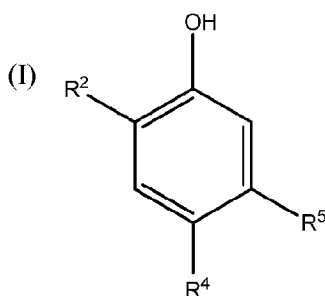
20. A compound of Claim 19, wherein:

R^2 is selected from the group consisting of trifluoroalkyl and cycloalkyl

R^5 is selected from the group consisting of trifluoroalkyl and cycloalkyl.

21. A compound selected from the group consisting of: 5-(1,2-dimethyl-propyl)-2-methyl-phenol; 5-isobutyl-2-methyl-phenol; 5-cyclopentyl-2-methyl-phenol; 5-*sec*-butyl-2-ethyl-phenol; 5-butyl-2-propyl-phenol; 5-isopropyl-2-propyl-phenol; 5-*sec*-butyl-2-propyl-phenol; 5-*tert*-butyl-2-propyl-phenol; 2-butyl-5-isopropyl-phenol; 2-butyl-5-*sec*-butyl-phenol; 5-(*tert*-butyl)-2-butylphenol; 2-isopropyl-5-propyl-phenol; 5-*sec*-butyl-2-isopropyl-phenol; 2-*sec*-butyl-5-ethyl-phenol; 2-*sec*-butyl-5-propyl-phenol; 5-butyl-2-*sec*-butyl-phenol; 2-*sec*-butyl-5-isopropyl-phenol; 5-*sec*-butyl-2-*tert*-butyl-phenol; 2-methyl-5-(2,2,2-trifluoro-1-methyl-ethyl)-phenol; 5-(2-fluoro-1-methyl-ethyl)-2-methyl-phenol; 2-methyl-5-(2,2,2-trifluoro-1-trifluoromethyl-ethyl)-phenol; 2-trifluoromethyl-5-(2,2,2-trifluoro-1-methyl-ethyl)-phenol; 5-isopropyl-2-(1-methyl-butyl)-phenol; 2-isopropyl-5-isopropyl-phenol; 2-cyclopropyl-5-isopropyl-phenol; and 2,5-dicyclopropyl-phenol.

22. A compound or pharmaceutically acceptable salt of the compound, wherein the compound has the structure of Formula (I):



wherein:

R^2 is selected from the group consisting of methyl, cycloalkyl, and $-\text{CF}_3$;

R^4 is halo;

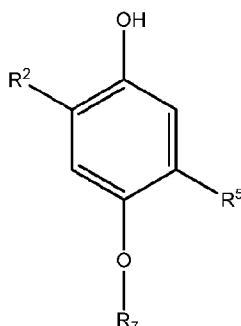
R^5 is selected from the group consisting of fluoroalkyl and a three, four, or five carbon cycloalkyl.

23. The compound of Claim 22, wherein:

R^4 is selected from the group consisting of Br, Cl, and F.

24. A compound or pharmaceutically acceptable salt of the compound, wherein the compound has the structure of Formula (III):

5 (III)



wherein:

10 R^2 and R^5 are each independently selected from the group consisting of alkyl and cycloalkyl, wherein at least one of R^2 and R^5 is cycloalkyl; and

R_7 is selected from the group consisting of isopropyl, *tert*-butyl, and haloalkyl.

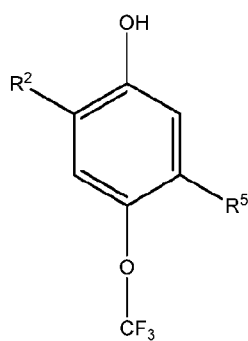
25. A compound of Claim 24, wherein:

R_7 is selected from the group consisting of isopropyl and *tert*-butyl.

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26. A compound or pharmaceutically acceptable salt of the compound of Claim 22, wherein the compound has the structure of Formula (IV):

(IV)



20

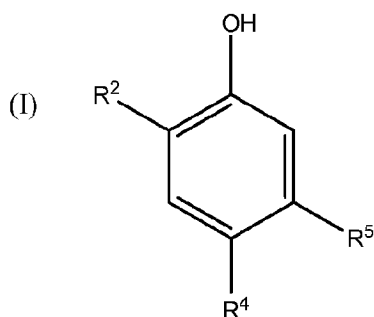
25 wherein:

R^2 is selected from the group consisting of alkyl, and cycloalkyl; and

R^5 is selected from the group consisting of alkyl, and cycloalkyl.

30

27. A method of treating epilepsy, seizures, or convulsions, the method comprising administering a therapeutically effective amount of a compound or of a pharmaceutically acceptable salt of the compound, wherein the compound has the structure of Formula (I):



wherein:

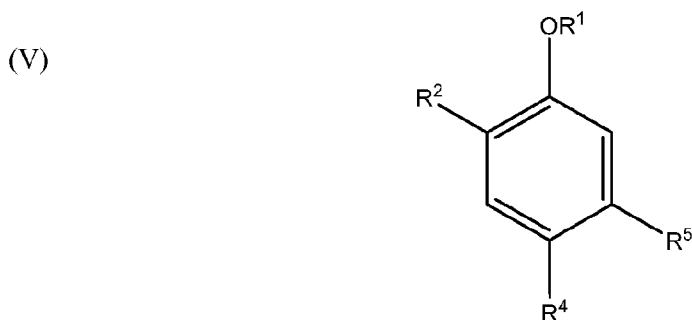
R^2 and R^5 are each independently selected from the group consisting of methyl, isopropyl, and *tert*-butyl; and

R^4 is selected from the group consisting of Br, Cl, and F.

28. The method of any one of Claims 1–16 or 27, wherein the compound is deuterated.

29. The compound or pharmaceutically acceptable salt of any one of Claims 17–26, wherein the compound is deuterated.

30. A method of treating a neurological or an inflammatory condition comprising administering a therapeutically effective amount of a compound or pharmaceutically acceptable salt of the compound, wherein the compound has a structure of Formula (V):



wherein:

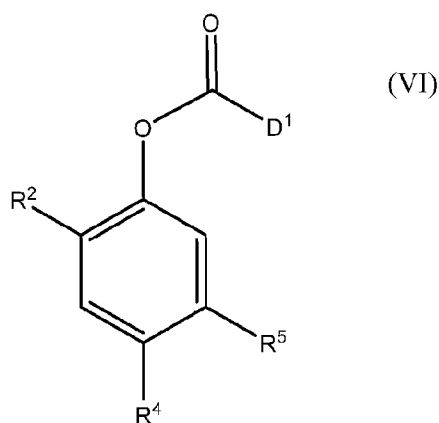
R^1 is selected from the group consisting of an ester, a carbonate, a phosphate, a carbamate, a sulfamate, and an acylmethylester;

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

R^4 is selected from the group consisting of H, halo, and alkoxy, wherein the alkoxy may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl and halo, and wherein R^4 is not methyl; and

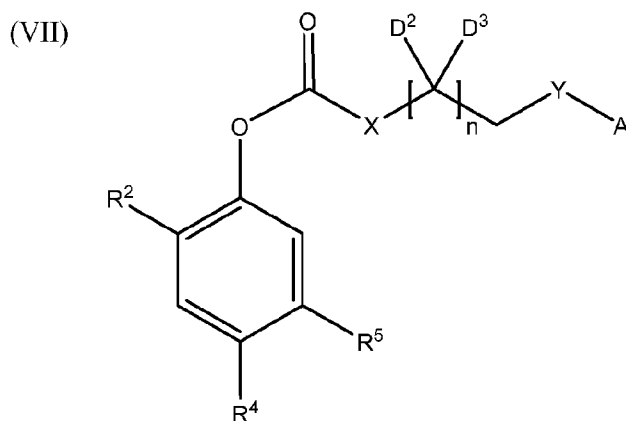
R^5 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl.

31. The method of Claim 30, wherein the compound has a structure of Formula (VI):



wherein D^1 is alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroalkyl, heteroaryl, heteroaralkyl, carbonylalkyl, or phosphonooxyalkyl, optionally substituted with one or more substituents selected from the group consisting of alkyl, carboxylate, heteroalkyl, monocyclic ring, bicyclic ring, and hydroxyl moieties.

32. The method of Claim 31, wherein the compound has a structure of Formula (VII):



wherein:

D^2 and D^3 together with the carbon atom to which they are bonded form a cycloalkyl or cycloheteroalkyl ring, or alternatively D^2 and D^3 are each independently selected from the group consisting of hydrogen, alkyl, and heteroalkyl;

A , Y , and one of D^2 or D^3 together with the atoms to which they are bonded to form a cycloheteroalkyl ring, or alternatively A is selected from the group consisting of hydrogen, phosphono, alkyl, aryl, arylalkyl, heteroalkyl, heteroaryl, and heteroarylalkyl;

X is selected from the group consisting of $-ND^4-$, $-O-$, $-CH_2-$, and $-S-$;

Y is selected from the group consisting of $-O-$ and $-ND^4-$;

n is an integer from 1 to 5; and

D^4 is selected from the group consisting of hydrogen, alkyl, and arylalkyl.

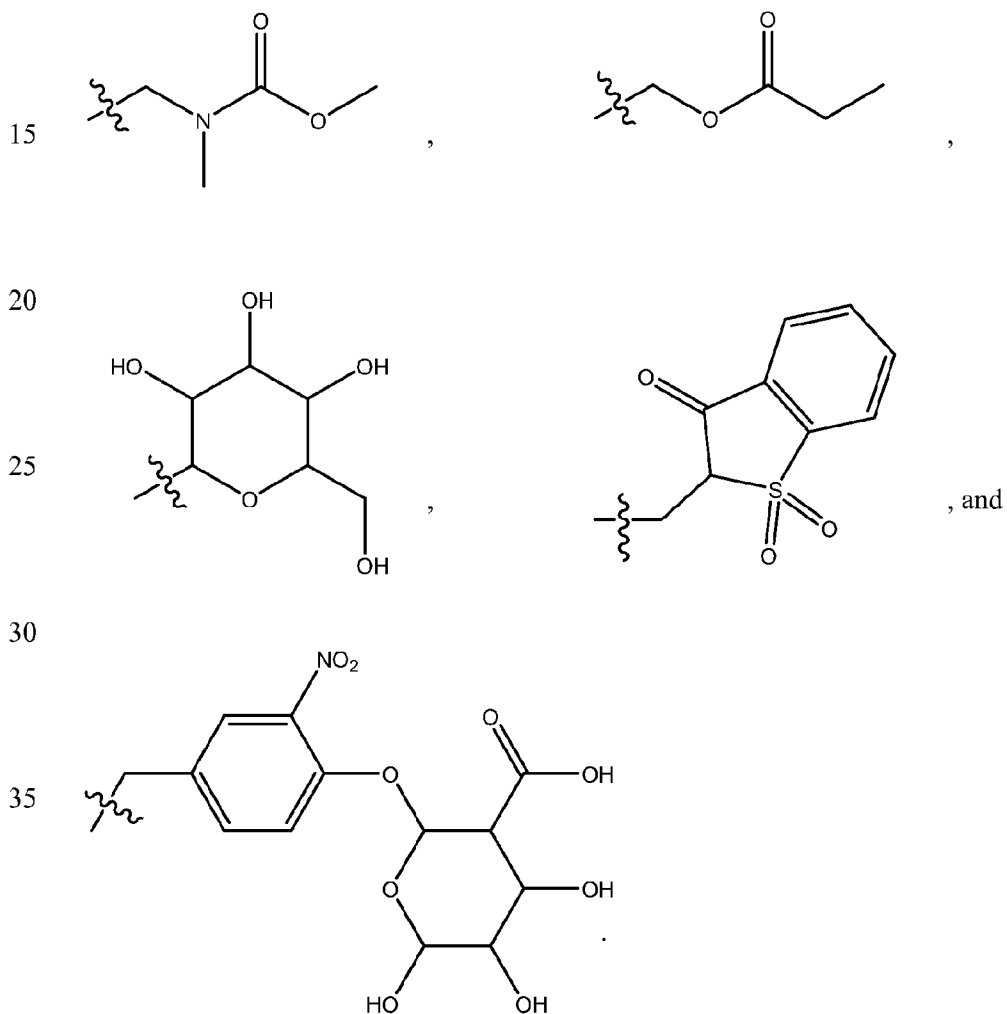
33. The method of Claim 32, wherein D^2 and D^3 are each hydrogen, X is $-CH_2-$, Y is $-O-$, A is phosphono, and $n=1$.

34. The method of Claim 30, wherein R^1 is selected from the group consisting of $-P-(O)(OD^5)_2$,

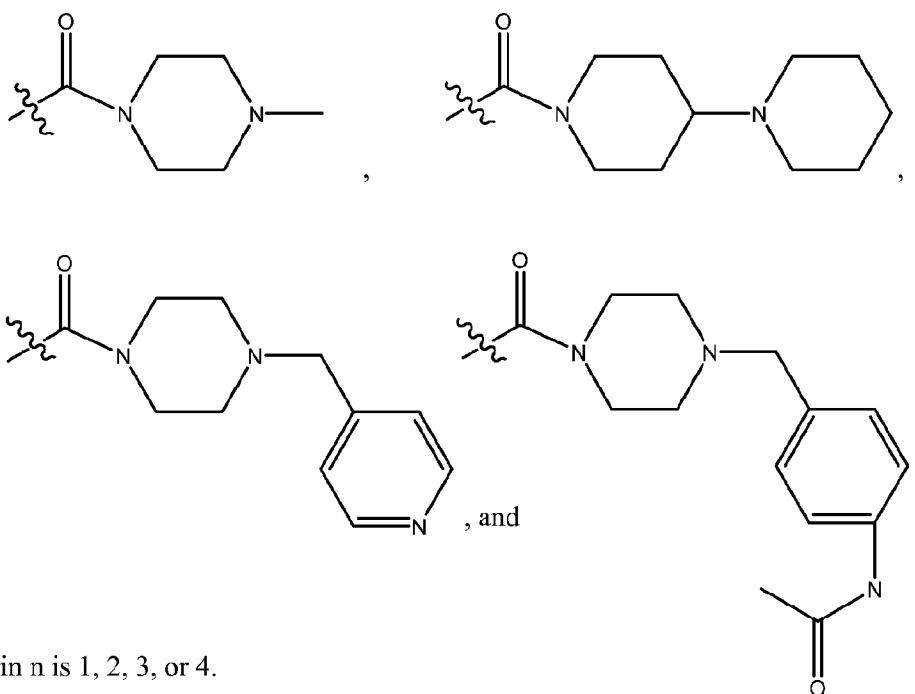
5 $-CH_2-O-P-(O)(OD^5)_2$, $-(CH_2)_2-O-P-(O)(OD^5)_2$, and $-CH_2-O-P-(O)(OD^5)_2$, and further wherein D^5 is H or a pharmaceutically acceptable cation.

35. The method of Claim 34, wherein the pharmaceutically acceptable cation is selected from the group consisting of Li^+ , Na^+ , and K^+ .

36. The method of Claim 30, wherein R^1 is selected from the group consisting of



37. The method of Claim 30, wherein R^1 is selected from the group consisting of
 $-\text{CONHCH}_2(\text{CH}_2)_n\text{CH}_3$, $-\text{CON}(\text{CH}_3)_2$, $-\text{CON}(\text{C}_2\text{H}_5)_2$, $-\text{CON}(\text{CH}(\text{CH}_3)_2)_2$, $-\text{CONNH}_2$
 CH_3



wherein n is 1, 2, 3, or 4.

38. The method of Claim 30, wherein R^1 is $-\text{S}(=\text{O})_2\text{NH}_2$.

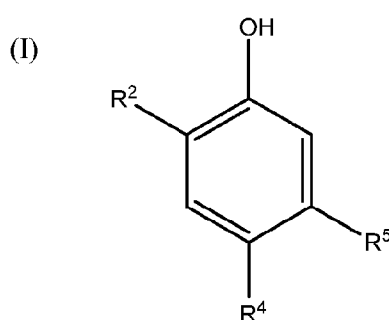
39. The method of any one of the previous claims wherein:

alkyl is selected from the group consisting of methyl, ethyl, propyl, isopropyl, butyl, isobutyl, *tert*-butyl, *sec*-butyl, pentanyl, isopentanyl, and neopentanyl;

haloalkyl is selected from the group consisting of fluoromethyl, 1-fluoroethyl, 2-fluoroethyl, 1-fluoropropyl, 2-fluoropropyl, 3-fluoropropyl, chloromethyl, 1-chloroethyl, 2-chloroethyl, 1-chloropropyl, 2-chloropropyl, 3-chloropropyl, bromomethyl, 1-bromoethyl, 2-bromoethyl, 1-bromopropyl, 2-bromopropyl, and 3-bromopropyl; and

cycloalkyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

40. A method of treating a neurological or an inflammatory condition comprising administering a therapeutically effective amount of a compound or pharmaceutically acceptable salt of the compound, wherein the compound has a structure of Formula (I):



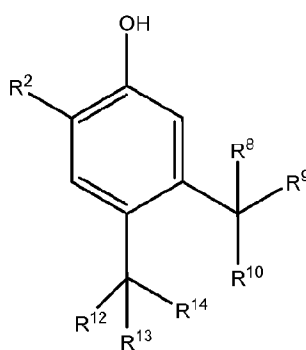
wherein:

- R² is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl, wherein the alkyl or haloalkyl is optionally substituted with one or more cycloalkyl substituents;
- R⁴ is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl, wherein the alkyl or haloalkyl is optionally substituted with one or more cycloalkyl substituents, and wherein R⁴ is not methyl; and
- R⁵ is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl.
41. The method of Claim 40 wherein each of R², R⁴, and R⁵ has between one and five carbons.
42. The method of Claim 41 wherein the condition is epilepsy, seizures, or convulsions.
43. The method of Claim 40 wherein the condition is neuropathic pain or fibromyalgia.
44. The method of Claim 40 wherein the condition is a psychological disorder.
45. The method of Claim 44 wherein the psychological disorder is anxiety, mania, bipolar disorder, or depression.

46. The method of Claim 40, wherein the condition is Alzheimer's Disease, Huntington's Disease, Multiple Sclerosis, Parkinson's disease, Tourette's Syndrome, tinnitus, and tremors.

47. The method of Claim 40, wherein the compound has a structure of Formula (II):

(II)



wherein:

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

R^8 and R^9 form a cycloalkyl of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 carbons or R^8 and

R^9 are each independently selected from the group consisting of H, alkyl, and haloalkyl;

R^{10} is selected from the group consisting of H, alkyl, and haloalkyl;

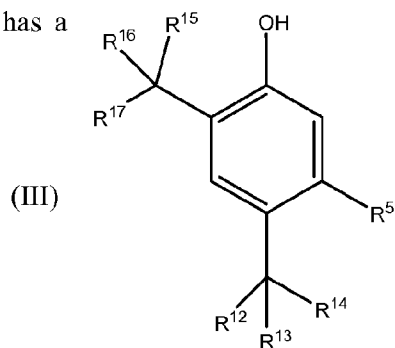
R^{12} and R^{13} form a cycloalkyl of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 carbons or R^{12} and R^{13} are each independently selected from the group consisting of H, alkyl, and haloalkyl; and

R^{14} is selected from the group consisting of H, alkyl, and haloalkyl.

48. The method of Claim 47, wherein halo is chloro, bromo, or fluoro.

49. The method of Claim 48, wherein the halo is fluoro.

50. The method of Claim 40, wherein the compound has a structure of Formula (III):



wherein:

R^5 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

R^{12} and R^{13} form a cycloalkyl of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 carbons or R^{12} and R^{13} are each independently selected from the group consisting of H, alkyl, and haloalkyl; and

5 R^{14} is selected from the group consisting of H, alkyl, and haloalkyl;

R^{15} and R^{16} form a cycloalkyl of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 carbons or R^{15} and R^{16} are each independently selected from the group consisting of H, alkyl, and haloalkyl; and

R^{17} is selected from the group consisting of H, alkyl, and haloalkyl.

10 51. The method of Claim 50, wherein halo is chloro, bromo, or fluoro.

52. The method of Claim 51, wherein the halo is fluoro.

53. The method of Claim 47, wherein:

15 R^{12} and R^{13} form a cycloalkyl moiety; and

R^{14} is selected from the group consisting of alkyl and haloalkyl.

54. The method of Claim 50, wherein:

R^{12} and R^{13} form a cycloalkyl moiety;

20 R^{15} and R^{16} form a cycloalkyl moiety; and

R^{14} and R^{17} are each independently selected from the group consisting of alkyl and haloalkyl.

55. The method of Claim 42, wherein:

R^5 is selected from the group consisting of methyl and isopropyl;

25 R^{12} is selected from the group consisting of H, halo, methyl, and cycloalkyl comprising R^{13} ;

R^{13} is selected from the group consisting of H, halo, methyl, trihalomethyl, and cycloalkyl comprising R^{12} ;

R^{14} is selected from the group consisting of halo, methyl, trihalomethyl and pentahaloethyl;

R^{15} is selected from the group consisting of H, methyl, and trihalomethyl.

30 R^{16} is selected from the group consisting of H and cycloalkyl comprising R^{17} ; and

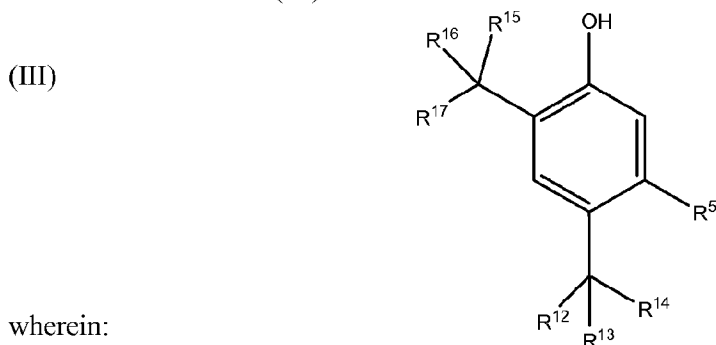
R^{17} is selected from the group consisting of H, methyl, and cycloalkyl comprising R^{16} .

56. The method of Claim 55 wherein the halo is chloro, bromo, or fluoro.

57. The method of Claim 56, wherein the halo is fluoro.

58. The method of Claim 57, wherein the compound is selected from the group consisting of: 5-isopropyl-2-methyl-4-trifluoromethyl-phenol; 2,5-diisopropyl-4-trifluoromethyl-phenol; 4-(1,1-difluoroethyl)-2-isopropyl-5-methyl-phenol; 2-isopropyl-5-methyl-4-trifluoromethyl-phenol; 2-isopropyl-5-methyl-4-(1-methyl-cyclopropyl)-phenol; 2-isopropyl-5-methyl-4-(1-trifluoro-methyl-cyclopropyl)-phenol; 2-isopropyl-5-methyl-4-(2,2,3,3,3-pentafluoro-propyl)-phenol; 2-isopropyl-5-methyl-4-pentafluoroethyl-phenol; 2-isopropyl-5-methyl-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol; 4-*tert*-butyl-5-methyl-2-(2,2,2-trifluoro-1-methyl-ethyl)-phenol; 4-*tert*-butyl-5-methyl-2-(1-methyl-cyclopropyl)-phenol; and 4-*tert*-butyl-5-methyl-2-(1-trifluoro-methyl-cyclopropyl)-phenol.

59. A compound or pharmaceutically acceptable salt of the compound, wherein the compound has a structure of Formula (III):



wherein:

R⁵ is selected from the group consisting of methyl and isopropyl;

R¹² is selected from the group consisting of H, halo, methyl, and cycloalkyl comprising R¹³;

R¹³ is selected from the group consisting of H, halo, methyl, trihalomethyl, and cycloalkyl comprising R¹²;

R¹⁴ is selected from the group consisting of halo, methyl, trihalomethyl and pentahaloethyl;

R¹⁵ is selected from the group consisting of H, methyl, and trihalomethyl.

R¹⁶ is selected from the group consisting of H and cycloalkyl comprising R¹⁷; and

R¹⁷ is selected from the group consisting of H, methyl, and cycloalkyl comprising R¹⁶.

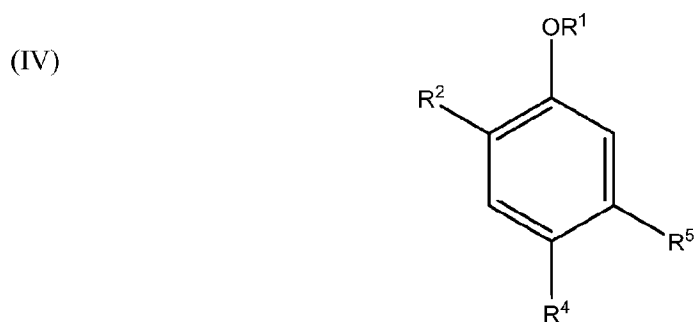
60. A compound or pharmaceutically acceptable salt of the compound, wherein the compound is selected from the group consisting of the species of Table 1, except 4-*tert*-butyl-5-ethyl-2-methyl-phenol.

5 61. The compound or pharmaceutically acceptable salt of Claim 60, wherein the compound is selected from the group consisting of 5-isopropyl-2-methyl-4-trifluoromethyl-phenol; 2,5-diisopropyl-4-trifluoromethyl-phenol; 4-(1,1-difluoroethyl)-2-isopropyl-5-methyl-phenol; 2-isopropyl-5-methyl-4-trifluoromethyl-phenol; 2-isopropyl-5-methyl-4-(1-methyl-cyclopropyl)-phenol; 2-isopropyl-5-methyl-4-(1-trifluoro-methyl-cyclopropyl)-phenol; 2-isopropyl-5-methyl-4-
10 (2,2,3,3,3-pentafluoro-propyl)-phenol; 2-isopropyl-5-methyl-4-pentafluoroethyl-phenol; 2-isopropyl-5-methyl-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol; 4-*tert*-butyl-5-methyl-2-(2,2,2-trifluoro-1-methyl-ethyl)-phenol; 4-*tert*-butyl-5-methyl-2-(1-methyl-cyclopropyl)-phenol; and 4-*tert*-butyl-5-methyl-2-(1-trifluoro-methyl-cyclopropyl)-phenol.

15 62. The method of any one of Claims 40–58, wherein the compound is deuterated.

63. The compound or pharmaceutically acceptable salt of any one of Claims 59–61, wherein the compound is deuterated.

20 64. A method of treating a neurological or an inflammatory condition comprising administering a therapeutically effective amount of a compound or pharmaceutically acceptable salt of the compound, wherein the compound has a structure of Formula (IV):



30 wherein:

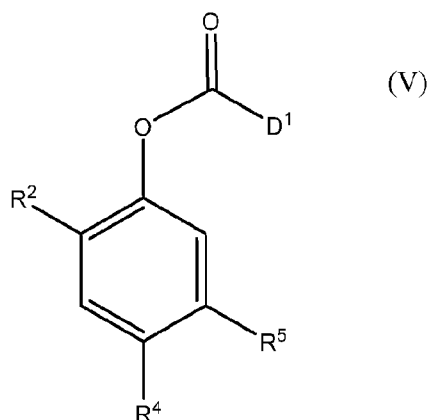
R¹ is selected from the group consisting of an ester, a carbonate, a phosphate, a carbamate, a sulfamate, and an acylmethylester;

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl, wherein the alkyl or haloalkyl is optionally substituted with one or more cycloalkyl substituents;

R^4 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl, wherein the alkyl or haloalkyl is optionally substituted with one or more cycloalkyl substituents, and wherein R^4 is not methyl; and

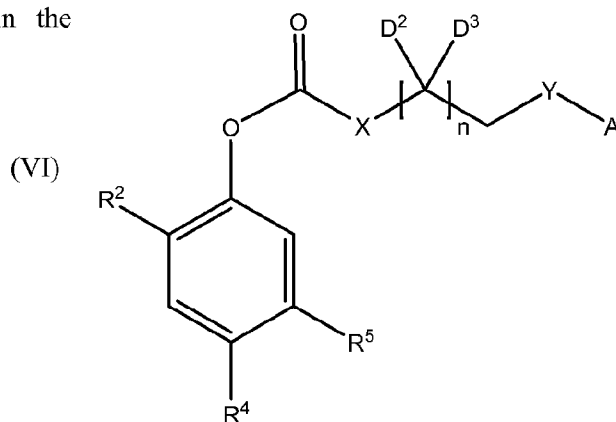
R^5 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl.

65. The method of Claim 64, wherein the compound has a structure of Formula (V):



wherein D^1 is alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroalkyl, heteroaryl, heteroaralkyl, carbonylalkyl, or phosphonooxyalkyl, optionally substituted with one or more substituents selected from the group consisting of alkyl, carboxylate, heteroalkyl, monocyclic ring, bicyclic ring, and hydroxyl moieties.

66. The method of Claim 65, wherein the compound has a structure of Formula (VI):



wherein:

D^2 and D^3 together with the carbon atom to which they are bonded form a cycloalkyl or cycloheteroalkyl ring, or alternatively D^2 and D^3 are each independently selected from the group consisting of hydrogen, alkyl, and heteroalkyl;

5 A, Y, and one of D^2 or D^3 together with the atoms to which they are bonded to form a cycloheteroalkyl ring, or alternatively A is selected from the group consisting of hydrogen, phosphono, alkyl, aryl, arylalkyl, heteroalkyl, heteroaryl, and heteroarylalkyl;

X is selected from the group consisting of $—ND^4—$, $—O—$, $—CH_2—$, and $—S—$;

Y is selected from the group consisting of $—O—$ and $—ND^4—$;

10 n is an integer from 1 to 5; and

D^4 is selected from the group consisting of hydrogen, alkyl, and arylalkyl.

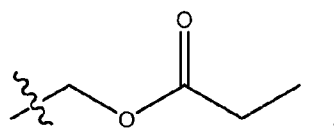
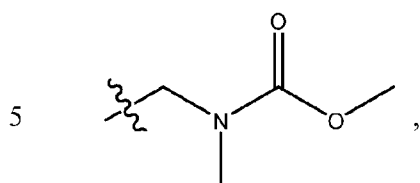
67. The method of Claim 66, wherein D^2 and D^3 are each hydrogen, X is $—CH_2—$, Y is $—O—$, A is phosphono, and $n=1$.

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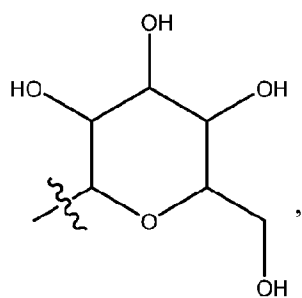
68. The method of Claim 64, wherein R^1 is selected from the group consisting of $—P(O)(OD^5)_2$, $—CH_2—O—P(O)(OD^5)_2$, $—(CH_2)_2—O—P(O)(OD^5)_2$, and $—\overset{CH_3}{\underset{|}{CH_2}}—O—P(O)(OD^5)_2$, and further wherein
20 D^5 is H or a pharmaceutically acceptable cation.

69. The method of Claim 68, wherein the pharmaceutically acceptable cation is selected from the group consisting of Li^+ , Na^+ , and K^+ .

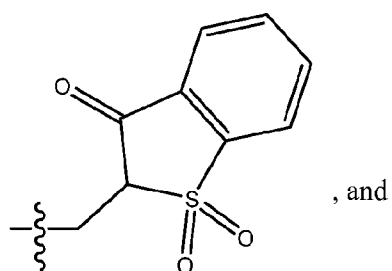
70. The method of Claim 64, wherein R¹ is selected from the group consisting of



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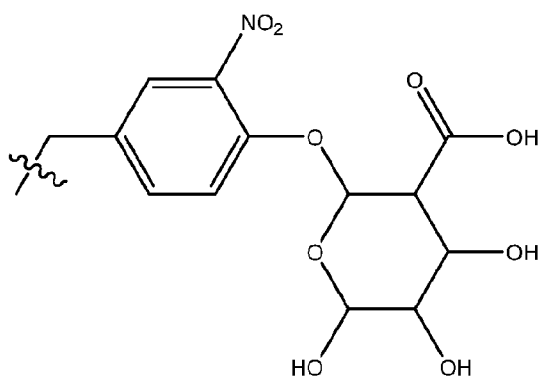
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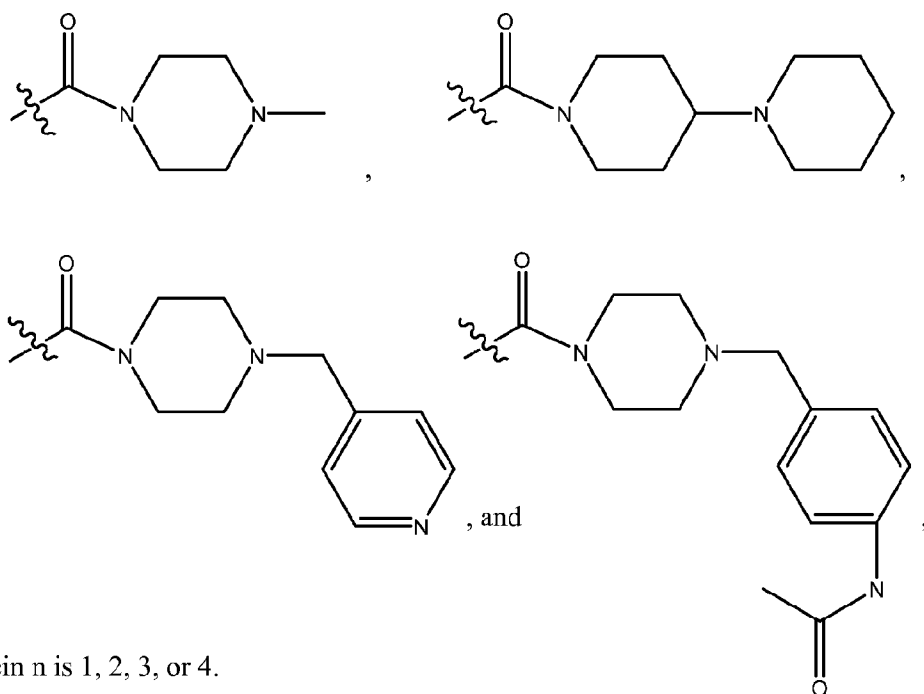
, and

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25



40. The method of Claim 64, wherein R^1 is selected from the group consisting of
 $-\text{CONHCH}_2(\text{CH}_2)_n\text{CH}_3$, $-\text{CON}(\text{CH}_3)_2$, $-\text{CON}(\text{C}_2\text{H}_5)_2$, $-\text{CON}(\text{CH}(\text{CH}_3)_2)_2$, $-\text{CONNH}_2$
 CH_3



wherein n is 1, 2, 3, or 4.

71. The method of Claim 64, wherein R^1 is $-\text{S}(=\text{O})_2\text{NH}_2$.

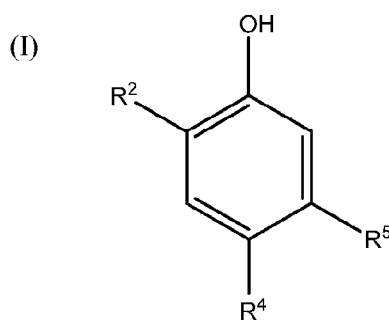
72. The method of any one of the previous claims wherein:

alkyl is selected from the group consisting of methyl, ethyl, propyl, isopropyl, butyl, isobutyl, *tert*-butyl, *sec*-butyl, pentanyl, isopentanyl, and neopentanyl;

haloalkyl is selected from the group consisting of fluoromethyl, 1-fluoroethyl, 2-fluoroethyl, 1-fluoropropyl, 2-fluoropropyl, 3-fluoropropyl, chloromethyl, 1-chloroethyl, 2-chloroethyl, 1-chloropropyl, 2-chloropropyl, 3-chloropropyl, bromomethyl, 1-bromoethyl, 2-bromoethyl, 1-bromopropyl, 2-bromopropyl, and 3-bromopropyl; and

cycloalkyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

73. A method of treating a neurological or an inflammatory condition comprising administering a therapeutically effective amount of a compound or pharmaceutically acceptable salt of the compound, wherein the compound has a structure of Formula (I):



wherein,

R² is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl, wherein the alkyl or haloalkyl is optionally substituted with one or more cycloalkyl substituents;

R⁴ is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl, wherein the alkyl or haloalkyl is optionally substituted with one or more cycloalkyl substituents, and wherein R⁴ is not methyl; and

R⁵ is selected from the group consisting of halo, and alkoxy, wherein the alkoxy may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl and halo.

74. The method of Claim 73 wherein each of R², R⁴, and R⁵ has between one and five carbons.

75. The method of Claim 73 wherein the condition is epilepsy, seizures, or convulsions.

76. The method of Claim 73 wherein the condition is neuropathic pain or fibromyalgia.

77. The method of Claim 73 wherein the condition is a psychological disorder.

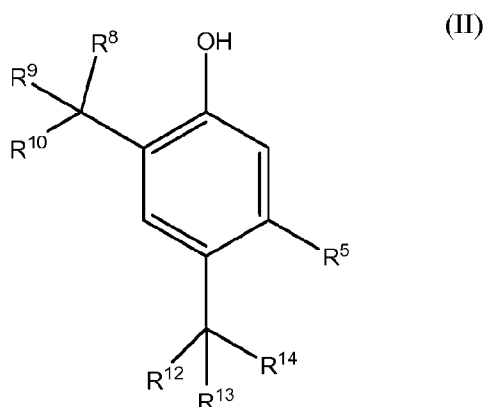
78. The method of Claim 77 wherein the psychological disorder is anxiety, mania, bipolar disorder, or depression.

79. The method of Claim 73, wherein the condition is Alzheimer's Disease, Huntington's Disease, Multiple Sclerosis, Parkinson's disease, Tourette's Syndrome, tinnitus, and tremors.

80. The method of Claim 74, wherein R^2 and R^4 are not identical.

5

81. The method of Claim 74, wherein the compound has a structure of Formula (II):



10

wherein,

15

R^5 is halo;

R^8 and R^9 form a cycloalkyl of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 carbons or R^8 and R^9 are each independently selected from the group consisting of H, alkyl, halo, and haloalkyl;

R^{10} is selected from the group consisting of H, alkyl, halo, and haloalkyl;

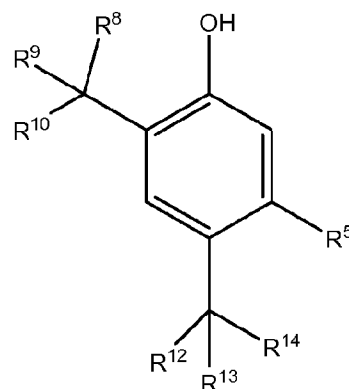
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R^{12} and R^{13} form a cycloalkyl of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 carbons or R^{12} and R^{13} are each independently selected from the group consisting of H, alkyl, halo, and haloalkyl; and

R^{14} is selected from the group consisting of H, alkyl, halo, and haloalkyl.

25

82. The method of Claim 80, wherein the compound has a structure of Formula (II)



30

wherein,

R^5 is halo;

R^8 and R^9 form a cycloalkyl of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 carbons or R^8 and R^9 are each independently selected from the group consisting of H, alkyl, halo, and haloalkyl;

5 R^{10} is selected from the group consisting of H, alkyl, halo, and haloalkyl;

R^{12} and R^{13} form a cycloalkyl of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 carbons or R^{12} and R^{13} are each independently selected from the group consisting of H, alkyl, halo, and haloalkyl; and

R^{14} is selected from the group consisting of H, alkyl, halo, and haloalkyl.

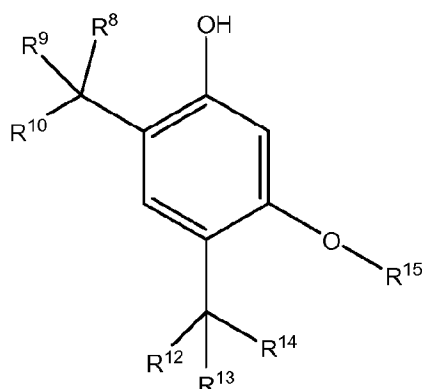
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83. The method of Claim 82, wherein halo is bromo, chloro, or fluoro.

84. The method of Claim 74, wherein the compound has a structure of Formula (III):

(III)

15



20

wherein,

R^{15} is selected from the group consisting of methyl, trihalomethyl, and isopropyl;

R^8 and R^9 form a cycloalkyl of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 carbons or R^8 and R^9 are each independently selected from the group consisting of H, alkyl, halo, and haloalkyl;

25

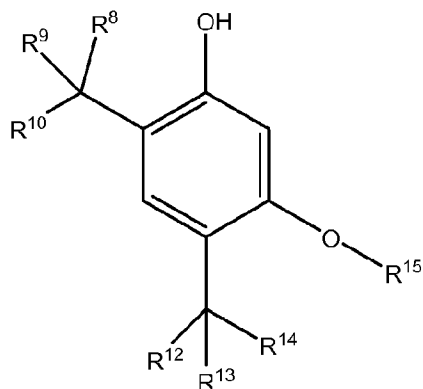
R^{10} is selected from the group consisting of H, alkyl, halo, and haloalkyl;

R^{12} and R^{13} form a cycloalkyl of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 carbons or R^{12} and R^{13} are each independently selected from the group consisting of H, alkyl, halo, and haloalkyl; and

R^{14} is selected from the group consisting of H, alkyl, halo, and haloalkyl.

30

85. The method of Claim 80, wherein the compound has a structure of Formula (III):



wherein,

R^{15} is selected from the group consisting of methyl, trihalomethyl, and isopropyl;

R^8 and R^9 form a cycloalkyl of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 carbons or R^8 and R^9 are each independently selected from the group consisting of H, alkyl, halo, and haloalkyl;

R^{10} is selected from the group consisting of H, alkyl, halo, and haloalkyl;

R^{12} and R^{13} form a cycloalkyl of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 carbons or R^{12} and R^{13} are each independently selected from the group consisting of H, alkyl, halo, and haloalkyl; and

R^{14} is selected from the group consisting of H, alkyl, halo, and haloalkyl.

86. The method of Claim 85, wherein halo is bromo, chloro, or fluoro.

87. The method of Claim 81, wherein:

R^{12} and R^{13} form a cycloalkyl moiety; and

R^{14} is selected from the group consisting of alkyl and haloalkyl.

88. The method of Claim 87, wherein:

R^9 and R^{10} form a cycloalkyl moiety; and

R^8 is selected from the group consisting of alkyl and haloalkyl.

89. The method of Claim 84, wherein:

R^{12} and R^{13} form a cycloalkyl moiety; and

R^{14} is selected from the group consisting of alkyl and haloalkyl.

90. The method of Claim 89, wherein:

R⁹ and R¹⁰ form a cycloalkyl moiety; and

R⁸ is selected from the group consisting of alkyl and haloalkyl

5 91. A compound or pharmaceutically acceptable salt of the compound, wherein the compound is selected from the group consisting of the species of Table 1.

92. The method of Claim 75, wherein the compound is selected from the group consisting of 5-bromo-4-tert-butyl-2-methyl-phenol, 5-bromo-4-tert-butyl-2-isopropyl-phenol, 4-tert-butyl-5-chloro-2-isopropyl-phenol, 4-tert-butyl-2-isopropyl-5-trifluoromethoxy-phenol, 5-bromo-2-(tert-butyl)-4-(1,1-difluoroethyl)phenol, 5-bromo-4-tert-butyl-2-cyclopropyl-phenol, 5-bromo-2-cyclopropyl-4-trifluoromethyl-phenol, 5-bromo-2-isopropyl-4-(1-trifluoromethyl-cyclopropyl)-phenol, 5-bromo-2-isopropyl-4-(1-methyl-cyclopropyl)-phenol, 5-bromo-2-isopropyl-4-(1-pentafluoroethyl-cyclopropyl)-phenol, 5-bromo-2-isopropyl-4-pentafluoroethyl-phenol, 5-bromo-2-isopropyl-4-(2,2,3,3,3-pentafluoro-propyl)-phenol, 5-bromo-2-isopropyl-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol, 5-fluoro-2,4-bis-(1-methyl-cyclopropyl)-phenol, 5-bromo-4-(1-methyl-cyclopropyl)-2-(1-trifluoromethyl-cyclopropyl)-phenol, 5-fluoro-4-(1-methyl-cyclopropyl)-2-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol, 2,4-bis-(1-methyl-cyclopropyl)-5-trifluoromethoxy-phenol, 2-[1-(2,2,2-Trifluoro-ethyl)-cyclopropyl]-5-trifluoromethoxy-4-(1-trifluoromethyl-cyclopropyl)-phenol, 2-Isopropyl-5-trifluoromethoxy-4-(1-trifluoromethyl-cyclopropyl)-phenol, and 2-cyclopropyl-5-methoxy-4-(1-trifluoromethyl-cyclopropyl)-phenol.

93. The compound or pharmaceutically acceptable salt of Claim 91, wherein the compound is selected from the group consisting of 5-bromo-4-tert-butyl-2-methyl-phenol, 5-bromo-4-tert-butyl-2-isopropyl-phenol, 4-tert-butyl-5-chloro-2-isopropyl-phenol, 4-tert-butyl-2-isopropyl-5-trifluoromethoxy-phenol, 5-bromo-2-(tert-butyl)-4-(1,1-difluoroethyl)phenol, 5-bromo-4-tert-butyl-2-cyclopropyl-phenol, 5-bromo-2-cyclopropyl-4-trifluoromethyl-phenol, 5-bromo-2-isopropyl-4-(1-trifluoromethyl-cyclopropyl)-phenol, 5-bromo-2-isopropyl-4-(1-methyl-cyclopropyl)-phenol, 5-bromo-2-isopropyl-4-(1-pentafluoroethyl-cyclopropyl)-phenol, 5-bromo-2-isopropyl-4-pentafluoroethyl-phenol, 5-bromo-2-isopropyl-4-(2,2,3,3,3-pentafluoro-propyl)-phenol, 5-bromo-2-isopropyl-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol, 5-fluoro-2,4-bis-(1-methyl-cyclopropyl)-phenol, 5-bromo-4-(1-methyl-cyclopropyl)-2-(1-trifluoromethyl-cyclopropyl)-phenol, 5-fluoro-4-(1-methyl-

cyclopropyl)-2-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol, 2,4-bis-(1-methyl-cyclopropyl)-5-trifluoromethoxy-phenol, 2-[1-(2,2,2-Trifluoro-ethyl)-cyclopropyl]-5-trifluoromethoxy-4-(1-trifluoromethyl-cyclopropyl)-phenol, 2-Isopropyl-5-trifluoromethoxy-4-(1-trifluoromethyl-cyclopropyl)-phenol, and 2-cyclopropyl-5-methoxy-4-(1-trifluoromethyl-cyclopropyl)-phenol.

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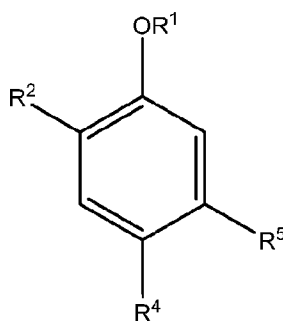
94. The method of any one of Claims 73–90 or 92 wherein the compound is deuterated.

95. The compound or pharmaceutically acceptable salt of Claim 91 or 93, wherein the compound is deuterated.

10

96. A method of treating a neurological or an inflammatory condition comprising administering a therapeutically effective amount of a compound or pharmaceutically acceptable salt of the compound, wherein the compound has a structure of Formula (IV):

15 (IV)



20

wherein:

R^1 is selected from the group consisting of an ester, a carbonate, a phosphate, a carbamate, a sulfamate, and an acylmethylester;

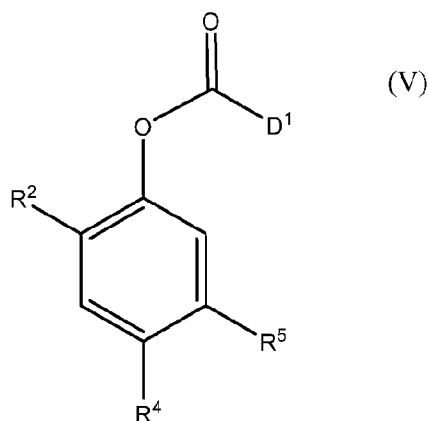
R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl, wherein the alkyl or haloalkyl is optionally substituted with one or more cycloalkyl substituents;

R^4 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl, wherein the alkyl or haloalkyl is optionally substituted with one or more cycloalkyl substituents, and wherein R^4 is not methyl; and

R^5 is selected from the group consisting of halo, and alkoxy, wherein the alkoxy may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl and halo.

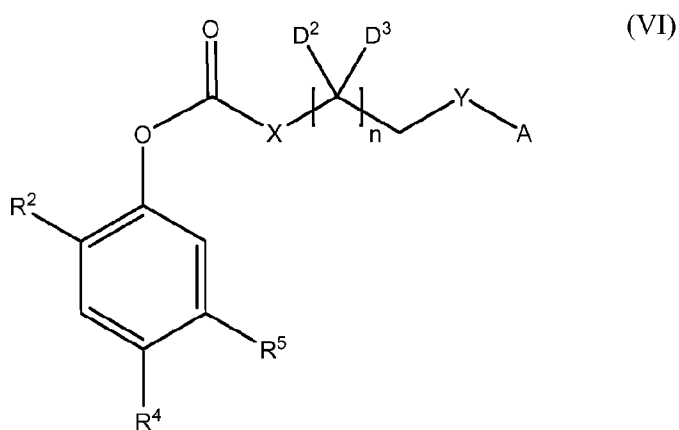
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97. The method of Claim 96, wherein the compound has a structure of Formula (V):



wherein D^1 is alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroalkyl, heteroaryl, heteroaralkyl, carbonylalkyl, or phosphonooxyalkyl, optionally substituted with one or more substituents selected from the group consisting of alkyl, carboxylate, heteroalkyl, monocyclic ring, bicyclic ring, and hydroxyl moieties.

98. The method of Claim 97, wherein the compound has a structure of Formula (VI):



wherein:

D^2 and D^3 together with the carbon atom to which they are bonded form a cycloalkyl or cycloheteroalkyl ring, or alternatively D^2 and D^3 are each independently selected from the group consisting of hydrogen, alkyl, and heteroalkyl;

A, Y, and one of D² or D³ together with the atoms to which they are bonded to form a cycloheteroalkyl ring, or alternatively A is selected from the group consisting of hydrogen, phosphono, alkyl, aryl, arylalkyl, heteroalkyl, heteroaryl, and heteroarylalkyl;

X is selected from the group consisting of —ND⁴—, —O—, —CH₂—, and —S—;

5 Y is selected from the group consisting of —O— and —ND⁴—;

n is an integer from 1 to 5; and

D⁴ is selected from the group consisting of hydrogen, alkyl, and arylalkyl.

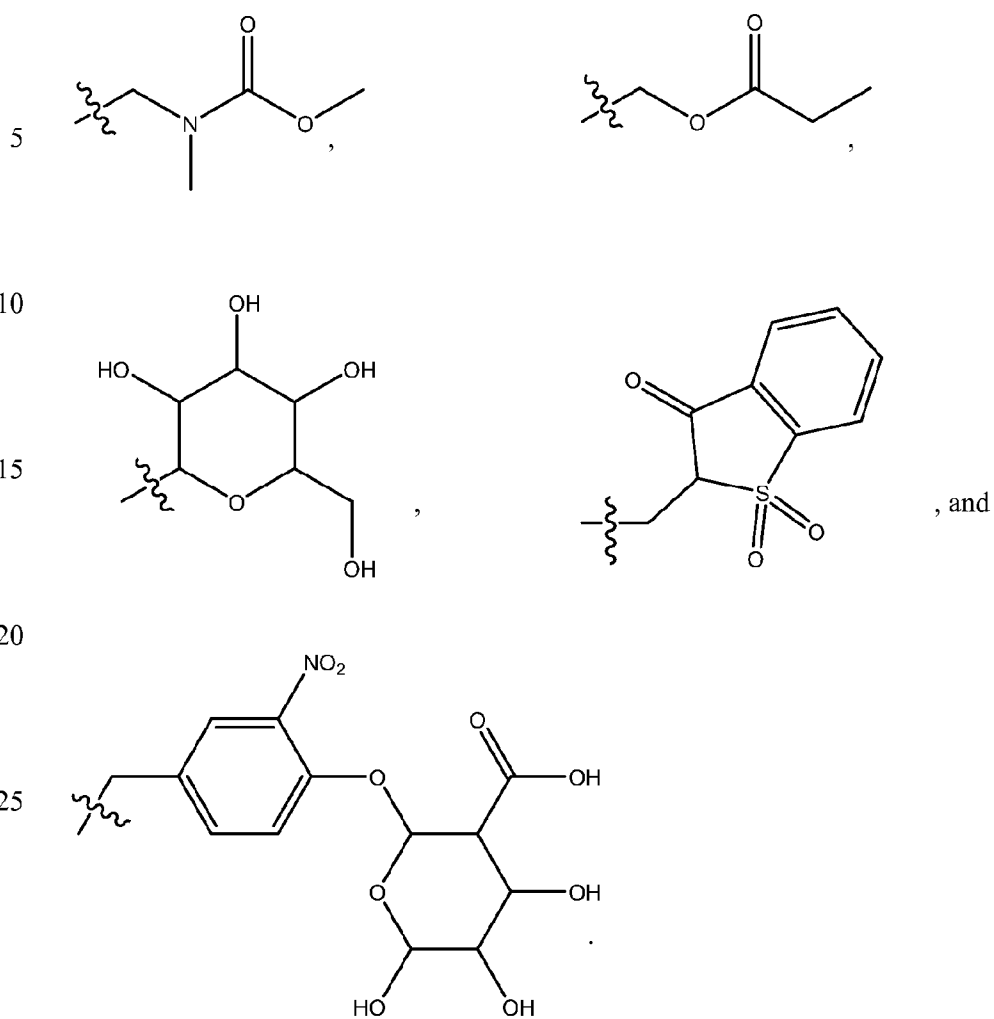
99. The method of Claim 98, wherein D² and D³ are each hydrogen, X is —CH₂—, Y is —O—, A
10 is phosphono, and n=1.

100. The method of Claim 96, wherein R¹ is selected from the group consisting of —P—(O)(OD⁵)₂,
—CH₂—O—P—(O)(OD⁵)₂, —(CH₂)₂—O—P—(O)(OD⁵)₂, and $\overset{\text{CH}_3}{\underset{|}{\text{—CH}_2\text{—O—P—(O)(OD}^5\text{)}_2}}$, and further wherein
15 D⁵ is H or a pharmaceutically acceptable cation.

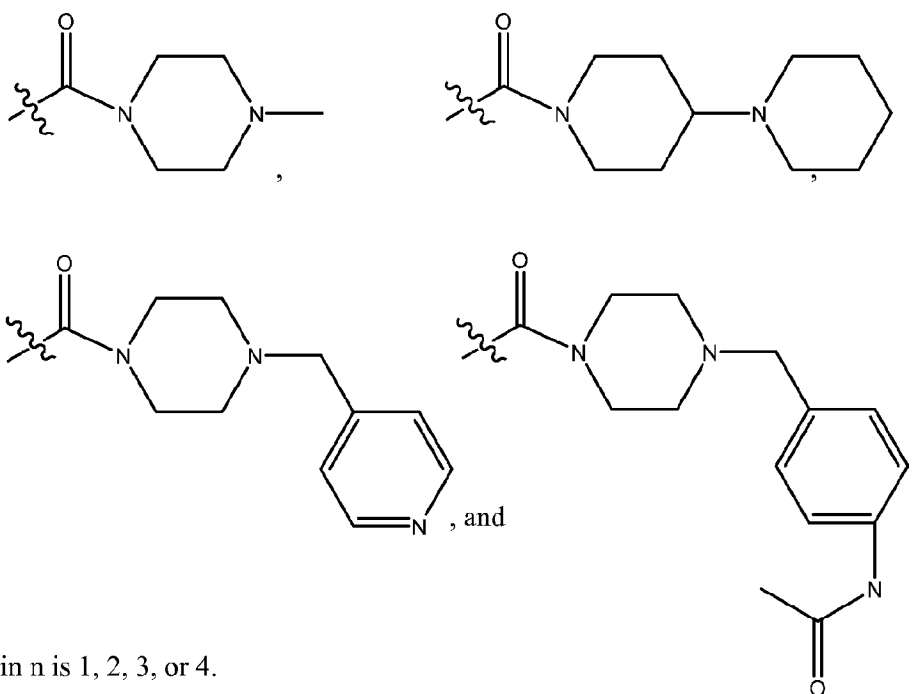
101. The method of Claim 100, wherein the pharmaceutically acceptable cation is selected from the group consisting of Li⁺, Na⁺, and K⁺.

20

102. The method of Claim 96, wherein R¹ is selected from the group consisting of



103. The method of Claim 96, wherein R^1 is selected from the group consisting of
 $-\text{CONHCH}_2(\text{CH}_2)_n\text{CH}_3$, $-\text{CON}(\text{CH}_3)_2$, $-\text{CON}(\text{C}_2\text{H}_5)_2$, $-\text{CON}(\text{CH}(\text{CH}_3)_2)_2$, $-\text{CONNH}_2$
 CH_3



wherein n is 1, 2, 3, or 4.

104. The method of Claim 24, wherein R^1 is $-\text{S}(=\text{O})_2\text{NH}_2$.

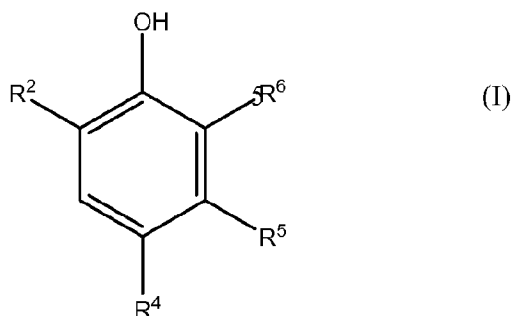
105. The method of any one of the previous claims wherein:

alkyl is selected from the group consisting of methyl, ethyl, propyl, isopropyl, butyl, isobutyl, *tert*-butyl, *sec*-butyl, pentanyl, isopentanyl, and neopentanyl;

haloalkyl is selected from the group consisting of fluoromethyl, 1-fluoroethyl, 2-fluoroethyl, 1-fluoropropyl, 2-fluoropropyl, 3-fluoropropyl, chloromethyl, 1-chloroethyl, 2-chloroethyl, 1-chloropropyl, 2-chloropropyl, 3-chloropropyl, bromomethyl, 1-bromoethyl, 2-bromoethyl, 1-bromopropyl, 2-bromopropyl, and 3-bromopropyl; and

cycloalkyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

106. A method of treating a neurological or an inflammatory condition comprising administering a therapeutically effective amount of a compound or pharmaceutically acceptable salt of the compound, wherein the compound has a structure of Formula (I):



10 wherein:

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl, wherein the alkyl or haloalkyl is optionally substituted with one or more cycloalkyl substituents;

R^4 is selected from the group consisting of H, halo, alkyl, alkoxy, haloalkyl, haloalkoxy and cycloalkyl, wherein alkyl or haloalkyl is optionally substituted with one or more cycloalkyl substituents, wherein alkoxy alkyl hydrogens may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl and halo, and wherein R^4 is not methyl;

15

R^5 is selected from the group consisting of alkyl, haloalkyl, cycloalkyl, halo, and alkoxy, wherein the alkoxy may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl and haloalkyl; and

20

R^6 is halo.

107. The method of Claim 106, wherein each of R^2 , R^4 , and R^5 has between one and five carbons.

25 108. The method of Claim 106, wherein the condition is epilepsy, seizures, or convulsions.

109. The method of Claim 106, wherein the condition is neuropathic pain or fibromyalgia.

110. The method of Claim 106, wherein the condition is a psychological disorder.

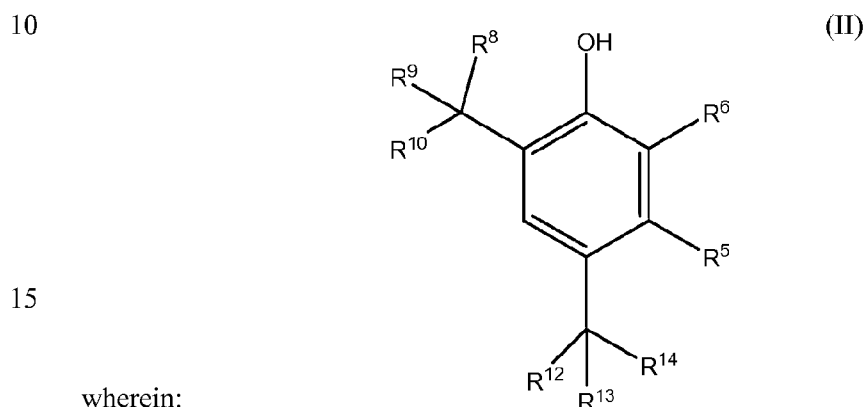
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111. The method of Claim 110, wherein the psychological disorder is anxiety, mania, bipolar disorder, or depression.

112. The method of Claim 106, wherein the condition is Alzheimer's Disease, Huntington's Disease, Multiple Sclerosis, Parkinson's disease, Tourette's Syndrome, tinnitus, and tremors.

113. The method of Claim 107, wherein R^2 and R^4 are not identical.

114. The method of Claim 107, wherein the compound has a structure of Formula (II):



wherein:

R^5 is halo;

R^6 is halo;

20 R^8 , R^9 , and R^{10} are each independently selected from the group consisting of H, alkyl, halo, haloalkyl, cycloalkyl comprising R^8 and R^9 , and cycloalkyl comprising R^9 and R^{10} ; and

R^{12} , R^{13} , and R^{14} are each independently selected from the group consisting of H, alkyl, halo, haloalkyl, cycloalkyl comprising R^{12} and R^{13} , and cycloalkyl comprising R^{13} and R^{14} .

25 115. The method of Claim 113, wherein the compound has a structure of Formula (II), wherein:

R^5 is halo;

R^6 is halo;

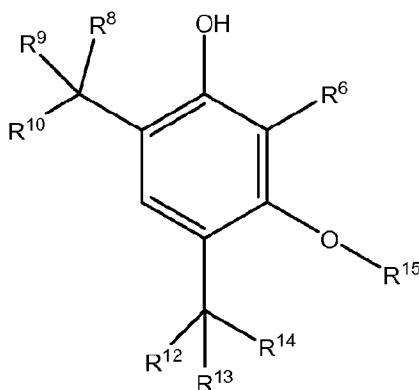
R^8 , R^9 , and R^{10} are each independently selected from the group consisting of H, alkyl, halo, haloalkyl, cycloalkyl comprising R^8 and R^9 , and cycloalkyl comprising R^9 and R^{10} ; and

30 R^{12} , R^{13} , and R^{14} are each independently selected from the group consisting of H, alkyl, halo, haloalkyl, cycloalkyl comprising R^{12} and R^{13} , and cycloalkyl comprising R^{13} and R^{14} .

116. The method of Claim 114, wherein halo is Br, Cl, or F.

117. The method of Claim 107, wherein the compound has a structure of Formula (III):

5 (III)



10

wherein:

R⁶ is halo;

15 R⁸, R⁹, and R¹⁰ are each independently selected from the group consisting of H, alkyl, halo, haloalkyl, cycloalkyl comprising R⁸ and R⁹, and cycloalkyl comprising R⁹ and R¹⁰;

R¹², R¹³, and R¹⁴ are each independently selected from the group consisting of H, alkyl, halo, haloalkyl, cycloalkyl comprising R¹² and R¹³, and cycloalkyl comprising R¹³ and R¹⁴; and

R¹⁵ is selected from the group consisting of methyl, trihalomethyl, and isopropyl.

20 118. The method of Claim 113, wherein the compound has a structure of Formula (III) and wherein:

R¹⁵ is selected from the group consisting of methyl, trihalomethyl, and isopropyl;

R⁸, R⁹, and R¹⁰ are each independently selected from the group consisting of H, alkyl, halo, haloalkyl, cycloalkyl comprising R⁸ and R⁹, and cycloalkyl comprising R⁹ and R¹⁰; and

25 R¹², R¹³, and R¹⁴ are each independently selected from the group consisting of H, alkyl, halo, haloalkyl, cycloalkyl comprising R¹² and R¹³, and cycloalkyl comprising R¹³ and R¹⁴.

119. The method of Claim 117, wherein halo is bromo, chloro, or fluoro.

30 120. The method of Claim 114, wherein:

R¹² and R¹³ form a cycloalkyl moiety; and

R¹⁴ is selected from the group consisting of alkyl and haloalkyl.

121. The method of Claim 120, wherein:

R^9 and R^{10} form a cycloalkyl moiety; and

R^8 is selected from the group consisting of alkyl and haloalkyl.

5 122. The method of Claim 117, wherein:

R^{12} and R^{13} form a cycloalkyl moiety; and

R^{14} is selected from the group consisting of alkyl and haloalkyl.

123. The method of Claim 122, wherein:

10 R^9 and R^{10} form a cycloalkyl moiety; and

R^8 is selected from the group consisting of alkyl and haloalkyl.

124. The method of Claim 108, wherein the compound is selected from the group consisting of the species of Table 1.

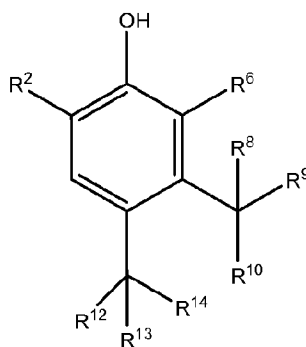
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125. A compound or pharmaceutically acceptable salt of the compound, wherein the compound is selected from the group consisting of the species of Table 1.

126. The method of Claim 106, wherein the compound has a structure of Formula (IV):

20

(IV)



25

wherein:

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

R^6 is halo;

30 R^8 , R^9 , and R^{10} are each independently selected from the group consisting of H, alkyl, haloalkyl, cycloalkyl comprising R^8 and R^9 , and cycloalkyl comprising R^9 and R^{10} ; and

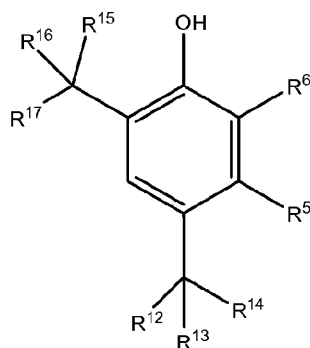
R^{12} , R^{13} , and R^{14} are each independently selected from the group consisting of H, alkyl, haloalkyl, cycloalkyl comprising R^{12} and R^{13} , and cycloalkyl comprising R^{13} and R^{14} .

127. The method of Claim 126, wherein halo is chloro, bromo, or fluoro.

128. The method of Claim 127, wherein the halo is fluoro.

129. The method of Claim 106, wherein the compound has a structure of Formula (V):

(V)



wherein:

R^5 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

R^6 is halo;

R^{12} and R^{13} form a cycloalkyl of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 carbons or R^{12}

and R^{13} are each independently selected from the group consisting of H, alkyl, and haloalkyl;

R^{14} is selected from the group consisting of H, alkyl, and haloalkyl;

R^{15} and R^{16} form a cycloalkyl of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 carbons or R^{15}

and R^{16} are each independently selected from the group consisting of H, alkyl, and haloalkyl; and

R^{17} is selected from the group consisting of H, alkyl, and haloalkyl.

130. The method of Claim 129, wherein halo is chloro, bromo, or fluoro.

131. The method of Claim 130, wherein the halo is fluoro.

132. The method of Claim 126, wherein:

R^{12} and R^{13} form a cycloalkyl moiety; and

R¹⁴ is selected from the group consisting of alkyl and haloalkyl.

133. The method of Claim 129, wherein:

R¹² and R¹³ form a cycloalkyl moiety;

5 R¹⁵ and R¹⁶ form a cycloalkyl moiety; and

R¹⁴ and R¹⁷ are each independently selected from the group consisting of alkyl and haloalkyl.

134. The method of Claim 129, wherein the compound has a structure of Formula (V), and wherein:

10 R⁵ is selected from the group consisting of methyl and isopropyl;

R¹² is selected from the group consisting of H, halo, methyl, and cycloalkyl comprising R¹³;

R¹³ is selected from the group consisting of H, halo, methyl, trihalomethyl, and cycloalkyl comprising R¹²;

R¹⁴ is selected from the group consisting of halo, methyl, trihalomethyl and pentahaloethyl;

15 R¹⁵ is selected from the group consisting of H, methyl, and trihalomethyl.

R¹⁶ is selected from the group consisting of H and cycloalkyl comprising R¹⁷; and

R¹⁷ is selected from the group consisting of H, methyl, and cycloalkyl comprising R¹⁶.

135. The method of Claim 134, wherein the halo is chloro, bromo, or fluoro.

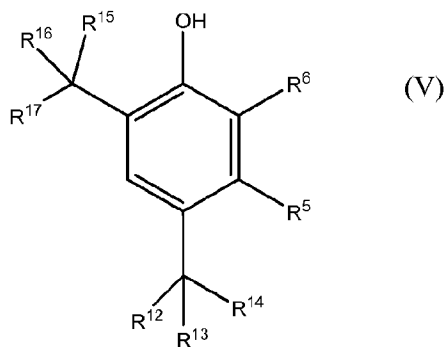
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136. The method of Claim 135, wherein the halo is fluoro.

137. The method of Claim 135, wherein the compound is selected from the group consisting of the species of Table 2.

25

138. A compound or pharmaceutically acceptable salt of the compound, wherein the compound has a structure of Formula (V)



wherein:

10 R^5 is selected from the group consisting of methyl and isopropyl;

R^{12} is selected from the group consisting of H, halo, methyl, and cycloalkyl comprising R^{13} ;

R^{13} is selected from the group consisting of H, halo, methyl, trihalomethyl, and cycloalkyl comprising R^{12} ;

R^{14} is selected from the group consisting of halo, methyl, trihalomethyl and pentahaloethyl;

15 R^{15} is selected from the group consisting of H, methyl, and trihalomethyl.

R^{16} is selected from the group consisting of H and cycloalkyl comprising R^{17} ; and

R^{17} is selected from the group consisting of H, methyl, and cycloalkyl comprising R^{16} .

139. The compound or pharmaceutically acceptable salt of Claim 138, wherein the compound is
20 selected from the group consisting of the species of Table 2.

140. The method of Claim 106, wherein:

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl; and

R^4 is halo.

141. The method of Claim 140, wherein:

R^4 is selected from the group consisting of Br, Cl, and F.

142. The method of Claim 141, wherein:

30 R^2 is alkyl; and

R^5 is alkyl having two or more carbons.

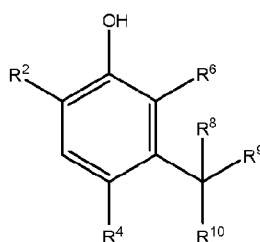
143. The method of Claim 142, wherein the compound is selected from the group consisting of 4-bromo-2-fluoro-3-isopropyl-6-methyl-phenol, 4-chloro-2-fluoro-3-isopropyl-6-methyl-phenol, 2,4-difluoro-3-isopropyl-6-methyl-phenol, 4-bromo-2-fluoro-3-isopropyl-6-trifluoromethyl-phenol, 4-bromo-2-fluoro-6-trifluoromethyl-3-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 4-bromo-6-cyclopropyl-2-fluoro-3-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 4-bromo-3-cyclopropyl-2-fluoro-6-methyl-phenol, 4-bromo-3-cyclopropyl-2-fluoro-6-trifluoromethyl-phenol, 4-bromo-3,6-dicyclopropyl-2-fluoro-phenol, 4-bromo-2-chloro-3-isopropyl-6-methyl-phenol, 2-fluoro-3-isopropyl-6-methyl-4-trifluoromethoxy-phenol, 2-bromo-3-isopropyl-6-methyl-4-trifluoro-methoxy-phenol, 2-chloro-3-isopropyl-6-methyl-4-trifluoromethoxy-phenol, 4-tert-butoxy-2-fluoro-3-isopropyl-6-methyl-phenol, 2-bromo-4-tert-butoxy-3-isopropyl-6-methyl-phenol, 4-bromo-3-(2,2-difluoro-1-methyl-ethyl)-2-fluoro-6-isopropyl-phenol, 4-bromo-2-fluoro-6-iso-propyl-3-pentafluoroethyl-phenol, 4-bromo-2-fluoro-6-isopropyl-3-(2,2,2-trifluoro-ethyl)-phenol, 4-bromo-3-ethyl-2-fluoro-6-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol, 4-bromo-2-fluoro-6-isopropyl-3-(2,2,2-trifluoro-1-trifluoromethyl-ethyl)-phenol, 4-bromo-2-fluoro-6-iso-propyl-3-(2,2,3,3,3-pentafluoro-propyl)-phenol, 2-fluoro-6-isopropyl-3-(2,2,3,3,3-pentafluoro-propyl)-4-trifluoro-methoxy-phenol, 2-fluoro-4-isopropoxy-6-isopropyl-3-(2,2,2-trifluoro-ethyl)-phenol, 2-fluoro-6-isopropyl-4-methoxy-3-(2,2,2-trifluoro-ethyl)-phenol, 3-ethyl-2-fluoro-6-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-4-trifluoro methoxy-phenol, 2-fluoro-6-isopropyl-4-methoxy-3-(2,2,2-trifluoro-ethyl)-phenol, 4-tert-butoxy-3-(2,2-difluoro-1-methyl-ethyl)-2-fluoro-6-isopropyl-phenol, 2-bromo-3-isopropyl-4-trifluoromethoxy-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 3-ethyl-2-fluoro-6-(2,2,2-trifluoro-ethyl)-4-trifluoro methoxy-phenol, 4-tert-butoxy-3-ethyl-2-fluoro-6-(2,2,2-trifluoro-ethyl)-phenol, and 3-ethyl-2-fluoro-4-isopropoxy-6-(2,2,2-trifluoro-ethyl)-phenol.

144. The method of Claim 108, wherein the compound is selected from the group consisting of 4-bromo-2-fluoro-3-isopropyl-6-methyl-phenol, 4-chloro-2-fluoro-3-isopropyl-6-methyl-phenol, 2,4-difluoro-3-isopropyl-6-methyl-phenol, 4-bromo-2-fluoro-3-isopropyl-6-trifluoromethyl-phenol, 4-bromo-2-fluoro-6-trifluoromethyl-3-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 4-bromo-6-cyclopropyl-2-fluoro-3-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 4-bromo-3-cyclopropyl-2-fluoro-6-methyl-phenol, 4-bromo-3,6-dicyclopropyl-2-fluoro-phenol, 2,4-dibromo-3-isopropyl-6-methyl-phenol, 4-bromo-2-chloro-3-isopropyl-6-methyl-phenol, 2,4-dichloro-3-isopropyl-6-methyl-phenol, 2,4-dibromo-3-isopropyl-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 4-bromo-3-(1,1-difluoroethyl)-

2-fluoro-6-isopropyl-phenol, 2-fluoro-6-isopropyl-3-(2,2,3,3,3-pentafluoro-propyl)-4-trifluoromethoxy-phenol, 2-fluoro-4-isopropoxy-6-isopropyl-3-(2,2,2-trifluoroethyl)-phenol, 2-fluoro-6-isopropyl-4-methoxy-3-(2,2,2-trifluoroethyl)-phenol, 4-tert-butoxy-3-ethyl-2-fluoro-6-(2,2,2-trifluoroethyl)-phenol, 2-fluoro-3-isopropyl-6-methyl-4-trifluoromethoxy-phenol, 2-bromo-3-isopropyl-6-methyl-4-trifluoromethoxy-phenol, and 2-chloro-3-isopropyl-6-methyl-4-trifluoromethoxy-phenol.

145. The method of Claim 106, wherein the compound has the structure of Formula (VI):

(VI)



wherein:

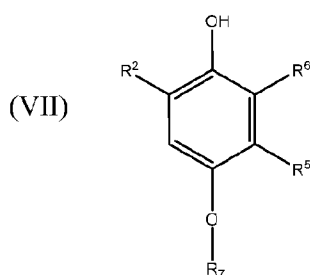
R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

R^4 is selected from the group consisting of Br, Cl, and F;

R^6 is halo; and

R^8 , R^9 and R^{10} are each independently selected from the group consisting of H, alkyl, and haloalkyl.

146. The method of Claim 106, wherein the compound has the structure of Formula (VII):



wherein:

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

R^5 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

R^6 is halo; and

R_7 is selected from the group consisting of alkyl and haloalkyl.

147. The method of Claim 145, wherein:

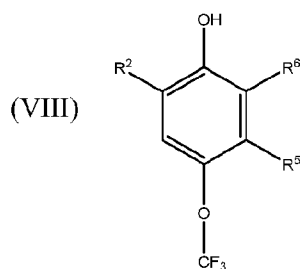
R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

R^5 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl; and

R_7 is alkyl.

5

148. The method of Claim 146, wherein the compound has the structure of Formula (VIII):



10

wherein:

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl; and

R^5 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl.

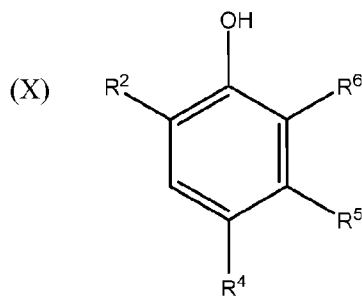
15 149. The method of Claim 148, wherein:

R^2 is selected from the group consisting of alkyl and cycloalkyl; and

R^5 is selected from the group consisting of alkyl and cycloalkyl.

150. A compound or pharmaceutically acceptable salt of the compound, wherein the compound has the structure of Formula (X):

20



25

wherein:

R^2 is selected from the group consisting of methyl, cycloalkyl, and $-CF_3$;

R^4 is halo;

R^5 is selected from the group consisting of fluoroalkyl and a three, four, or five carbon cycloalkyl;

30

R^6 is halo; and

R^4 and R^6 are not both Br or both Cl.

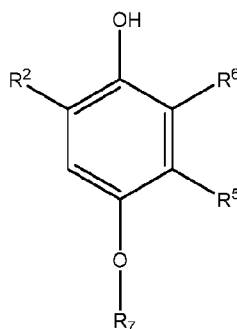
151. The compound or pharmaceutically acceptable salt of Claim 150, wherein:

R^4 is selected from the group consisting of Br, Cl, and F.

5

152. A compound or pharmaceutically acceptable salt of the compound, wherein the compound has the structure of Formula (XI):

10 (XI)



wherein:

15 R^2 and R^5 are each independently selected from the group consisting of alkyl and cycloalkyl, wherein at least one of R^2 and R^5 is cycloalkyl;

R^6 is halo; and

R^7 is selected from the group consisting of isopropyl, *tert*-butyl, and haloalkyl.

153. The compound or pharmaceutically acceptable salt of Claim 152, wherein:

20 R^7 is selected from the group consisting of isopropyl and *tert*-butyl.

154. The compound or pharmaceutically acceptable salt of Claim 152, wherein:

R^2 is selected from the group consisting of alkyl, and cycloalkyl;

R^5 is selected from the group consisting of alkyl, and cycloalkyl; and

25 R^7 is trifluoromethyl.

155. The method of Claim 109, wherein:

R^2 and R^5 are each independently selected from the group consisting of methyl, isopropyl, and *tert*-butyl; and

30 R^4 and R^6 are each independently selected from the group consisting of Br, Cl, and F.

156. The compound or pharmaceutically acceptable salt of Claim 151, wherein the compound is selected from the group consisting of 4-bromo-2-fluoro-3-isopropyl-6-methyl-phenol, 4-chloro-2-fluoro-3-isopropyl-6-methyl-phenol, 2,4-difluoro-3-isopropyl-6-methyl-phenol, 4-bromo-2-fluoro-3-isopropyl-6-trifluoromethyl-phenol, 4-bromo-2-fluoro-6-trifluoromethyl-3-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 4-bromo-6-cyclopropyl-2-fluoro-3-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 4-bromo-3-cyclopropyl-2-fluoro-6-methyl-phenol, 4-bromo-3-cyclopropyl-2-fluoro-6-trifluoromethyl-phenol, 4-bromo-3,6-dicyclopropyl-2-fluoro-phenol, 4-bromo-2-chloro-3-isopropyl-6-methyl-phenol, 2-fluoro-3-isopropyl-6-methyl-4-trifluoromethoxy-phenol, 2-bromo-3-isopropyl-6-methyl-4-trifluoromethoxy-phenol, 2-chloro-3-isopropyl-6-methyl-4-trifluoromethoxy-phenol, 4-tert-butoxy-2-fluoro-3-isopropyl-6-methyl-phenol, 2-bromo-4-tert-butoxy-3-isopropyl-6-methyl-phenol, 4-bromo-3-(2,2-difluoro-1-methyl-ethyl)-2-fluoro-6-isopropyl-phenol, 4-bromo-2-fluoro-6-isopropyl-3-pentafluoroethyl-phenol, 4-bromo-2-fluoro-6-isopropyl-3-(2,2,2-trifluoro-ethyl)-phenol, 4-bromo-3-ethyl-2-fluoro-6-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol, 4-bromo-2-fluoro-6-isopropyl-3-(2,2,2-trifluoro-1-trifluoromethyl-ethyl)-phenol, 4-bromo-2-fluoro-6-isopropyl-3-(2,2,3,3,3-pentafluoro-propyl)-phenol, 2-fluoro-6-isopropyl-3-(2,2,3,3,3-pentafluoro-propyl)-4-trifluoromethoxy-phenol, 2-fluoro-4-isopropoxy-6-isopropyl-3-(2,2,2-trifluoro-ethyl)-phenol, 2-fluoro-6-isopropyl-4-methoxy-3-(2,2,2-trifluoro-ethyl)-phenol, 3-ethyl-2-fluoro-6-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-4-trifluoromethoxy-phenol, 2-fluoro-6-isopropyl-4-methoxy-3-(2,2,2-trifluoro-ethyl)-phenol, 4-tert-butoxy-3-(2,2-difluoro-1-methyl-ethyl)-2-fluoro-6-isopropyl-phenol, 2-bromo-3-isopropyl-4-trifluoromethoxy-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 3-ethyl-2-fluoro-6-(2,2,2-trifluoro-ethyl)-4-trifluoromethoxy-phenol, 4-tert-butoxy-3-ethyl-2-fluoro-6-(2,2,2-trifluoro-ethyl)-phenol, and 3-ethyl-2-fluoro-4-isopropoxy-6-(2,2,2-trifluoro-ethyl)-phenol.

157. The compound or pharmaceutically acceptable salt of Claim 156, wherein the compound is selected from the group consisting of 4-bromo-2-fluoro-3-isopropyl-6-methyl-phenol, 4-chloro-2-fluoro-3-isopropyl-6-methyl-phenol, 2,4-difluoro-3-isopropyl-6-methyl-phenol, 4-bromo-2-fluoro-3-isopropyl-6-trifluoromethyl-phenol, 4-bromo-2-fluoro-6-trifluoromethyl-3-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 4-bromo-6-cyclopropyl-2-fluoro-3-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 4-bromo-3-cyclopropyl-2-fluoro-6-methyl-phenol, 4-bromo-3,6-dicyclopropyl-2-fluoro-phenol, 4-bromo-2-chloro-3-isopropyl-6-methyl-phenol, 2,4-dibromo-3-isopropyl-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 4-bromo-3-(1,1-difluoroethyl)-2-fluoro-6-isopropyl-phenol, 2-fluoro-6-isopropyl-3-(2,2,3,3,3-pentafluoro-propyl)-4-trifluoromethoxy-phenol, 2-fluoro-4-isopropoxy-6-isopropyl-3-

(2,2,2-trifluoroethyl)-phenol, 2-fluoro-6-isopropyl-4-methoxy-3-(2,2,2-trifluoroethyl)-phenol, 4-tert-butoxy-3-ethyl-2-fluoro-6-(2,2,2-trifluoro-ethyl)-phenol, 2-fluoro-3-isopropyl-6-methyl-4-trifluoro-methoxy-phenol, 2-bromo-3-isopropyl-6-methyl-4-trifluoromethoxy-phenol, and 2-chloro-3-isopropyl-6-methyl-4-trifluoromethoxy-phenol.

5

158. The method of Claim 108, wherein the compound is selected from the group consisting of 4-tert-butyl-2-fluoro-6-isopropyl-3-methyl-phenol, 4-tert-butyl-2-fluoro-6-isopropyl-3-trifluoromethyl-phenol, 2-fluoro-6-isopropyl-3-methyl-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol, 2-bromo-6-isopropyl-3-methyl-4-trifluoromethyl-phenol, 4-tert-butyl-6-cyclopropyl-2-fluoro-3-trifluoromethyl-phenol, 2-fluoro-6-isopropyl-3-methyl-4-(1-methyl-cyclopropyl)-phenol, 2-fluoro-6-isopropyl-3-methyl-4-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol, 2-fluoro-6-isopropyl-3-methyl-4-(1-pentafluoroethyl-cyclopropyl)-phenol, 2-fluoro-3-methyl-4-(2,2,3,3,3-pentafluoro-propyl)-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 2-fluoro-3-methyl-4-pentafluoroethyl-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 3-cyclopropyl-2-fluoro-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-6-(1-trifluoromethyl-cyclopropyl)-phenol, 2-fluoro-3-methyl-4,6-bis-(1-methyl-cyclopropyl)-phenol, 2-fluoro-3-methyl-4-(1-methyl-cyclopropyl)-6-(1-trifluoromethyl-cyclopropyl)-phenol, 2-fluoro-3-methyl-4,6-bis-(1-trifluoromethyl-cyclopropyl)-phenol, and 2-fluoro-3-methyl-6-(1-methyl-cyclopropyl)-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol.

159. The compound or pharmaceutically acceptable salt of Claim 139, wherein the compound is selected from the group consisting of 4-tert-butyl-2-fluoro-6-isopropyl-3-methyl-phenol, 4-tert-butyl-2-fluoro-6-isopropyl-3-trifluoromethyl-phenol, 2-fluoro-6-isopropyl-3-methyl-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol, 2-bromo-6-isopropyl-3-methyl-4-trifluoromethyl-phenol, 4-tert-butyl-6-cyclopropyl-2-fluoro-3-trifluoromethyl-phenol, 2-fluoro-6-isopropyl-3-methyl-4-(1-methyl-cyclopropyl)-phenol, 2-fluoro-6-isopropyl-3-methyl-4-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol, 2-fluoro-6-isopropyl-3-methyl-4-(1-pentafluoroethyl-cyclopropyl)-phenol, 2-fluoro-3-methyl-4-(2,2,3,3,3-pentafluoro-propyl)-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 2-fluoro-3-methyl-4-pentafluoroethyl-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 3-cyclopropyl-2-fluoro-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-6-(1-trifluoromethyl-cyclopropyl)-phenol, 2-fluoro-3-methyl-4,6-bis-(1-methyl-cyclopropyl)-phenol, 2-fluoro-3-methyl-4-(1-methyl-cyclopropyl)-6-(1-trifluoromethyl-cyclopropyl)-phenol, 2-fluoro-3-methyl-4,6-bis-(1-trifluoromethyl-cyclopropyl)-phenol, and 2-fluoro-3-methyl-6-(1-methyl-cyclopropyl)-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol.

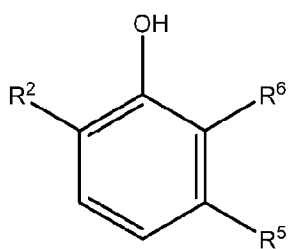
160. The method of Claim 108, wherein the compound is selected from the group consisting of 3-bromo-4-tert-butyl-2-fluoro-6-isopropyl-phenol, 4-tert-butyl-3-chloro-2-fluoro-6-isopropyl-phenol, 4-tert-butyl-2,3-difluoro-6-isopropyl-phenol, 3-bromo-6-cyclopropyl-2-fluoro-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol, 3-bromo-2-fluoro-6-isopropyl-4-trifluoromethyl-phenol, 3-bromo-2-fluoro-6-isopropyl-4-(1-methyl-cyclopropyl)-phenol, 3-bromo-2-fluoro-6-isopropyl-4-(1-trifluoromethyl-cyclopropyl)-phenol, 3-bromo-6-cyclopropyl-2-fluoro-4-(1-trifluoromethyl-cyclopropyl)-phenol, 4-tert-butyl-2-fluoro-6-isopropyl-3-trifluoromethoxy-phenol, 3-tert-butoxy-2-fluoro-6-isopropyl-4-trifluoromethyl-phenol, 2-fluoro-6-isopropyl-4-(1-methyl-cyclopropyl)-3-trifluoromethoxy-phenol, 3-bromo-2-fluoro-4-pentafluoroethyl-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 3-bromo-2-fluoro-4-pentafluoroethyl-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 3-bromo-2-fluoro-6-isopropyl-4-(2,2,3,3,3-pentafluoro-propyl)-phenol, 3-bromo-2-fluoro-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-6-(1-trifluoromethyl-cyclopropyl)-phenol, 3-bromo-2-fluoro-4-(1-methyl-cyclopropyl)-6-(1-trifluoromethyl-cyclopropyl)-phenol, 3-bromo-2-fluoro-6-(1-methyl-cyclopropyl)-4-(1-trifluoromethyl-cyclopropyl)-phenol, 3-bromo-2-fluoro-4,6-bis-(1-trifluoromethyl-cyclopropyl)-phenol, 3-bromo-2-fluoro-6-(1-methyl-cyclopropyl)-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol, and 3-bromo-2-fluoro-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-6-(1-trifluoromethyl-cyclopropyl)-phenol.

161. The compound or pharmaceutically acceptable salt of Claim 125, wherein the compound is selected from the group consisting of 3-bromo-4-tert-butyl-2-fluoro-6-isopropyl-phenol, 4-tert-butyl-3-chloro-2-fluoro-6-isopropyl-phenol, 4-tert-butyl-2,3-difluoro-6-isopropyl-phenol, 3-bromo-6-cyclopropyl-2-fluoro-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol, 3-bromo-2-fluoro-6-isopropyl-4-trifluoromethyl-phenol, 3-bromo-2-fluoro-6-isopropyl-4-(1-methyl-cyclopropyl)-phenol, 3-bromo-2-fluoro-6-isopropyl-4-(1-trifluoromethyl-cyclopropyl)-phenol, 3-bromo-6-cyclopropyl-2-fluoro-4-(1-trifluoromethyl-cyclopropyl)-phenol, 4-tert-butyl-2-fluoro-6-isopropyl-3-trifluoromethoxy-phenol, 3-tert-butoxy-2-fluoro-6-isopropyl-4-trifluoromethyl-phenol, 2-fluoro-6-isopropyl-4-(1-methyl-cyclopropyl)-3-trifluoromethoxy-phenol, 3-bromo-2-fluoro-4-pentafluoroethyl-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 3-bromo-2-fluoro-4-pentafluoroethyl-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 3-bromo-2-fluoro-6-isopropyl-4-(2,2,3,3,3-pentafluoro-propyl)-phenol, 3-bromo-2-fluoro-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-6-(1-trifluoromethyl-cyclopropyl)-phenol, 3-bromo-2-fluoro-4-(1-methyl-cyclopropyl)-6-(1-trifluoromethyl-cyclopropyl)-phenol, 3-bromo-2-fluoro-6-(1-methyl-cyclopropyl)-4-(1-trifluoromethyl-cyclopropyl)-phenol, 3-bromo-2-fluoro-4,6-bis-(1-trifluoromethyl-cyclopropyl)-phenol, 3-bromo-2-fluoro-6-(1-methyl-cyclopropyl)-4-(2,2,2-trifluoro-

1,1-dimethyl-ethyl)-phenol, and 3-bromo-2-fluoro-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-6-(1-trifluoromethyl-cyclopropyl)-phenol.

162. A compound or pharmaceutically acceptable salt of the compound, wherein the compound has the structure of Formula (IX):

(IX)



wherein:

R² is selected from the group consisting of haloalkyl and cycloalkyl;

R⁵ is selected from the group consisting of haloalkyl and cycloalkyl; and

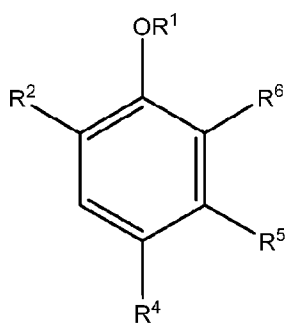
R⁶ is halo.

163. The method of any one of Claims 106–124, 126–137, 140–148, 155, 158, or 160, wherein the compound is deuterated.

164. The compound or pharmaceutically acceptable salt of any one of Claims 125, 138, 139, 149–154, or 156–161 wherein the compound is deuterated.

165. A method of treating a neurological or an inflammatory condition comprising administering a therapeutically effective amount of a compound or pharmaceutically acceptable salt of the compound, wherein the compound has a structure of Formula (XII):

(XII)



wherein:

R^1 is selected from the group consisting of an ester, a carbonate, a phosphate, a carbamate, a sulfamate, and an acylmethylester;

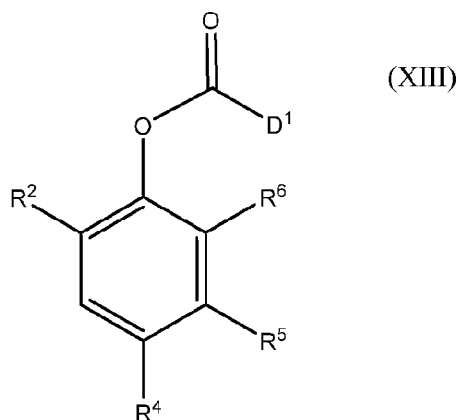
R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl, wherein the alkyl or haloalkyl is optionally substituted with one or more cycloalkyl substituents;

5 R^4 is selected from the group consisting of H, halo, alkyl, alkoxy, haloalkyl, haloalkoxy and cycloalkyl, wherein alkyl or haloalkyl is optionally substituted with one or more cycloalkyl substituents, wherein alkoxy alkyl hydrogens may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl and halo, and wherein R^4 is not methyl;

10 R^5 is selected from the group consisting of alkyl, haloalkyl, cycloalkyl, halo, and alkoxy, wherein the alkoxy may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl and haloalkyl; and

R^6 is halo.

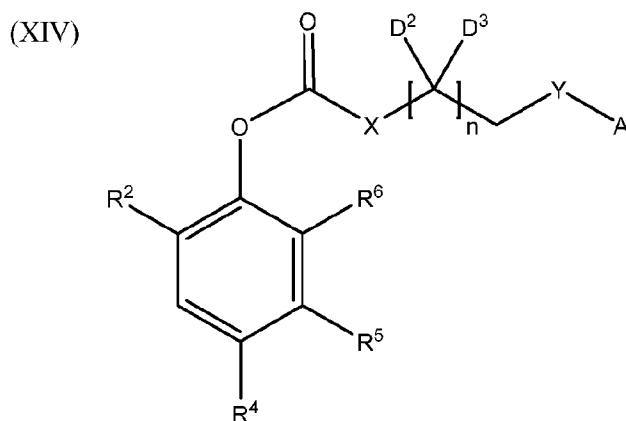
15 166. The method of Claim 165, wherein the compound has a structure of Formula (XIII):



wherein D^1 is alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroalkyl, heteroaryl, heteroaralkyl, carbonylalkyl, or phosphonooxyalkyl, optionally substituted with one or more substituents selected from the group consisting of alkyl, carboxylate, heteroalkyl, monocyclic ring, bicyclic ring, and hydroxyl moieties.

30

167. The method of Claim 166, wherein the compound has a structure of Formula (XIV):



wherein:

D^2 and D^3 together with the carbon atom to which they are bonded form a cycloalkyl or cycloheteroalkyl ring, or alternatively D^2 and D^3 are each independently selected from the group consisting of hydrogen, alkyl, and heteroalkyl;

A , Y , and one of D^2 or D^3 together with the atoms to which they are bonded to form a cycloheteroalkyl ring, or alternatively A is selected from the group consisting of hydrogen, phosphono, alkyl, aryl, arylalkyl, heteroalkyl, heteroaryl, and heteroarylalkyl;

X is selected from the group consisting of $-ND^4-$, $-O-$, $-CH_2-$, and $-S-$;

Y is selected from the group consisting of $-O-$ and $-ND^4-$;

n is an integer from 1 to 5; and

D^4 is selected from the group consisting of hydrogen, alkyl, and arylalkyl.

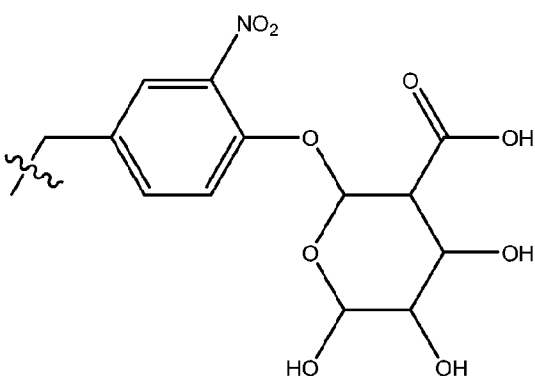
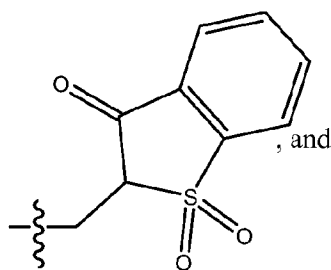
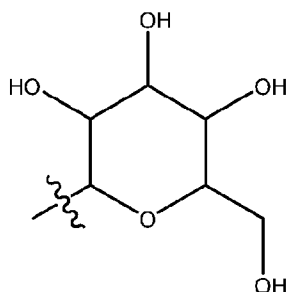
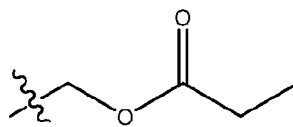
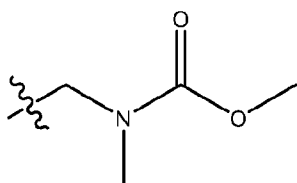
168. The method of Claim 167, wherein D^2 and D^3 are each hydrogen, X is $-CH_2-$, Y is $-O-$,

A is phosphono, and $n=1$.

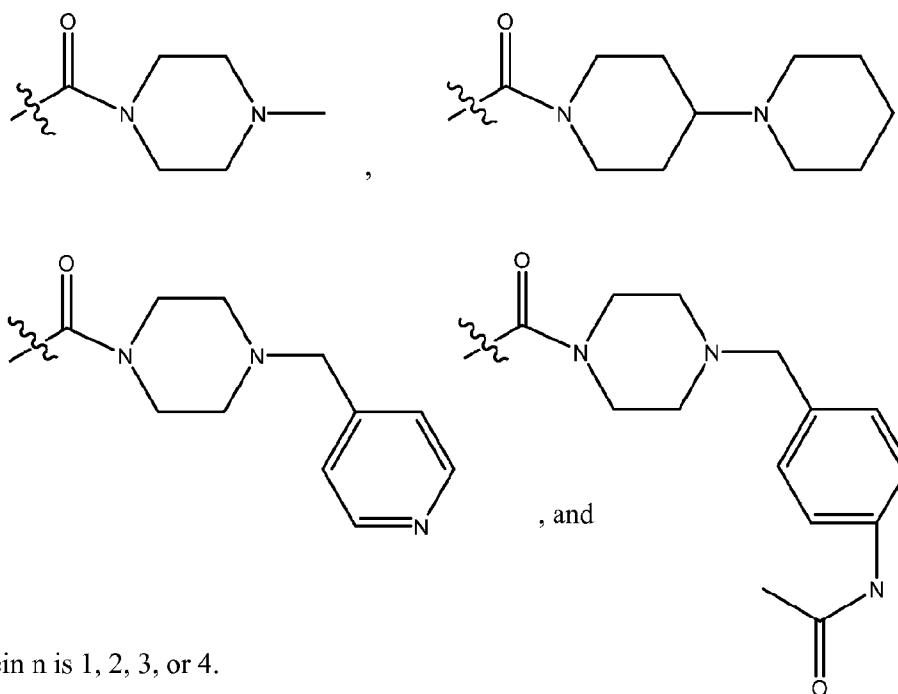
169. The method of Claim 165, wherein R^1 is selected from the group consisting of $-P(O)(OD^5)_2$, $-CH_2-O-P(O)(OD^5)_2$, $-(CH_2)_2-O-P(O)(OD^5)_2$, and $-CH_2-O-P(O)(OD^5)_2$, and further wherein D^5 is H or a pharmaceutically acceptable cation.

170. The method of Claim 169, wherein the pharmaceutically acceptable cation is selected from the group consisting of Li^+ , Na^+ , and K^+ .

171. The method of Claim 165, wherein R^1 is selected from the group consisting of



172. The method of Claim 165, wherein R^1 is selected from the group consisting of
 $-\text{CONHCH}_2(\text{CH}_2)_n\text{CH}_3$, $-\text{CON}(\text{CH}_3)_2$, $-\text{CON}(\text{C}_2\text{H}_5)_2$, $-\text{CON}(\text{CH}(\text{CH}_3)_2)_2$, $-\text{CONNH}_2$
 CH_3



wherein n is 1, 2, 3, or 4.

173. The method of Claim 165, wherein R^1 is $-\text{S}(=\text{O})_2\text{NH}_2$.

174. The method of any one of the previous claims wherein:

alkyl is selected from the group consisting of methyl, ethyl, propyl, isopropyl, butyl, isobutyl, *tert*-butyl, *sec*-butyl, pentanyl, isopentanyl, and neopentanyl;

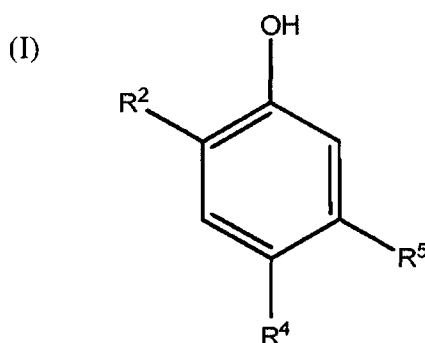
haloalkyl is selected from the group consisting of fluoromethyl, 1-fluoroethyl, 2-fluoroethyl, 1-fluoropropyl, 2-fluoropropyl, 3-fluoropropyl, chloromethyl, 1-chloroethyl, 2-chloroethyl, 1-chloropropyl, 2-chloropropyl, 3-chloropropyl, bromomethyl, 1-bromoethyl, 2-bromoethyl, 1-bromopropyl, 2-bromopropyl, and 3-bromopropyl; and

cycloalkyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

AMENDED CLAIMS
received by the International Bureau on 24 March 2016 (24.03.2016)

What is claimed is:

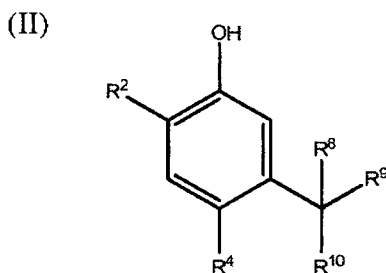
1. A method of treating a neurological or an inflammatory condition comprising administering a therapeutically effective amount of a compound or pharmaceutically acceptable salt of the compound, wherein the compound has the structure of Formula (I):



wherein:

- R² is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;
- R⁴ is selected from the group consisting of halo and alkoxy, wherein the alkoxy may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl and halo, and wherein R⁴ is not methyl; and
- R⁵ is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl.
2. The method of claim 1 wherein each of R² and R⁵ has between one and five carbons.
 3. The method of claim 1 wherein the condition is epilepsy, seizures, or convulsions.
 4. The method of claim 1 wherein the condition is neuropathic pain or fibromyalgia.
 5. The method of claim 1 wherein the condition is a psychological disorder.
 6. The method of claim 5 wherein the psychological disorder is anxiety, mania, bipolar disorder, or depression.

7. The method of claim 1, wherein the condition is Alzheimer's Disease, Huntington's Disease, Multiple Sclerosis, Parkinson's disease, Tourette's Syndrome, tinnitus, or tremors.
8. The method of Claims 1 or 3, wherein:
 R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;
 R^4 is halo.
9. The method of Claim 8, wherein:
 R^4 is selected from the group consisting of Br, Cl, and F.
10. The method of Claim 9, wherein:
 R^2 is alkyl; and
 R^5 is alkyl having two or more carbons.
11. The method of Claim 10, wherein the compound is selected from a group consisting of: 4-chloro-5-*tert*-butyl-2-methyl-phenol; 4-chloro-2-isopropyl-5-methyl-phenol; 4-fluoro-2-isopropyl-5-methyl-phenol; 4-chloro-2,5-diisopropyl-phenol; 4-bromo-5-isopropyl-2-methylphenol; 4-bromo-2-isopropyl-5-methyl-phenol; 4-bromo-2-*tert*-butyl-5-isopropyl-phenol; 4-bromo-5-*tert*-butyl-2-methyl-phenol; and 4-fluoro-5-*tert*-butyl-2-methyl-phenol.
12. The method of Claim 1, wherein the compound has the structure of Formula (II):

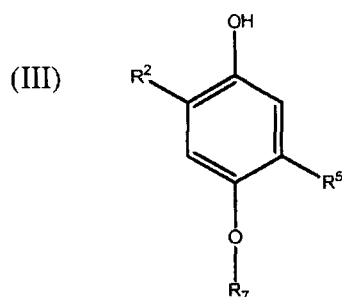


wherein:

- R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;
 R^4 is selected from the group consisting of Br, Cl, and F; and

R^8 , R^9 and R^{10} are each independently selected from the group consisting of H, alkyl, and haloalkyl.

13. The method of Claim 1, wherein the compound has the structure of Formula (III):



wherein:

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

R^5 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl; and

R_7 is selected from the group consisting of alkyl and haloalkyl.

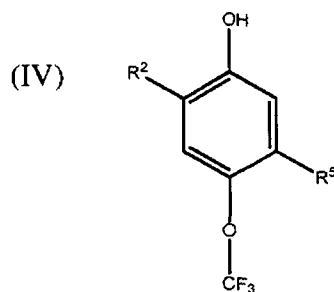
14. The method of Claim 13, wherein:

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

R^5 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl; and

R_7 is alkyl.

15. The method of Claim 14, wherein the compound has the structure of Formula (IV):



wherein:

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl; and

R^5 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl.

16. The method of Claim 15, wherein:

R^2 is selected from the group consisting of alkyl and cycloalkyl; and

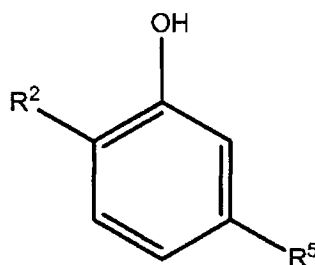
R^5 is selected from the group consisting of alkyl and cycloalkyl.

17. A compound selected from the group consisting of: 4-bromo-5-ethyl-2-methyl-phenol; 4-fluoro-5-isopropyl-2-methyl-phenol; 4-bromo-5-*tert*-butyl-2-methyl-phenol; 4-bromo-5-cyclopropyl-2-methyl-phenol; 4-bromo-2-ethyl-5-isopropyl-phenol; 4-chloro-2-ethyl-5-isopropyl-phenol; 2-ethyl-4-fluoro-5-isopropyl phenol; 4-bromo-5-isopropyl-2-propyl-phenol, 5-isopropyl-2-propyl-phenol; and 4-bromo-2,5-isopropyl-phenol.

18. A compound selected from the group consisting of: 4-bromo-2-methyl-5-(2,2,2-trifluoro-1-methyl-ethyl)-phenol; 4-bromo-5-(2-fluoro-1-methyl-ethyl)-2-methyl-phenol; 4-bromo-2-methyl-5-(2,2,2-trifluoro-1-trifluoromethyl-ethyl)-phenol; 4-bromo-2-trifluoromethyl-5-(2,2,2-trifluoro-1-methyl-ethyl)-phenol; 4-bromo-2-cyclopropyl-5-isopropyl-phenol; 4-bromo-2,5-dicyclopropyl-phenol; 5-isopropyl-2-methyl-4-trifluoromethoxy-phenol; 2-cyclopropyl-5-isopropyl-4-trifluoromethoxy-phenol; 5-cyclopropyl-2-methyl-4-trifluoromethoxy-phenol; 2,5-dicyclopropyl-4-trifluoromethoxy-phenol; 4-*tert*-butoxy-5-cyclopropyl-2-methyl-phenol; 4-*tert*-butoxy-5-cyclopropyl-5-methyl-phenol; 4-*tert*-butoxy-2,5-dicyclopropyl-phenol; 4-isopropoxy-5-isopropyl-2-methyl-phenol; 4-bromo-5-isopropyl-2-trifluoromethyl-phenol; 4-bromo-5-(2-fluoro-1-methyl-ethyl)-2-methyl-phenol; and 4-*tert*-butoxy-5-isopropyl-2-methyl-phenol.

19. A compound or pharmaceutically acceptable salt of the compound, wherein the compound has the structure of Formula (V):

(V)



wherein:

R^2 is selected from the group consisting of haloalkyl and cycloalkyl; and

R^5 is selected from the group consisting of haloalkyl and cycloalkyl.

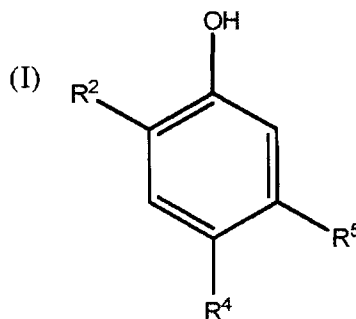
20. A compound of Claim 19, wherein:

R^2 is selected from the group consisting of trifluoroalkyl and cycloalkyl

R^5 is selected from the group consisting of trifluoroalkyl and cycloalkyl.

21. A compound selected from the group consisting of: 5-(1,2-dimethyl-propyl)-2-methyl-phenol; 5-isobutyl-2-methyl-phenol; 5-cyclopentyl-2-methyl-phenol; 5-*sec*-butyl-2-ethyl-phenol; 5-butyl-2-propyl-phenol; 5-isopropyl-2-propyl-phenol; 5-*sec*-butyl-2-propyl-phenol; 5-*tert*-butyl-2-propyl-phenol; 2-butyl-5-isopropyl-phenol; 2-butyl-5-*sec*-butyl-phenol; 5-(*tert*-butyl)-2-butylphenol; 2-isopropyl-5-propyl-phenol; 5-*sec*-butyl-2-isopropyl-phenol; 2-*sec*-butyl-5-ethyl-phenol; 2-*sec*-butyl-5-propyl-phenol; 5-butyl-2-*sec*-butyl-phenol; 2-*sec*-butyl-5-isopropyl-phenol; 5-*sec*-butyl-2-*tert*-butyl-phenol; 2-methyl-5-(2,2,2-trifluoro-1-methyl-ethyl)-phenol; 5-(2-fluoro-1-methyl-ethyl)-2-methyl-phenol; 2-methyl-5-(2,2,2-trifluoro-1-trifluoromethyl-ethyl)-phenol; 2-trifluoromethyl-5-(2,2,2-trifluoro-1-methyl-ethyl)-phenol; 5-isopropyl-2-(1-methyl-butyl)-phenol; 2-isopropyl-5-isopropyl-phenol; 2-cyclopropyl-5-isopropyl-phenol; and 2,5-dicyclopropyl-phenol.

22. A compound or pharmaceutically acceptable salt of the compound, wherein the compound has the structure of Formula (I):



wherein:

R^2 is selected from the group consisting of methyl, cycloalkyl, and $-CF_3$;

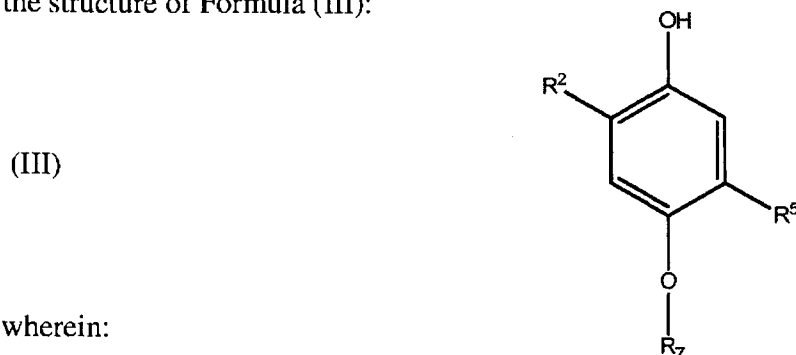
R^4 is halo;

R^5 is selected from the group consisting of fluoroalkyl and a three, four, or five carbon cycloalkyl.

23. The compound of Claim 22, wherein:

R^4 is selected from the group consisting of Br, Cl, and F.

24. A compound or pharmaceutically acceptable salt of the compound, wherein the compound has the structure of Formula (III):



wherein:

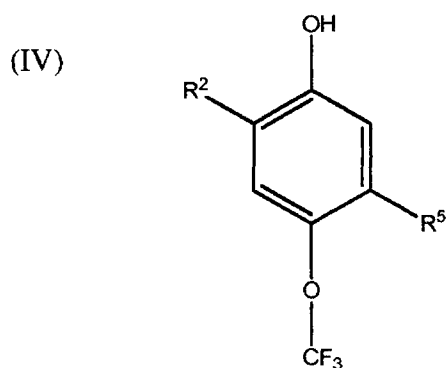
R^2 and R^5 are each independently selected from the group consisting of alkyl and cycloalkyl, wherein at least one of R^2 and R^5 is cycloalkyl; and

R_7 is selected from the group consisting of isopropyl, *tert*-butyl, and haloalkyl.

25. A compound of Claim 24, wherein:

R_7 is selected from the group consisting of isopropyl and *tert*-butyl.

26. A compound or pharmaceutically acceptable salt of the compound of Claim 22, wherein the compound has the structure of Formula (IV):

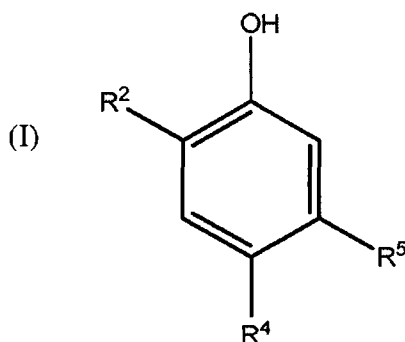


wherein:

R^2 is selected from the group consisting of alkyl, and cycloalkyl; and

R^5 is selected from the group consisting of alkyl, and cycloalkyl.

27. A method of treating epilepsy, seizures, or convulsions, the method comprising administering a therapeutically effective amount of a compound or of a pharmaceutically acceptable salt of the compound, wherein the compound has the structure of Formula (I):



wherein:

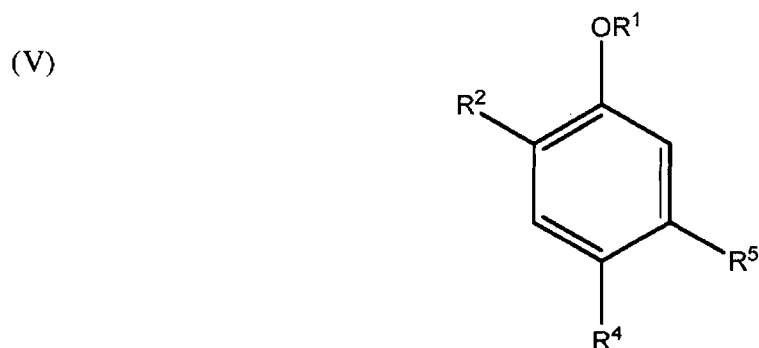
R^2 and R^5 are each independently selected from the group consisting of methyl, isopropyl, and *tert*-butyl; and

R^4 is selected from the group consisting of Br, Cl, and F.

28. The method of any one of Claims 1–16 or 27, wherein the compound is deuterated.

29. The compound or pharmaceutically acceptable salt of any one of Claims 17–26, wherein the compound is deuterated.

30. A method of treating a neurological or an inflammatory condition comprising administering a therapeutically effective amount of a compound or pharmaceutically acceptable salt of the compound, wherein the compound has a structure of Formula (V):



wherein:

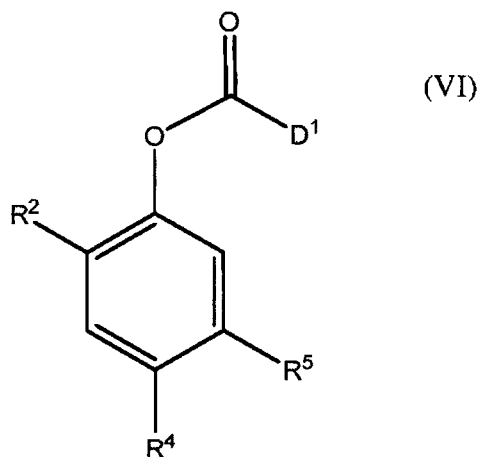
R^1 is selected from the group consisting of an ester, a carbonate, a phosphate, a carbamate, a sulfamate, and an acylmethylester;

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

R^4 is selected from the group consisting of H, halo, and alkoxy, wherein the alkoxy may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl and halo, and wherein R^4 is not methyl; and

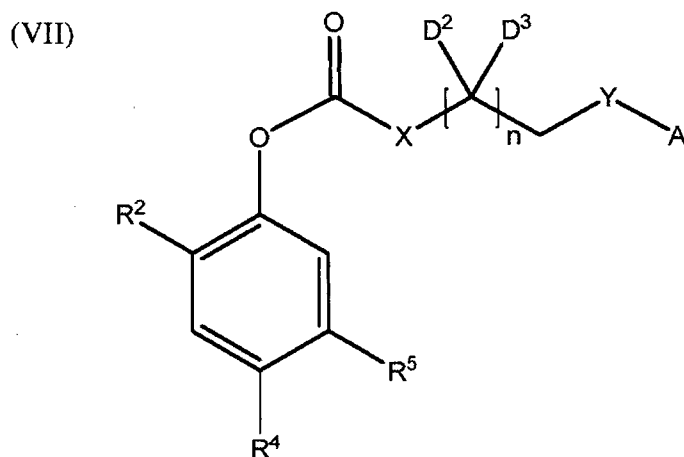
R^5 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl.

31. The method of Claim 30, wherein the compound has a structure of Formula (VI):



wherein D^1 is alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroalkyl, heteroaryl, heteroaralkyl, carbonylalkyl, or phosphonoxyalkyl, optionally substituted with one or more substituents selected from the group consisting of alkyl, carboxylate, heteroalkyl, monocyclic ring, bicyclic ring, and hydroxyl moieties.

32. The method of Claim 31, wherein the compound has a structure of Formula (VII):



wherein:

D^2 and D^3 together with the carbon atom to which they are bonded form a cycloalkyl or cycloheteroalkyl ring, or alternatively D^2 and D^3 are each independently selected from the group consisting of hydrogen, alkyl, and heteroalkyl,;

A, Y, and one of D^2 or D^3 together with the atoms to which they are bonded to form a cycloheteroalkyl ring, or alternatively A is selected from the group consisting of hydrogen, phosphono, alkyl, aryl, arylalkyl, heteroalkyl, heteroaryl, and heteroarylalkyl;

X is selected from the group consisting of $-\text{ND}^4-$, $-\text{O}-$, $-\text{CH}_2-$, and $-\text{S}-$;

Y is selected from the group consisting of $-\text{O}-$ and $-\text{ND}^4-$;

n is an integer from 1 to 5; and

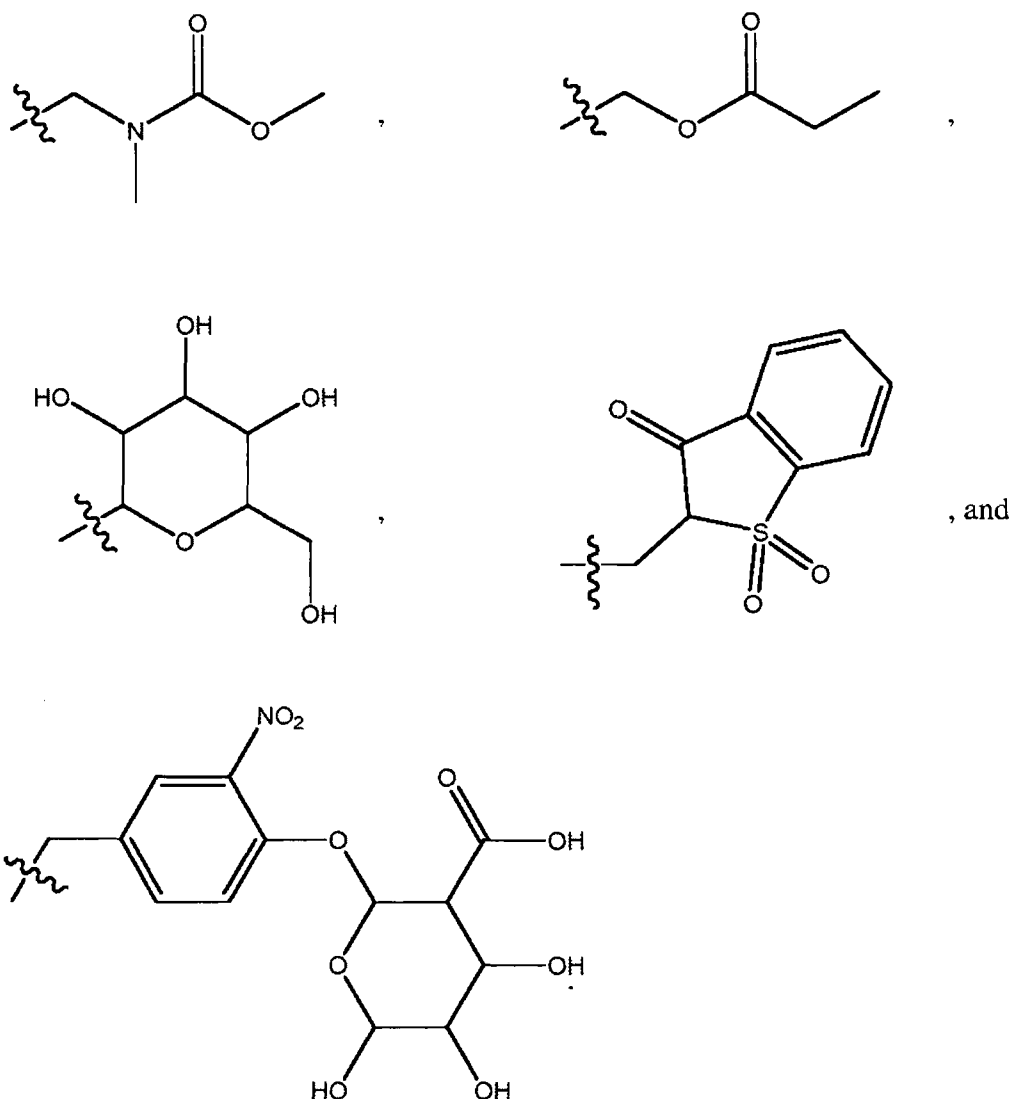
D^4 is selected from the group consisting of hydrogen, alkyl, and arylalkyl.

33. The method of Claim 32, wherein D^2 and D^3 are each hydrogen, X is $-\text{CH}_2-$, Y is $-\text{O}-$, A is phosphono, and $n=1$.

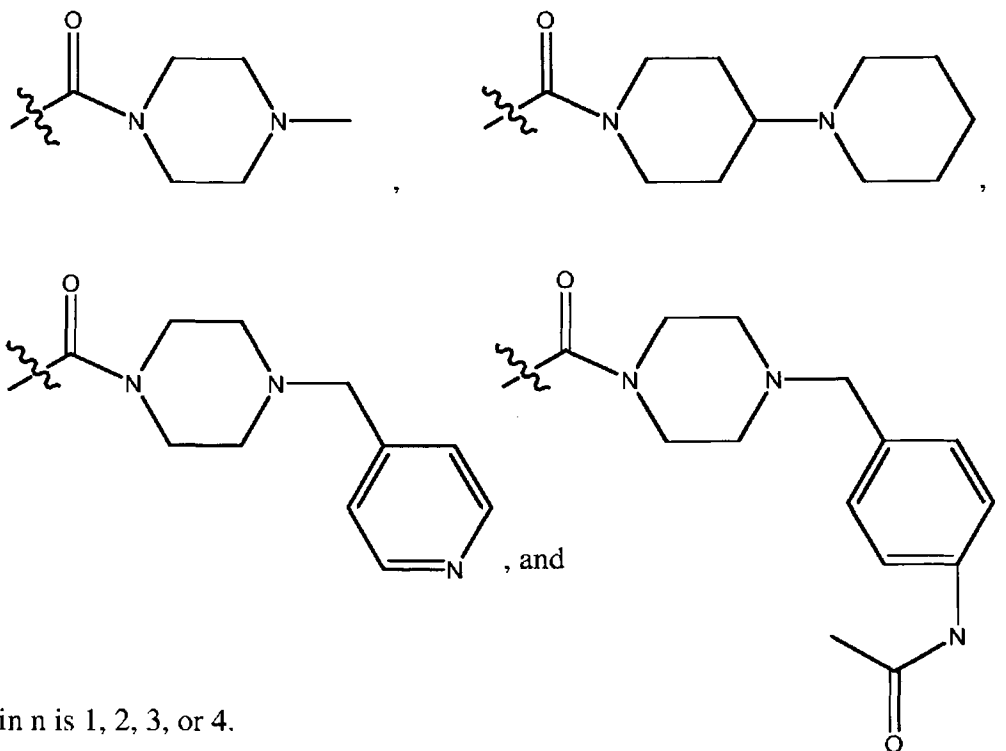
34. The method of Claim 30, wherein R^1 is selected from the group consisting of $-P-(O)(OD^5)_2$, $-CH_2-O-P-(O)(OD^5)_2$, $-(CH_2)_2-O-P-(O)(OD^5)_2$, and $-CH_2-O-P-(O)(OD^5)_2$, and further wherein D^5 is H or a pharmaceutically acceptable cation.

35. The method of Claim 34, wherein the pharmaceutically acceptable cation is selected from the group consisting of Li^+ , Na^+ , and K^+ .

36. The method of Claim 30, wherein R^1 is selected from the group consisting of



37. The method of Claim 30, wherein R^1 is selected from the group consisting of $-\text{CONHCH}_2(\text{CH}_2)_n\text{CH}_3$, $-\text{CON}(\text{CH}_3)_2$, $-\text{CON}(\text{C}_2\text{H}_5)_2$, $-\text{CON}(\text{CH}(\text{CH}_3)_2)_2$, $-\text{CONNH}_2$, $-\text{CON}(\text{CH}_3)$, and $-\text{CON}(\text{CH}_3)_2$.



wherein n is 1, 2, 3, or 4.

38. The method of Claim 30, wherein R^1 is $-\text{S}(=\text{O})_2\text{NH}_2$.

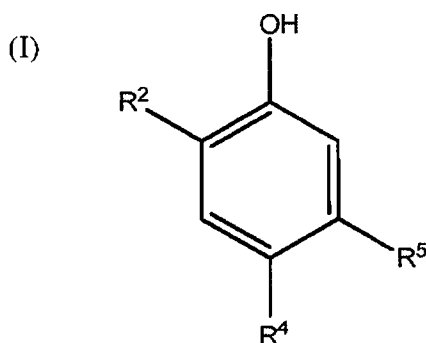
39. The method of any one of the previous claims wherein:

alkyl is selected from the group consisting of methyl, ethyl, propyl, isopropyl, butyl, isobutyl, *tert*-butyl, *sec*-butyl, pentanyl, isopentanyl, and neopentanyl;

haloalkyl is selected from the group consisting of fluoromethyl, 1-fluoroethyl, 2-fluoroethyl, 1-fluoropropyl, 2-fluoropropyl, 3-fluoropropyl, chloromethyl, 1-chloroethyl, 2-chloroethyl, 1-chloropropyl, 2-chloropropyl, 3-chloropropyl, bromomethyl, 1-bromoethyl, 2-bromoethyl, 1-bromopropyl, 2-bromopropyl, and 3-bromopropyl; and

cycloalkyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

40. A method of treating a neurological or an inflammatory condition comprising administering a therapeutically effective amount of a compound or pharmaceutically acceptable salt of the compound, wherein the compound has a structure of Formula (I):



wherein:

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl, wherein the alkyl or haloalkyl is optionally substituted with one or more cycloalkyl substituents;

R^4 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl, wherein the alkyl or haloalkyl is optionally substituted with one or more cycloalkyl substituents, and wherein R^4 is not methyl; and

R^5 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl.

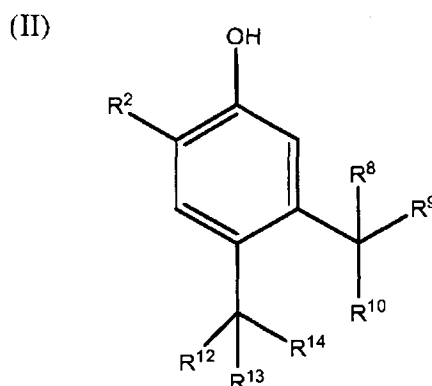
41. The method of Claim 40 wherein each of R^2 , R^4 , and R^5 has between one and five carbons.

42. The method of Claim 41 wherein the condition is epilepsy, seizures, or convulsions.

43. The method of Claim 40 wherein the condition is neuropathic pain or fibromyalgia.

44. The method of Claim 40 wherein the condition is a psychological disorder.

45. The method of Claim 44 wherein the psychological disorder is anxiety, mania, bipolar disorder, or depression.
46. The method of Claim 40, wherein the condition is Alzheimer's Disease, Huntington's Disease, Multiple Sclerosis, Parkinson's disease, Tourette's Syndrome, tinnitus, or tremors.
47. The method of Claim 40, wherein the compound has a structure of Formula (II):

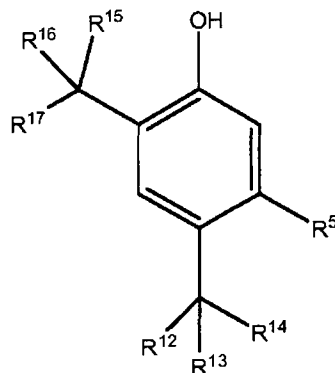


wherein:

- R² is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;
- R⁸ and R⁹ form a cycloalkyl of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 carbons or R⁸ and R⁹ are each independently selected from the group consisting of H, alkyl, and haloalkyl;
- R¹⁰ is selected from the group consisting of H, alkyl, and haloalkyl;
- R¹² and R¹³ form a cycloalkyl of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 carbons or R¹² and R¹³ are each independently selected from the group consisting of H, alkyl, and haloalkyl; and
- R¹⁴ is selected from the group consisting of H, alkyl, and haloalkyl.

48. The method of Claim 47, wherein halo is chloro, bromo, or fluoro.
49. The method of Claim 48, wherein the halo is fluoro.
50. The method of Claim 40, wherein the compound has a structure of Formula (III):

(III)



wherein:

R^5 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

R^{12} and R^{13} form a cycloalkyl of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 carbons or R^{12} and R^{13} are each independently selected from the group consisting of H, alkyl, and haloalkyl; and

R^{14} is selected from the group consisting of H, alkyl, and haloalkyl;

R^{15} and R^{16} form a cycloalkyl of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 carbons or R^{15} and R^{16} are each independently selected from the group consisting of H, alkyl, and haloalkyl; and

R^{17} is selected from the group consisting of H, alkyl, and haloalkyl.

51. The method of Claim 50, wherein halo is chloro, bromo, or fluoro.

52. The method of Claim 51, wherein the halo is fluoro.

53. The method of Claim 47, wherein:

R^{12} and R^{13} form a cycloalkyl moiety; and

R^{14} is selected from the group consisting of alkyl and haloalkyl.

54. The method of Claim 50, wherein:

R^{12} and R^{13} form a cycloalkyl moiety;

R^{15} and R^{16} form a cycloalkyl moiety; and

R^{14} and R^{17} are each independently selected from the group consisting of alkyl and haloalkyl.

55. The method of Claim 50, wherein:

R^5 is selected from the group consisting of methyl and isopropyl;

R^{12} is selected from the group consisting of H, halo, methyl, and cycloalkyl comprising R^{13} ;

R^{13} is selected from the group consisting of H, halo, methyl, trihalomethyl, and cycloalkyl comprising R^{12} ;

R^{14} is selected from the group consisting of halo, methyl, trihalomethyl and pentahaloethyl;

R^{15} is selected from the group consisting of H, methyl, and trihalomethyl.

R^{16} is selected from the group consisting of H and cycloalkyl comprising R^{17} ; and

R^{17} is selected from the group consisting of H, methyl, and cycloalkyl comprising R^{16} .

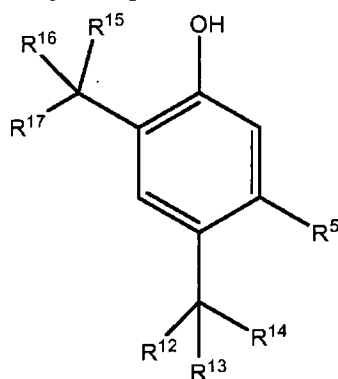
56. The method of Claim 55 wherein the halo is chloro, bromo, or fluoro.

57. The method of Claim 56, wherein the halo is fluoro.

58. The method of Claim 57, wherein the compound is selected from the group consisting of: 5-isopropyl-2-methyl-4-trifluoromethyl-phenol; 2,5-diisopropyl-4-trifluoromethyl-phenol; 4-(1,1-difluoroethyl)-2-isopropyl-5-methyl-phenol; 2-isopropyl-5-methyl-4-trifluoromethyl-phenol; 2-isopropyl-5-methyl-4-(1-methyl-cyclopropyl)-phenol; 2-isopropyl-5-methyl-4-(1-trifluoro-methyl-cyclopropyl)-phenol; 2-isopropyl-5-methyl-4-(2,2,3,3,3-pentafluoro-propyl)-phenol; 2-isopropyl-5-methyl-4-pentafluoroethyl-phenol; 2-isopropyl-5-methyl-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol; 4-*tert*-butyl-5-methyl-2-(2,2,2-trifluoro-1-methyl-ethyl)-phenol; 4-*tert*-butyl-5-methyl-2-(1-methyl-cyclopropyl)-phenol; and 4-*tert*-butyl-5-methyl-2-(1-trifluoro-methyl-cyclopropyl)-phenol.

59. A compound or pharmaceutically acceptable salt of the compound, wherein the compound has a structure of Formula (III):

(III)



wherein:

R⁵ is selected from the group consisting of methyl and isopropyl;

R¹² is selected from the group consisting of H, halo, methyl, and cycloalkyl comprising R¹³;

R¹³ is selected from the group consisting of H, halo, methyl, trihalomethyl, and cycloalkyl comprising R¹²;

R¹⁴ is selected from the group consisting of halo, methyl, trihalomethyl and pentahaloethyl;

R¹⁵ is selected from the group consisting of H, methyl, and trihalomethyl.

R¹⁶ is selected from the group consisting of H and cycloalkyl comprising R¹⁷; and

R¹⁷ is selected from the group consisting of H, methyl, and cycloalkyl comprising R¹⁶.

60. A compound or pharmaceutically acceptable salt of the compound, wherein the compound is selected from the group consisting of the species of Table 1, except 4-*tert*-butyl-5-ethyl-2-methyl-phenol.

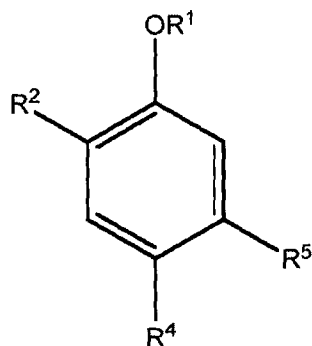
61. The compound or pharmaceutically acceptable salt of Claim 60, wherein the compound is selected from the group consisting of 5-isopropyl-2-methyl-4-trifluoromethyl-phenol; 2,5-diisopropyl-4-trifluoromethyl-phenol; 4-(1,1-difluoroethyl)-2-isopropyl-5-methyl-phenol; 2-isopropyl-5-methyl-4-trifluoromethyl-phenol; 2-isopropyl-5-methyl-4-(1-methyl-cyclopropyl)-phenol; 2-isopropyl-5-methyl-4-(1-trifluoro-methyl-cyclopropyl)-phenol; 2-isopropyl-5-methyl-4-(2,2,3,3,3-pentafluoro-propyl)-phenol; 2-isopropyl-5-methyl-4-pentafluoroethyl-phenol; 2-isopropyl-5-methyl-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol; 4-*tert*-butyl-5-methyl-2-(2,2,2-trifluoro-1-methyl-ethyl)-phenol; 4-*tert*-butyl-5-methyl-2-(1-methyl-cyclopropyl)-phenol; and 4-*tert*-butyl-5-methyl-2-(1-trifluoro-methyl-cyclopropyl)-phenol.

62. The method of any one of Claims 40–58, wherein the compound is deuterated.

63. The compound or pharmaceutically acceptable salt of any one of Claims 59–61, wherein the compound is deuterated.

64. A method of treating a neurological or an inflammatory condition comprising administering a therapeutically effective amount of a compound or pharmaceutically acceptable salt of the compound, wherein the compound has a structure of Formula (IV):

(IV)



wherein:

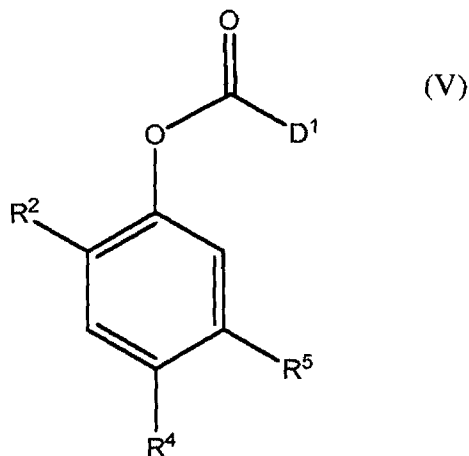
R^1 is selected from the group consisting of an ester, a carbonate, a phosphate, a carbamate, a sulfamate, and an acylmethylester;

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl, wherein the alkyl or haloalkyl is optionally substituted with one or more cycloalkyl substituents;

R^4 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl, wherein the alkyl or haloalkyl is optionally substituted with one or more cycloalkyl substituents, and wherein R^4 is not methyl; and

R^5 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl.

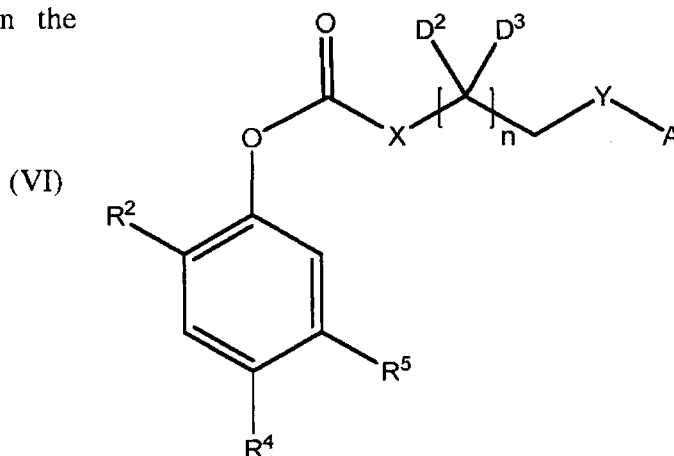
65. The method of Claim 64, wherein the compound has a structure of Formula (V):



wherein D^1 is alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroalkyl, heteroaryl, heteroaralkyl, carbonylalkyl, or phosphonooxyalkyl, optionally substituted with one or more substituents selected

from the group consisting of alkyl, carboxylate, heteroalkyl, monocyclic ring, bicyclic ring, and hydroxyl moieties.

66. The method of Claim 65, wherein the compound has a structure of Formula (VI):



wherein:

D² and D³ together with the carbon atom to which they are bonded form a cycloalkyl or cycloheteroalkyl ring, or alternatively D² and D³ are each independently selected from the group consisting of hydrogen, alkyl, and heteroalkyl;

A, Y, and one of D² or D³ together with the atoms to which they are bonded to form a cycloheteroalkyl ring, or alternatively A is selected from the group consisting of hydrogen, phosphono, alkyl, aryl, arylalkyl, heteroalkyl, heteroaryl, and heteroarylalkyl;

X is selected from the group consisting of —ND⁴—, —O—, —CH₂—, and —S—;

Y is selected from the group consisting of —O— and —ND⁴—;

n is an integer from 1 to 5; and

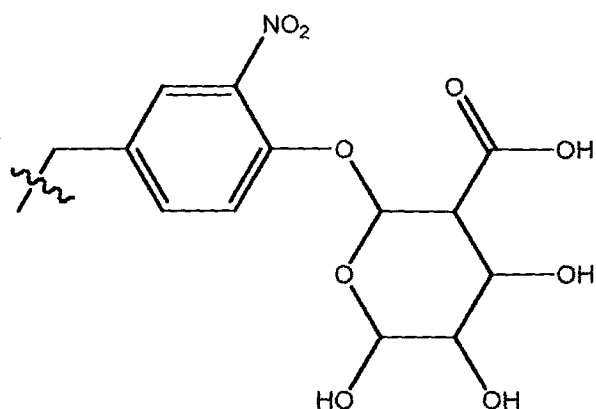
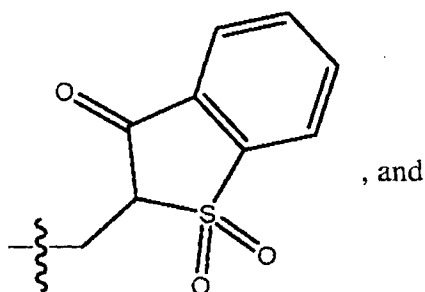
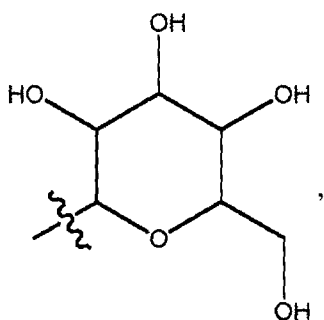
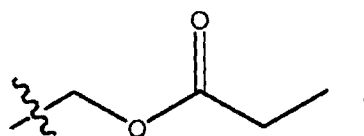
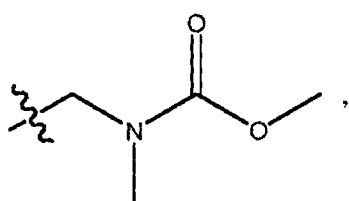
D⁴ is selected from the group consisting of hydrogen, alkyl, and arylalkyl.

67. The method of Claim 66, wherein D² and D³ are each hydrogen, X is —CH₂—, Y is —O—, A is phosphono, and n=1.

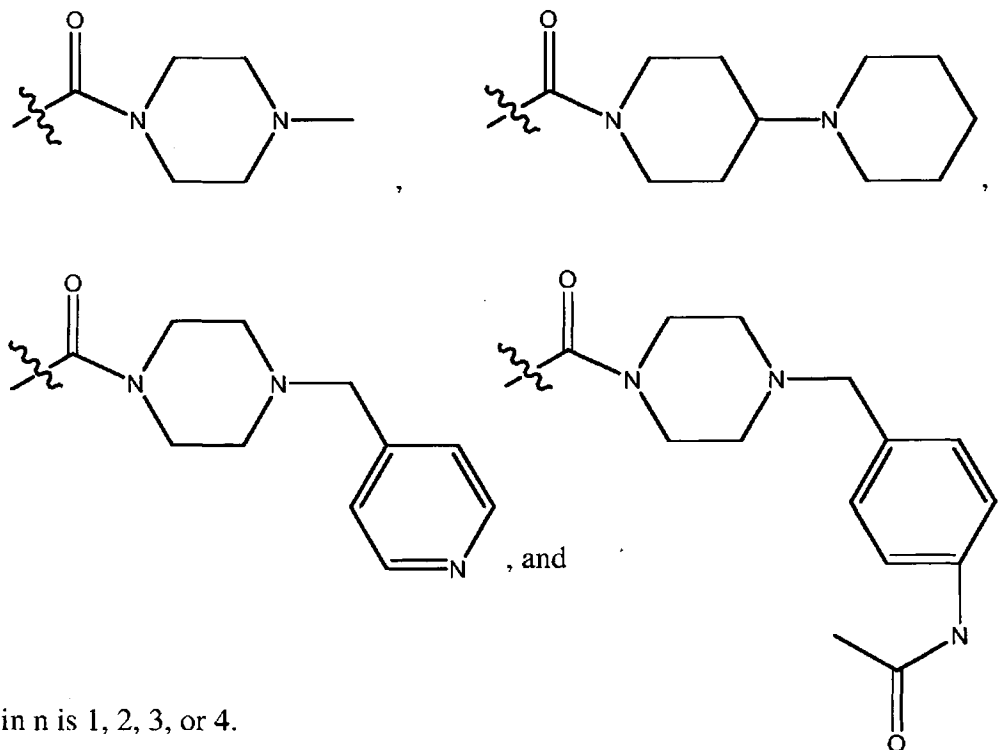
68. The method of Claim 64, wherein R^1 is selected from the group consisting of $-P-(O)(OD^5)_2$, $-CH_2-O-P-(O)(OD^5)_2$, $-(CH_2)_2-O-P-(O)(OD^5)_2$, and $-CH_2-O-P-(O)(OD^5)_2$, and further wherein D^5 is H or a pharmaceutically acceptable cation.

69. The method of Claim 68, wherein the pharmaceutically acceptable cation is selected from the group consisting of Li^+ , Na^+ , and K^+ .

70. The method of Claim 64, wherein R^1 is selected from the group consisting of



40. The method of Claim 64, wherein R^1 is selected from the group consisting of $-\text{CONHCH}_2(\text{CH}_2)_n\text{CH}_3$, $-\text{CON}(\text{CH}_3)_2$, $-\text{CON}(\text{C}_2\text{H}_5)_2$, $-\text{CON}(\text{CH}(\text{CH}_3)_2)_2$, $-\text{CONNH}_2$
 CH_3



wherein n is 1, 2, 3, or 4.

71. The method of Claim 64, wherein R^1 is $-\text{S}(=\text{O})_2\text{NH}_2$.

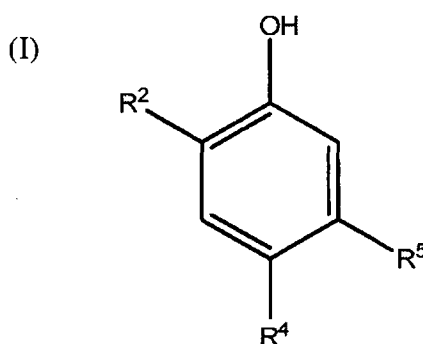
72. The method of any one of the previous claims wherein:

alkyl is selected from the group consisting of methyl, ethyl, propyl, isopropyl, butyl, isobutyl, *tert*-butyl, *sec*-butyl, pentanyl, isopentanyl, and neopentanyl;

haloalkyl is selected from the group consisting of fluoromethyl, 1-fluoroethyl, 2-fluoroethyl, 1-fluoropropyl, 2-fluoropropyl, 3-fluoropropyl, chloromethyl, 1-chloroethyl, 2-chloroethyl, 1-chloropropyl, 2-chloropropyl, 3-chloropropyl, bromomethyl, 1-bromoethyl, 2-bromoethyl, 1-bromopropyl, 2-bromopropyl, and 3-bromopropyl; and

cycloalkyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

73. A method of treating a neurological or an inflammatory condition comprising administering a therapeutically effective amount of a compound or pharmaceutically acceptable salt of the compound, wherein the compound has a structure of Formula (I):



wherein,

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl, wherein the alkyl or haloalkyl is optionally substituted with one or more cycloalkyl substituents;

R^4 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl, wherein the alkyl or haloalkyl is optionally substituted with one or more cycloalkyl substituents, and wherein R^4 is not methyl; and

R^5 is selected from the group consisting of halo, and alkoxy, wherein the alkoxy may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl and halo.

74. The method of Claim 73 wherein each of R^2 , R^4 , and R^5 has between one and five carbons.

75. The method of Claim 73 wherein the condition is epilepsy, seizures, or convulsions.

76. The method of Claim 73 wherein the condition is neuropathic pain or fibromyalgia.

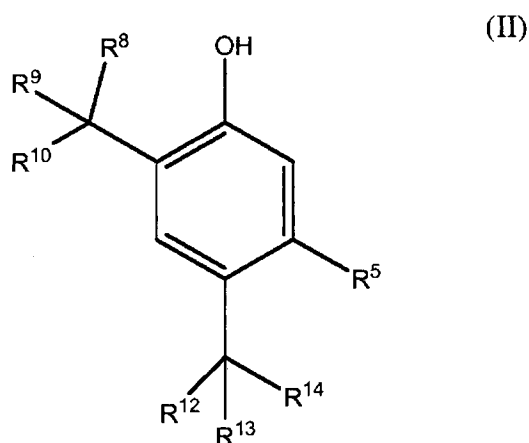
77. The method of Claim 73 wherein the condition is a psychological disorder.

78. The method of Claim 77 wherein the psychological disorder is anxiety, mania, bipolar disorder, or depression.

79. The method of Claim 73, wherein the condition is Alzheimer's Disease, Huntington's Disease, Multiple Sclerosis, Parkinson's disease, Tourette's Syndrome, tinnitus, or tremors.

80. The method of Claim 74, wherein R^2 and R^4 are not identical.

81. The method of Claim 74, wherein the compound has a structure of Formula (II):



wherein,

R^5 is halo;

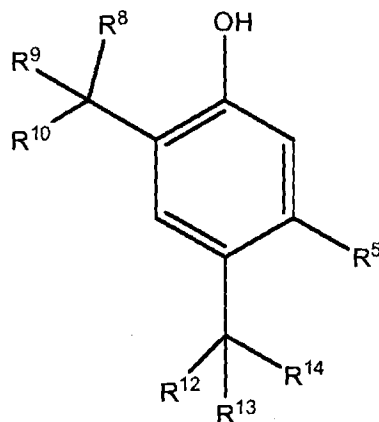
R^8 and R^9 form a cycloalkyl of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 carbons or R^8 and R^9 are each independently selected from the group consisting of H, alkyl, halo, and haloalkyl;

R^{10} is selected from the group consisting of H, alkyl, halo, and haloalkyl;

R^{12} and R^{13} form a cycloalkyl of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 carbons or R^{12} and R^{13} are each independently selected from the group consisting of H, alkyl, halo, and haloalkyl; and

R^{14} is selected from the group consisting of H, alkyl, halo, and haloalkyl.

82. The method of Claim 80, wherein the compound has a structure of Formula (II)



wherein,

R^5 is halo;

R^8 and R^9 form a cycloalkyl of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 carbons or R^8 and R^9 are each independently selected from the group consisting of H, alkyl, halo, and haloalkyl;

R^{10} is selected from the group consisting of H, alkyl, halo, and haloalkyl;

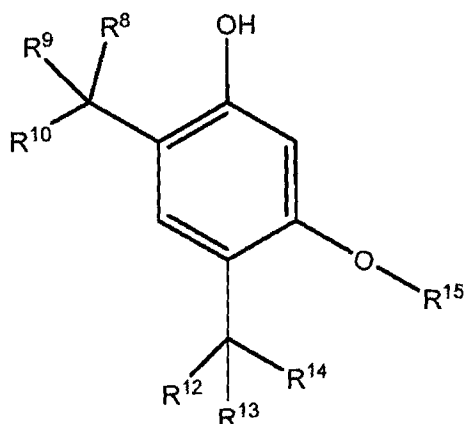
R^{12} and R^{13} form a cycloalkyl of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 carbons or R^{12} and R^{13} are each independently selected from the group consisting of H, alkyl, halo, and haloalkyl; and

R^{14} is selected from the group consisting of H, alkyl, halo, and haloalkyl.

83. The method of Claim 82, wherein halo is bromo, chloro, or fluoro.

84. The method of Claim 74, wherein the compound has a structure of Formula (III):

(III)



wherein,

R^{15} is selected from the group consisting of methyl, trihalomethyl, and isopropyl;

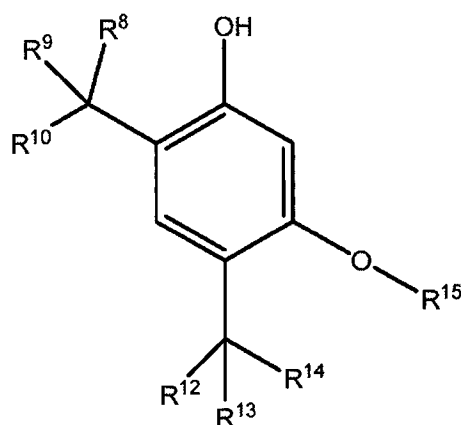
R^8 and R^9 form a cycloalkyl of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 carbons or R^8 and R^9 are each independently selected from the group consisting of H, alkyl, halo, and haloalkyl;

R^{10} is selected from the group consisting of H, alkyl, halo, and haloalkyl;

R^{12} and R^{13} form a cycloalkyl of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 carbons or R^{12} and R^{13} are each independently selected from the group consisting of H, alkyl, halo, and haloalkyl; and

R^{14} is selected from the group consisting of H, alkyl, halo, and haloalkyl.

85. The method of Claim 80, wherein the compound has a structure of Formula (III):



wherein,

R^{15} is selected from the group consisting of methyl, trihalomethyl, and isopropyl;

R^8 and R^9 form a cycloalkyl of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 carbons or R^8 and R^9 are each independently selected from the group consisting of H, alkyl, halo, and haloalkyl;

R^{10} is selected from the group consisting of H, alkyl, halo, and haloalkyl;

R^{12} and R^{13} form a cycloalkyl of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 carbons or R^{12} and R^{13} are each independently selected from the group consisting of H, alkyl, halo, and haloalkyl; and

R^{14} is selected from the group consisting of H, alkyl, halo, and haloalkyl.

86. The method of Claim 85, wherein halo is bromo, chloro, or fluoro.

87. The method of Claim 81, wherein:

R^{12} and R^{13} form a cycloalkyl moiety; and

R^{14} is selected from the group consisting of alkyl and haloalkyl.

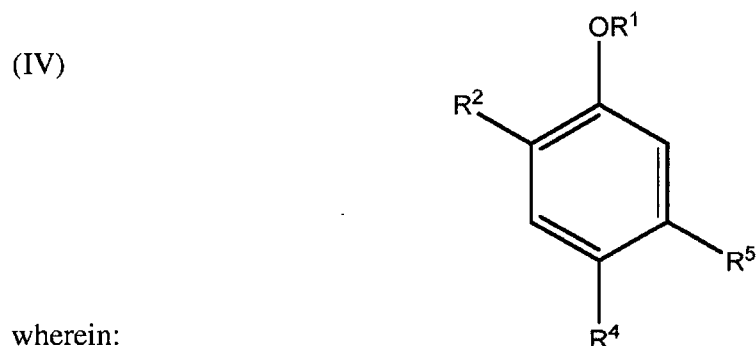
88. The method of Claim 87, wherein:
R⁹ and R¹⁰ form a cycloalkyl moiety; and
R⁸ is selected from the group consisting of alkyl and haloalkyl.
89. The method of Claim 84, wherein:
R¹² and R¹³ form a cycloalkyl moiety; and
R¹⁴ is selected from the group consisting of alkyl and haloalkyl.
90. The method of Claim 89, wherein:
R⁹ and R¹⁰ form a cycloalkyl moiety; and
R⁸ is selected from the group consisting of alkyl and haloalkyl.
91. A compound or pharmaceutically acceptable salt of the compound, wherein the compound is selected from the group consisting of the species of Table 1.
92. The method of Claim 75, wherein the compound is selected from the group consisting of 5-bromo-4-tert-butyl-2-methyl-phenol, 5-bromo-4-tert-butyl-2-isopropyl-phenol, 4-tert-butyl-5-chloro-2-isopropyl-phenol, 4-tert-butyl-2-isopropyl-5-trifluoromethoxy-phenol, 5-bromo-2-(tert-butyl)-4-(1,1-difluoroethyl)phenol, 5-bromo-4-tert-butyl-2-cyclopropyl-phenol, 5-bromo-2-cyclopropyl-4-trifluoromethyl-phenol, 5-bromo-2-isopropyl-4-(1-trifluoromethyl-cyclopropyl)-phenol, 5-bromo-2-isopropyl-4-(1-methyl-cyclopropyl)-phenol, 5-bromo-2-isopropyl-4-(1-pentafluoroethyl-cyclopropyl)-phenol, 5-bromo-2-isopropyl-4-pentafluoroethyl-phenol, 5-bromo-2-isopropyl-4-(2,2,3,3,3-pentafluoro-propyl)-phenol, 5-bromo-2-isopropyl-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol, 5-fluoro-2,4-bis-(1-methyl-cyclopropyl)-phenol, 5-bromo-4-(1-methyl-cyclopropyl)-2-(1-trifluoromethyl-cyclopropyl)-phenol, 5-fluoro-4-(1-methyl-cyclopropyl)-2-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol, 2,4-bis-(1-methyl-cyclopropyl)-5-trifluoromethoxy-phenol, 2-[1-(2,2,2-Trifluoro-ethyl)-cyclopropyl]-5-trifluoromethoxy-4-(1-trifluoromethyl-cyclopropyl)-phenol, 2-Isopropyl-5-trifluoromethoxy-4-(1-trifluoromethyl-cyclopropyl)-phenol, and 2-cyclopropyl-5-methoxy-4-(1-trifluoromethyl-cyclopropyl)-phenol.
93. The compound or pharmaceutically acceptable salt of Claim 91, wherein the compound is selected from the group consisting of 5-bromo-4-tert-butyl-2-methyl-phenol, 5-bromo-4-tert-butyl-

2-isopropyl-phenol, 4-tert-butyl-5-chloro-2-isopropyl-phenol, 4-tert-butyl-2-isopropyl-5-trifluoromethoxy-phenol, 5-bromo-2-(tert-butyl)-4-(1,1-difluoroethyl)phenol, 5-bromo-4-tert-butyl-2-cyclopropyl-phenol, 5-bromo-2-cyclopropyl-4-trifluoromethyl-phenol, 5-bromo-2-isopropyl-4-(1-trifluoromethyl-cyclopropyl)-phenol, 5-bromo-2-isopropyl-4-(1-methyl-cyclopropyl)-phenol, 5-bromo-2-isopropyl-4-(1-pentafluoroethyl-cyclopropyl)-phenol, 5-bromo-2-isopropyl-4-pentafluoroethyl-phenol, 5-bromo-2-isopropyl-4-(2,2,3,3,3-pentafluoro-propyl)-phenol, 5-bromo-2-isopropyl-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol, 5-fluoro-2,4-bis-(1-methyl-cyclopropyl)-phenol, 5-bromo-4-(1-methyl-cyclopropyl)-2-(1-trifluoromethyl-cyclopropyl)-phenol, 5-fluoro-4-(1-methyl-cyclopropyl)-2-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol, 2,4-bis-(1-methyl-cyclopropyl)-5-trifluoromethoxy-phenol, 2-[1-(2,2,2-Trifluoro-ethyl)-cyclopropyl]-5-trifluoromethoxy-4-(1-trifluoromethyl-cyclopropyl)-phenol, 2-Isopropyl-5-trifluoromethoxy-4-(1-trifluoromethyl-cyclopropyl)-phenol, and 2-cyclopropyl-5-methoxy-4-(1-trifluoromethyl-cyclopropyl)-phenol.

94. The method of any one of Claims 73–90 or 92 wherein the compound is deuterated.

95. The compound or pharmaceutically acceptable salt of Claim 91 or 93, wherein the compound is deuterated.

96. A method of treating a neurological or an inflammatory condition comprising administering a therapeutically effective amount of a compound or pharmaceutically acceptable salt of the compound, wherein the compound has a structure of Formula (IV):



wherein:

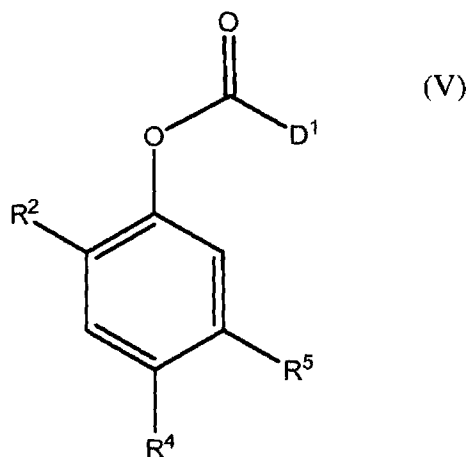
R¹ is selected from the group consisting of an ester, a carbonate, a phosphate, a carbamate, a sulfamate, and an acylmethylester;

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl, wherein the alkyl or haloalkyl is optionally substituted with one or more cycloalkyl substituents;

R^4 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl, wherein the alkyl or haloalkyl is optionally substituted with one or more cycloalkyl substituents, and wherein R^4 is not methyl; and

R^5 is selected from the group consisting of halo, and alkoxy, wherein the alkoxy may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl and halo.

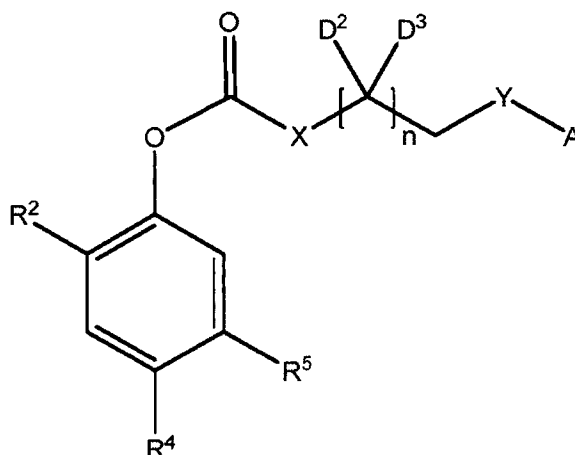
97. The method of Claim 96, wherein the compound has a structure of Formula (V):



wherein D^1 is alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroalkyl, heteroaryl, heteroaralkyl, carbonylalkyl, or phosphonooxyalkyl, optionally substituted with one or more substituents selected from the group consisting of alkyl, carboxylate, heteroalkyl, monocyclic ring, bicyclic ring, and hydroxyl moieties.

98. The method of Claim 97, wherein the compound has a structure of Formula (VI):

(VI)



wherein:

D^2 and D^3 together with the carbon atom to which they are bonded form a cycloalkyl or cycloheteroalkyl ring, or alternatively D^2 and D^3 are each independently selected from the group consisting of hydrogen, alkyl, and heteroalkyl;

A, Y, and one of D^2 or D^3 together with the atoms to which they are bonded to form a cycloheteroalkyl ring, or alternatively A is selected from the group consisting of hydrogen, phosphono, alkyl, aryl, arylalkyl, heteroalkyl, heteroaryl, and heteroarylalkyl;

X is selected from the group consisting of $-\text{ND}^4-$, $-\text{O}-$, $-\text{CH}_2-$, and $-\text{S}-$;

Y is selected from the group consisting of $-\text{O}-$ and $-\text{ND}^4-$;

n is an integer from 1 to 5; and

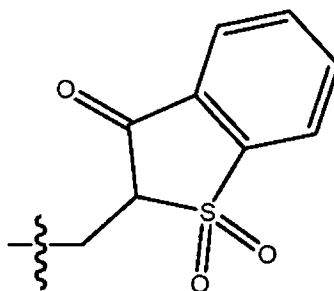
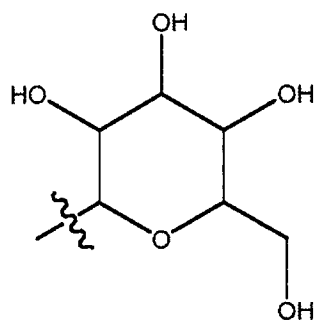
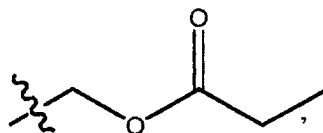
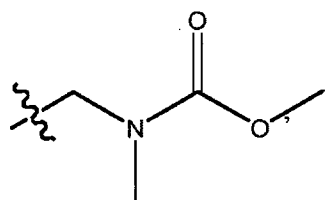
D^4 is selected from the group consisting of hydrogen, alkyl, and arylalkyl.

99. The method of Claim 98, wherein D^2 and D^3 are each hydrogen, X is $-\text{CH}_2-$, Y is $-\text{O}-$, A is phosphono, and $n=1$.

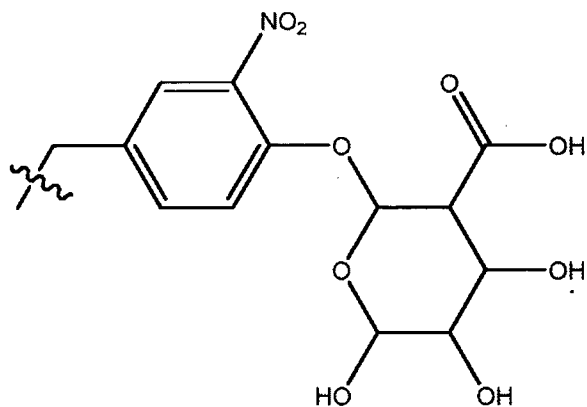
100. The method of Claim 96, wherein R^1 is selected from the group consisting of $-\text{P}-(\text{O})(\text{OD}^5)_2$, $-\text{CH}_2-\text{O}-\text{P}-(\text{O})(\text{OD}^5)_2$, $-(\text{CH}_2)_2-\text{O}-\text{P}-(\text{O})(\text{OD}^5)_2$, and $-\overset{\text{CH}_3}{\underset{|}{\text{CH}}}-\text{O}-\text{P}-(\text{O})(\text{OD}^5)_2$, and further wherein D^5 is H or a pharmaceutically acceptable cation.

101. The method of Claim 100, wherein the pharmaceutically acceptable cation is selected from the group consisting of Li^+ , Na^+ , and K^+ .

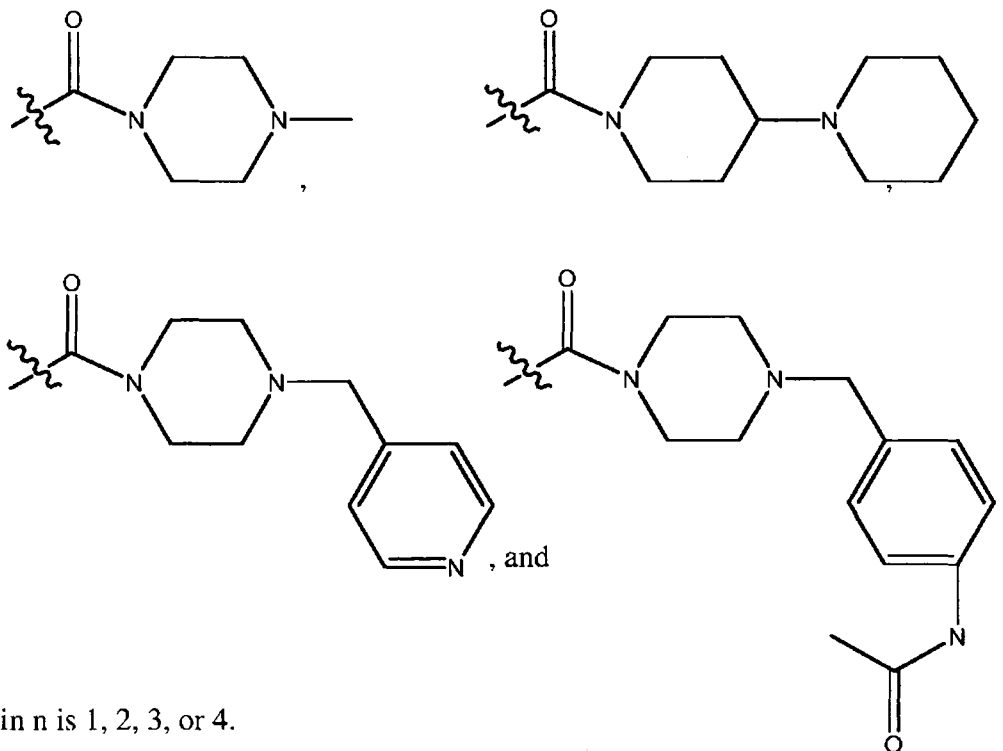
102. The method of Claim 96, wherein R^1 is selected from the group consisting of



, and



103. The method of Claim 96, wherein R^1 is selected from the group consisting of $-\text{CONHCH}_2(\text{CH}_2)_n\text{CH}_3$, $-\text{CON}(\text{CH}_3)_2$, $-\text{CON}(\text{C}_2\text{H}_5)_2$, $-\text{CON}(\text{CH}(\text{CH}_3)_2)_2$, $-\text{CONNH}_2$
 CH_3



wherein n is 1, 2, 3, or 4.

104. The method of Claim 24, wherein R^1 is $-\text{S}(=\text{O})_2\text{NH}_2$.

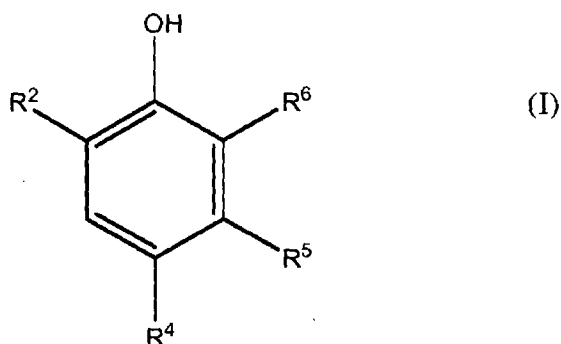
105. The method of any one of the previous claims wherein:

alkyl is selected from the group consisting of methyl, ethyl, propyl, isopropyl, butyl, isobutyl, *tert*-butyl, *sec*-butyl, pentanyl, isopentanyl, and neopentanyl;

haloalkyl is selected from the group consisting of fluoromethyl, 1-fluoroethyl, 2-fluoroethyl, 1-fluoropropyl, 2-fluoropropyl, 3-fluoropropyl, chloromethyl, 1-chloroethyl, 2-chloroethyl, 1-chloropropyl, 2-chloropropyl, 3-chloropropyl, bromomethyl, 1-bromoethyl, 2-bromoethyl, 1-bromopropyl, 2-bromopropyl, and 3-bromopropyl; and

cycloalkyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

106. A method of treating a neurological or an inflammatory condition comprising administering a therapeutically effective amount of a compound or pharmaceutically acceptable salt of the compound, wherein the compound has a structure of Formula (I):



wherein:

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl, wherein the alkyl or haloalkyl is optionally substituted with one or more cycloalkyl substituents;

R^4 is selected from the group consisting of H, halo, alkyl, alkoxy, haloalkyl, haloalkoxy and cycloalkyl, wherein alkyl or haloalkyl is optionally substituted with one or more cycloalkyl substituents, wherein alkoxy alkyl hydrogens may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl and halo, and wherein R^4 is not methyl;

R^5 is selected from the group consisting of alkyl, haloalkyl, cycloalkyl, halo, and alkoxy, wherein the alkoxy may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl and haloalkyl; and

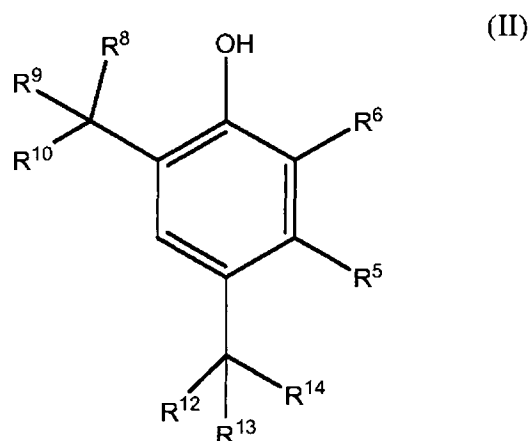
R^6 is halo.

107. The method of Claim 106, wherein each of R^2 , R^4 , and R^5 has between one and five carbons.

108. The method of Claim 106, wherein the condition is epilepsy, seizures, or convulsions.

109. The method of Claim 106, wherein the condition is neuropathic pain or fibromyalgia.

110. The method of Claim 106, wherein the condition is a psychological disorder.
111. The method of Claim 110, wherein the psychological disorder is anxiety, mania, bipolar disorder, or depression.
112. The method of Claim 106, wherein the condition is Alzheimer's Disease, Huntington's Disease, Multiple Sclerosis, Parkinson's disease, Tourette's Syndrome, tinnitus, and tremors.
113. The method of Claim 107, wherein R^2 and R^4 are not identical.
114. The method of Claim 107, wherein the compound has a structure of Formula (II):



wherein:

- R^5 is halo;
- R^6 is halo;
- R^8 , R^9 , and R^{10} are each independently selected from the group consisting of H, alkyl, halo, haloalkyl, cycloalkyl comprising R^8 and R^9 , and cycloalkyl comprising R^9 and R^{10} ; and
- R^{12} , R^{13} , and R^{14} are each independently selected from the group consisting of H, alkyl, halo, haloalkyl, cycloalkyl comprising R^{12} and R^{13} , and cycloalkyl comprising R^{13} and R^{14} .

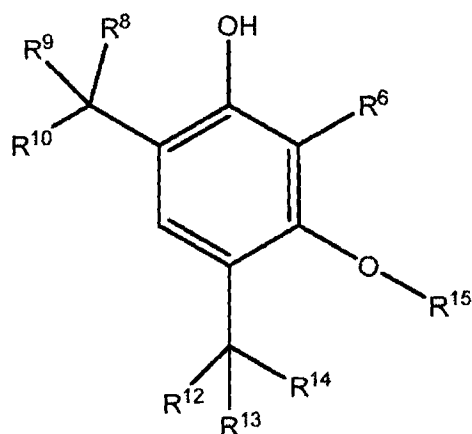
115. The method of Claim 113, wherein the compound has a structure of Formula (II), wherein:
- R^5 is halo;
 - R^6 is halo;
 - R^8 , R^9 , and R^{10} are each independently selected from the group consisting of H, alkyl, halo, haloalkyl, cycloalkyl comprising R^8 and R^9 , and cycloalkyl comprising R^9 and R^{10} ; and

R^{12} , R^{13} , and R^{14} are each independently selected from the group consisting of H, alkyl, halo, haloalkyl, cycloalkyl comprising R^{12} and R^{13} , and cycloalkyl comprising R^{13} and R^{14} .

116. The method of Claim 114, wherein halo is Br, Cl, or F.

117. The method of Claim 107, wherein the compound has a structure of Formula (III):

(III)



wherein:

R^6 is halo;

R^8 , R^9 , and R^{10} are each independently selected from the group consisting of H, alkyl, halo, haloalkyl, cycloalkyl comprising R^8 and R^9 , and cycloalkyl comprising R^9 and R^{10} ;

R^{12} , R^{13} , and R^{14} are each independently selected from the group consisting of H, alkyl, halo, haloalkyl, cycloalkyl comprising R^{12} and R^{13} , and cycloalkyl comprising R^{13} and R^{14} ; and

R^{15} is selected from the group consisting of methyl, trihalomethyl, and isopropyl.

118. The method of Claim 113, wherein the compound has a structure of Formula (III) and wherein:

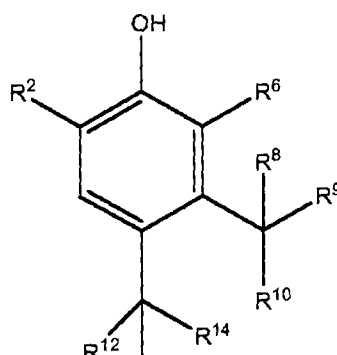
R^{15} is selected from the group consisting of methyl, trihalomethyl, and isopropyl;

R^8 , R^9 , and R^{10} are each independently selected from the group consisting of H, alkyl, halo, haloalkyl, cycloalkyl comprising R^8 and R^9 , and cycloalkyl comprising R^9 and R^{10} ; and

R^{12} , R^{13} , and R^{14} are each independently selected from the group consisting of H, alkyl, halo, haloalkyl, cycloalkyl comprising R^{12} and R^{13} , and cycloalkyl comprising R^{13} and R^{14} .

119. The method of Claim 117, wherein halo is bromo, chloro, or fluoro.
120. The method of Claim 114, wherein:
R¹² and R¹³ form a cycloalkyl moiety; and
R¹⁴ is selected from the group consisting of alkyl and haloalkyl.
121. The method of Claim 120, wherein:
R⁹ and R¹⁰ form a cycloalkyl moiety; and
R⁸ is selected from the group consisting of alkyl and haloalkyl.
122. The method of Claim 117, wherein:
R¹² and R¹³ form a cycloalkyl moiety; and
R¹⁴ is selected from the group consisting of alkyl and haloalkyl.
123. The method of Claim 122, wherein:
R⁹ and R¹⁰ form a cycloalkyl moiety; and
R⁸ is selected from the group consisting of alkyl and haloalkyl.
124. The method of Claim 108, wherein the compound is selected from the group consisting of the species of Table 1.
125. A compound or pharmaceutically acceptable salt of the compound, wherein the compound is selected from the group consisting of the species of Table 1.
126. The method of Claim 106, wherein the compound has a structure of Formula (IV):

(IV)



wherein:

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

R^6 is halo;

R^8 , R^9 , and R^{10} are each independently selected from the group consisting of H, alkyl, haloalkyl, cycloalkyl comprising R^8 and R^9 , and cycloalkyl comprising R^9 and R^{10} ; and

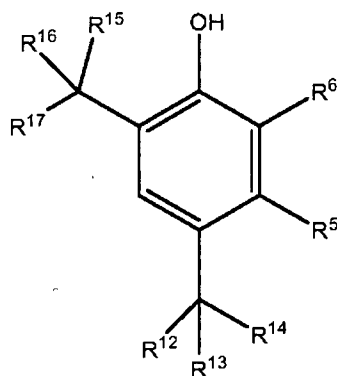
R^{12} , R^{13} , and R^{14} are each independently selected from the group consisting of H, alkyl, haloalkyl, cycloalkyl comprising R^{12} and R^{13} , and cycloalkyl comprising R^{13} and R^{14} .

127. The method of Claim 126, wherein halo is chloro, bromo, or fluoro.

128. The method of Claim 127, wherein the halo is fluoro.

129. The method of Claim 106, wherein the compound has a structure of Formula (V):

(V)



wherein:

R^5 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

R^6 is halo;

R^{12} and R^{13} form a cycloalkyl of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 carbons or R^{12} and R^{13} are each independently selected from the group consisting of H, alkyl, and haloalkyl;

R^{14} is selected from the group consisting of H, alkyl, and haloalkyl;

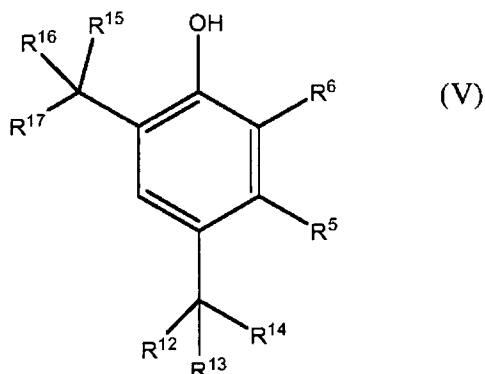
R^{15} and R^{16} form a cycloalkyl of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, or 14 carbons or R^{15} and R^{16} are each independently selected from the group consisting of H, alkyl, and haloalkyl; and

R^{17} is selected from the group consisting of H, alkyl, and haloalkyl.

130. The method of Claim 129, wherein halo is chloro, bromo, or fluoro.

131. The method of Claim 130, wherein the halo is fluoro.
132. The method of Claim 126, wherein:
R¹² and R¹³ form a cycloalkyl moiety; and
R¹⁴ is selected from the group consisting of alkyl and haloalkyl.
133. The method of Claim 129, wherein:
R¹² and R¹³ form a cycloalkyl moiety;
R¹⁵ and R¹⁶ form a cycloalkyl moiety; and
R¹⁴ and R¹⁷ are each independently selected from the group consisting of alkyl and haloalkyl.
134. The method of Claim 129, wherein the compound has a structure of Formula (V), and wherein:
R⁵ is selected from the group consisting of methyl and isopropyl;
R¹² is selected from the group consisting of H, halo, methyl, and cycloalkyl comprising R¹³;
R¹³ is selected from the group consisting of H, halo, methyl, trihalomethyl, and cycloalkyl comprising R¹²;
R¹⁴ is selected from the group consisting of halo, methyl, trihalomethyl and pentahaloethyl;
R¹⁵ is selected from the group consisting of H, methyl, and trihalomethyl.
R¹⁶ is selected from the group consisting of H and cycloalkyl comprising R¹⁷; and
R¹⁷ is selected from the group consisting of H, methyl, and cycloalkyl comprising R¹⁶.
135. The method of Claim 134, wherein the halo is chloro, bromo, or fluoro.
136. The method of Claim 135, wherein the halo is fluoro.
137. The method of Claim 135, wherein the compound is selected from the group consisting of the species of Table 2.

138. A compound or pharmaceutically acceptable salt of the compound, wherein the compound has a structure of Formula (V)



wherein:

R^5 is selected from the group consisting of methyl and isopropyl;

R^{12} is selected from the group consisting of H, halo, methyl, and cycloalkyl comprising R^{13} ;

R^{13} is selected from the group consisting of H, halo, methyl, trihalomethyl, and cycloalkyl comprising R^{12} ;

R^{14} is selected from the group consisting of halo, methyl, trihalomethyl and pentahaloethyl;

R^{15} is selected from the group consisting of H, methyl, and trihalomethyl.

R^{16} is selected from the group consisting of H and cycloalkyl comprising R^{17} ; and

R^{17} is selected from the group consisting of H, methyl, and cycloalkyl comprising R^{16} .

139. The compound or pharmaceutically acceptable salt of Claim 138, wherein the compound is selected from the group consisting of the species of Table 2.

140. The method of Claim 106, wherein:

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl; and

R^4 is halo.

141. The method of Claim 140, wherein:

R^4 is selected from the group consisting of Br, Cl, and F.

142. The method of Claim 141, wherein:

R^2 is alkyl; and

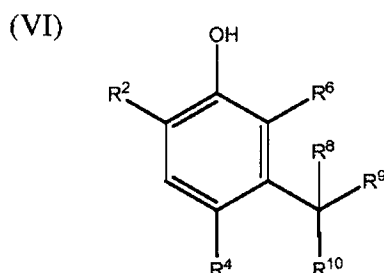
R^5 is alkyl having two or more carbons.

143. The method of Claim 142, wherein the compound is selected from the group consisting of 4-bromo-2-fluoro-3-isopropyl-6-methyl-phenol, 4-chloro-2-fluoro-3-isopropyl-6-methyl-phenol, 2,4-difluoro-3-isopropyl-6-methyl-phenol, 4-bromo-2-fluoro-3-isopropyl-6-trifluoromethyl-phenol, 4-bromo-2-fluoro-6-trifluoromethyl-3-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 4-bromo-6-cyclopropyl-2-fluoro-3-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 4-bromo-3-cyclopropyl-2-fluoro-6-methyl-phenol, 4-bromo-3-cyclopropyl-2-fluoro-6-trifluoromethyl-phenol, 4-bromo-3,6-dicyclopropyl-2-fluoro-phenol, 4-bromo-2-chloro-3-isopropyl-6-methyl-phenol, 2-fluoro-3-isopropyl-6-methyl-4-trifluoromethoxy-phenol, 2-bromo-3-isopropyl-6-methyl-4-trifluoro-methoxy-phenol, 2-chloro-3-isopropyl-6-methyl-4-trifluoromethoxy-phenol, 4-tert-butoxy-2-fluoro-3-isopropyl-6-methyl-phenol, 2-bromo-4-tert-butoxy-3-isopropyl-6-methyl-phenol, 4-bromo-3-(2,2-difluoro-1-methyl-ethyl)-2-fluoro-6-isopropyl-phenol, 4-bromo-2-fluoro-6-iso-propyl-3-pentafluoroethyl-phenol, 4-bromo-2-fluoro-6-isopropyl-3-(2,2,2-trifluoro-ethyl)-phenol, 4-bromo-3-ethyl-2-fluoro-6-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol, 4-bromo-2-fluoro-6-isopropyl-3-(2,2,2-trifluoro-1-trifluoromethyl-ethyl)-phenol, 4-bromo-2-fluoro-6-iso-propyl-3-(2,2,3,3,3-pentafluoro-propyl)-phenol, 2-fluoro-6-isopropyl-3-(2,2,3,3,3-pentafluoro-propyl)-4-trifluoro-methoxy-phenol, 2-fluoro-4-isopropoxy-6-isopropyl-3-(2,2,2-trifluoro-ethyl)-phenol, 2-fluoro-6-isopropyl-4-methoxy-3-(2,2,2-trifluoro-ethyl)-phenol, 3-ethyl-2-fluoro-6-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-4-trifluoro methoxy-phenol, 2-fluoro-6-isopropyl-4-methoxy-3-(2,2,2-trifluoro-ethyl)-phenol, 4-tert-butoxy-3-(2,2-difluoro-1-methyl-ethyl)-2-fluoro-6-isopropyl-phenol, 2-bromo-3-isopropyl-4-trifluoromethoxy-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 3-ethyl-2-fluoro-6-(2,2,2-trifluoro-ethyl)-4-trifluoro methoxy-phenol, 4-tert-butoxy-3-ethyl-2-fluoro-6-(2,2,2-trifluoro-ethyl)-phenol, and 3-ethyl-2-fluoro-4-isopropoxy-6-(2,2,2-trifluoro-ethyl)-phenol.

144. The method of Claim 108, wherein the compound is selected from the group consisting of 4-bromo-2-fluoro-3-isopropyl-6-methyl-phenol, 4-chloro-2-fluoro-3-isopropyl-6-methyl-phenol, 2,4-difluoro-3-isopropyl-6-methyl-phenol, 4-bromo-2-fluoro-3-isopropyl-6-trifluoromethyl-phenol, 4-bromo-2-fluoro-6-trifluoromethyl-3-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 4-bromo-6-cyclopropyl-2-fluoro-3-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 4-bromo-3-cyclopropyl-2-fluoro-6-methyl-phenol, 4-bromo-3,6-dicyclopropyl-2-fluoro-phenol, 2,4-dibromo-3-isopropyl-6-methyl-phenol, 4-bromo-2-chloro-3-isopropyl-6-methyl-phenol, 2,4-dichloro-3-isopropyl-6-methyl-phenol, 2,4-dibromo-3-isopropyl-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 4-bromo-3-(1,1-difluoroethyl)-

2-fluoro-6-isopropyl-phenol, 2-fluoro-6-isopropyl-3-(2,2,3,3,3-pentafluoro-propyl)-4-trifluoromethoxy-phenol, 2-fluoro-4-isopropoxy-6-isopropyl-3-(2,2,2-trifluoroethyl)-phenol, 2-fluoro-6-isopropyl-4-methoxy-3-(2,2,2-trifluoroethyl)-phenol, 4-tert-butoxy-3-ethyl-2-fluoro-6-(2,2,2-trifluoroethyl)-phenol, 2-fluoro-3-isopropyl-6-methyl-4-trifluoromethoxy-phenol, 2-bromo-3-isopropyl-6-methyl-4-trifluoromethoxy-phenol, and 2-chloro-3-isopropyl-6-methyl-4-trifluoromethoxy-phenol.

145. The method of Claim 106, wherein the compound has the structure of Formula (VI):



wherein:

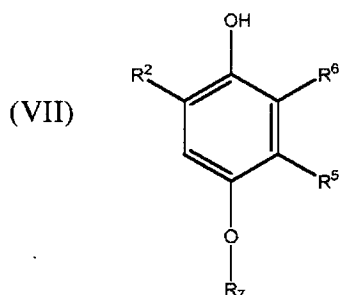
R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

R^4 is selected from the group consisting of Br, Cl, and F;

R^6 is halo; and

R^8 , R^9 and R^{10} are each independently selected from the group consisting of H, alkyl, and haloalkyl.

146. The method of Claim 106, wherein the compound has the structure of Formula (VII):



wherein:

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

R^5 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

R^6 is halo; and

R_7 is selected from the group consisting of alkyl and haloalkyl.

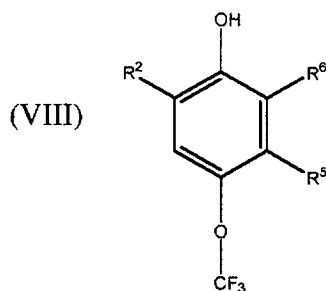
147. The method of Claim 145, wherein:

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

R^5 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl; and

R_7 is alkyl.

148. The method of Claim 146, wherein the compound has the structure of Formula (VIII):



wherein:

R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl;

R^5 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl; and

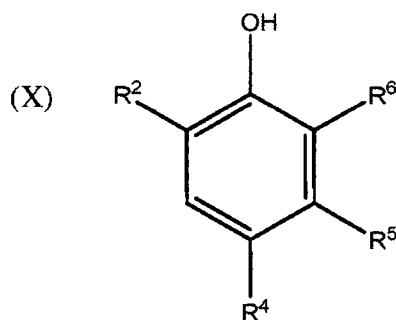
R^6 is halo.

149. The method of Claim 148, wherein:

R^2 is selected from the group consisting of alkyl and cycloalkyl; and

R^5 is selected from the group consisting of alkyl and cycloalkyl.

150. A compound or pharmaceutically acceptable salt of the compound, wherein the compound has the structure of Formula (X):



wherein:

R^2 is selected from the group consisting of methyl, cycloalkyl, and $-CF_3$;

R^4 is halo;

R^5 is selected from the group consisting of fluoroalkyl and a three, four, or five carbon cycloalkyl;

R^6 is halo; and

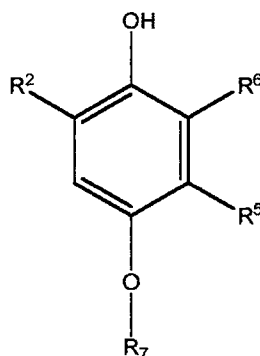
R^4 and R^6 are not both Br or both Cl.

151. The compound or pharmaceutically acceptable salt of Claim 150, wherein:

R^4 is selected from the group consisting of Br, Cl, and F.

152. A compound or pharmaceutically acceptable salt of the compound, wherein the compound has the structure of Formula (XI):

(XI)



wherein:

R^2 and R^5 are each independently selected from the group consisting of alkyl and cycloalkyl, wherein at least one of R^2 and R^5 is cycloalkyl;

R^6 is halo; and

R_7 is selected from the group consisting of isopropyl, *tert*-butyl, and haloalkyl.

153. The compound or pharmaceutically acceptable salt of Claim 152, wherein:

R_7 is selected from the group consisting of isopropyl and *tert*-butyl.

154. The compound or pharmaceutically acceptable salt of Claim 152, wherein:

R^2 is selected from the group consisting of alkyl, and cycloalkyl;

R^5 is selected from the group consisting of alkyl, and cycloalkyl; and

R^7 is trifluoromethyl.

155. The method of Claim 109, wherein:

R^2 and R^5 are each independently selected from the group consisting of methyl, isopropyl, and *tert*-butyl; and

R^4 and R^6 are each independently selected from the group consisting of Br, Cl, and F.

156. The compound or pharmaceutically acceptable salt of Claim 151, wherein the compound is selected from the group consisting of 4-bromo-2-fluoro-3-isopropyl-6-methyl-phenol, 4-chloro-2-fluoro-3-isopropyl-6-methyl-phenol, 2,4-difluoro-3-isopropyl-6-methyl-phenol, 4-bromo-2-fluoro-3-isopropyl-6-trifluoromethyl-phenol, 4-bromo-2-fluoro-6-trifluoromethyl-3-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 4-bromo-6-cyclopropyl-2-fluoro-3-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 4-bromo-3-cyclopropyl-2-fluoro-6-methyl-phenol, 4-bromo-3-cyclopropyl-2-fluoro-6-trifluoromethyl-phenol, 4-bromo-3,6-dicyclopropyl-2-fluoro-phenol, 4-bromo-2-chloro-3-isopropyl-6-methyl-phenol, 2-fluoro-3-isopropyl-6-methyl-4-trifluoromethoxy-phenol, 2-bromo-3-isopropyl-6-methyl-4-trifluoromethoxy-phenol, 2-chloro-3-isopropyl-6-methyl-4-trifluoromethoxy-phenol, 4-tert-butoxy-2-fluoro-3-isopropyl-6-methyl-phenol, 2-bromo-4-tert-butoxy-3-isopropyl-6-methyl-phenol, 4-bromo-3-(2,2-difluoro-1-methyl-ethyl)-2-fluoro-6-isopropyl-phenol, 4-bromo-2-fluoro-6-isopropyl-3-pentafluoroethyl-phenol, 4-bromo-2-fluoro-6-isopropyl-3-(2,2,2-trifluoro-ethyl)-phenol, 4-bromo-3-ethyl-2-fluoro-6-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol, 4-bromo-2-fluoro-6-isopropyl-3-(2,2,2-trifluoro-1-trifluoromethyl-ethyl)-phenol, 4-bromo-2-fluoro-6-isopropyl-3-(2,2,3,3,3-pentafluoro-propyl)-phenol, 2-fluoro-6-isopropyl-3-(2,2,3,3,3-pentafluoro-propyl)-4-trifluoromethoxy-phenol, 2-fluoro-4-isopropoxy-6-isopropyl-3-(2,2,2-trifluoro-ethyl)-phenol, 2-fluoro-6-isopropyl-4-methoxy-3-(2,2,2-trifluoro-ethyl)-phenol, 3-ethyl-2-fluoro-6-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-4-trifluoromethoxy-phenol, 2-fluoro-6-isopropyl-4-methoxy-3-(2,2,2-trifluoro-ethyl)-phenol, 4-tert-butoxy-3-(2,2-difluoro-1-methyl-ethyl)-2-fluoro-6-isopropyl-phenol, 2-bromo-3-isopropyl-4-trifluoromethoxy-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 3-ethyl-2-fluoro-6-(2,2,2-trifluoro-ethyl)-4-trifluoromethoxy-phenol, 4-tert-butoxy-3-ethyl-2-fluoro-6-(2,2,2-trifluoro-ethyl)-phenol, and 3-ethyl-2-fluoro-4-isopropoxy-6-(2,2,2-trifluoro-ethyl)-phenol.

157. The compound or pharmaceutically acceptable salt of Claim 156, wherein the compound is selected from the group consisting of 4-bromo-2-fluoro-3-isopropyl-6-methyl-phenol, 4-chloro-2-fluoro-3-isopropyl-6-methyl-phenol, 2,4-difluoro-3-isopropyl-6-methyl-phenol, 4-bromo-2-fluoro-3-isopropyl-6-trifluoromethyl-phenol, 4-bromo-2-fluoro-6-trifluoromethyl-3-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 4-bromo-6-cyclopropyl-2-fluoro-3-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 4-bromo-3-cyclopropyl-2-fluoro-6-methyl-phenol, 4-bromo-3,6-dicyclopropyl-2-fluoro-phenol, 4-bromo-2-chloro-3-isopropyl-6-methyl-phenol, 2,4-dibromo-3-isopropyl-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 4-bromo-3-(1,1-difluoroethyl)-2-fluoro-6-isopropyl-phenol, 2-fluoro-6-isopropyl-3-

(2,2,3,3,3-pentafluoro-propyl)-4-trifluoromethoxy-phenol, 2-fluoro-4-isopropoxy-6-isopropyl-3-(2,2,2-trifluoroethyl)-phenol, 2-fluoro-6-isopropyl-4-methoxy-3-(2,2,2-trifluoroethyl)-phenol, 4-tert-butoxy-3-ethyl-2-fluoro-6-(2,2,2-trifluoro-ethyl)-phenol, 2-fluoro-3-isopropyl-6-methyl-4-trifluoromethoxy-phenol, 2-bromo-3-isopropyl-6-methyl-4-trifluoromethoxy-phenol, and 2-chloro-3-isopropyl-6-methyl-4-trifluoromethoxy-phenol.

158. The method of Claim 108, wherein the compound is selected from the group consisting of 4-tert-butyl-2-fluoro-6-isopropyl-3-methyl-phenol, 4-tert-butyl-2-fluoro-6-isopropyl-3-trifluoromethyl-phenol, 2-fluoro-6-isopropyl-3-methyl-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol, 2-bromo-6-isopropyl-3-methyl-4-trifluoromethyl-phenol, 4-tert-butyl-6-cyclopropyl-2-fluoro-3-trifluoromethyl-phenol, 2-fluoro-6-isopropyl-3-methyl-4-(1-methyl-cyclopropyl)-phenol, 2-fluoro-6-isopropyl-3-methyl-4-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol, 2-fluoro-6-isopropyl-3-methyl-4-(1-pentafluoroethyl-cyclopropyl)-phenol, 2-fluoro-3-methyl-4-(2,2,3,3,3-pentafluoro-propyl)-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 2-fluoro-3-methyl-4-pentafluoroethyl-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 3-cyclopropyl-2-fluoro-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-6-(1-trifluoromethyl-cyclopropyl)-phenol, 2-fluoro-3-methyl-4,6-bis-(1-methyl-cyclopropyl)-phenol, 2-fluoro-3-methyl-4-(1-methyl-cyclopropyl)-6-(1-trifluoromethyl-cyclopropyl)-phenol, 2-fluoro-3-methyl-4,6-bis-(1-trifluoromethyl-cyclopropyl)-phenol, and 2-fluoro-3-methyl-6-(1-methyl-cyclopropyl)-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol.

159. The compound or pharmaceutically acceptable salt of Claim 139, wherein the compound is selected from the group consisting of 4-tert-butyl-2-fluoro-6-isopropyl-3-methyl-phenol, 4-tert-butyl-2-fluoro-6-isopropyl-3-trifluoromethyl-phenol, 2-fluoro-6-isopropyl-3-methyl-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol, 2-bromo-6-isopropyl-3-methyl-4-trifluoromethyl-phenol, 4-tert-butyl-6-cyclopropyl-2-fluoro-3-trifluoromethyl-phenol, 2-fluoro-6-isopropyl-3-methyl-4-(1-methyl-cyclopropyl)-phenol, 2-fluoro-6-isopropyl-3-methyl-4-[1-(2,2,2-trifluoro-ethyl)-cyclopropyl]-phenol, 2-fluoro-6-isopropyl-3-methyl-4-(1-pentafluoroethyl-cyclopropyl)-phenol, 2-fluoro-3-methyl-4-(2,2,3,3,3-pentafluoro-propyl)-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 2-fluoro-3-methyl-4-pentafluoroethyl-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 3-cyclopropyl-2-fluoro-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-6-(1-trifluoromethyl-cyclopropyl)-phenol, 2-fluoro-3-methyl-4,6-bis-(1-methyl-cyclopropyl)-phenol, 2-fluoro-3-methyl-4-(1-methyl-cyclopropyl)-6-(1-trifluoro-

methyl-cyclopropyl)-phenol, 2-fluoro-3-methyl-4,6-bis-(1-trifluoromethyl-cyclopropyl)-phenol, and 2-fluoro-3-methyl-6-(1-methyl-cyclopropyl)-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol.

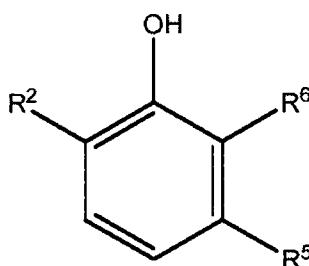
160. The method of Claim 108, wherein the compound is selected from the group consisting of 3-bromo-4-tert-butyl-2-fluoro-6-isopropyl-phenol, 4-tert-butyl-3-chloro-2-fluoro-6-isopropyl-phenol, 4-tert-butyl-2,3-difluoro-6-isopropyl-phenol, 3-bromo-6-cyclopropyl-2-fluoro-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol, 3-bromo-2-fluoro-6-isopropyl-4-trifluoromethyl-phenol, 3-bromo-2-fluoro-6-isopropyl-4-(1-methyl-cyclopropyl)-phenol, 3-bromo-2-fluoro-6-isopropyl-4-(1-trifluoromethyl-cyclopropyl)-phenol, 3-bromo-6-cyclopropyl-2-fluoro-4-(1-trifluoromethyl-cyclopropyl)-phenol, 4-tert-butyl-2-fluoro-6-isopropyl-3-trifluoromethoxy-phenol, 3-tert-butoxy-2-fluoro-6-isopropyl-4-trifluoromethyl-phenol, 2-fluoro-6-isopropyl-4-(1-methyl-cyclopropyl)-3-trifluoromethoxy-phenol, 3-bromo-2-fluoro-4-pentafluoroethyl-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 3-bromo-2-fluoro-4-pentafluoroethyl-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 3-bromo-2-fluoro-6-isopropyl-4-(2,2,3,3,3-pentafluoro-propyl)-phenol, 3-bromo-2-fluoro-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-6-(1-trifluoromethyl-cyclopropyl)-phenol, 3-bromo-2-fluoro-4-(1-methyl-cyclopropyl)-6-(1-trifluoromethyl-cyclopropyl)-phenol, 3-bromo-2-fluoro-6-(1-methyl-cyclopropyl)-4-(1-trifluoromethyl-cyclopropyl)-phenol, 3-bromo-2-fluoro-4,6-bis-(1-trifluoromethyl-cyclopropyl)-phenol, 3-bromo-2-fluoro-6-(1-methyl-cyclopropyl)-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol, and 3-bromo-2-fluoro-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-6-(1-trifluoromethyl-cyclopropyl)-phenol.

161. The compound or pharmaceutically acceptable salt of Claim 125, wherein the compound is selected from the group consisting of 3-bromo-4-tert-butyl-2-fluoro-6-isopropyl-phenol, 4-tert-butyl-3-chloro-2-fluoro-6-isopropyl-phenol, 4-tert-butyl-2,3-difluoro-6-isopropyl-phenol, 3-bromo-6-cyclopropyl-2-fluoro-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol, 3-bromo-2-fluoro-6-isopropyl-4-trifluoromethyl-phenol, 3-bromo-2-fluoro-6-isopropyl-4-(1-methyl-cyclopropyl)-phenol, 3-bromo-2-fluoro-6-isopropyl-4-(1-trifluoromethyl-cyclopropyl)-phenol, 3-bromo-6-cyclopropyl-2-fluoro-4-(1-trifluoromethyl-cyclopropyl)-phenol, 4-tert-butyl-2-fluoro-6-isopropyl-3-trifluoromethoxy-phenol, 3-tert-butoxy-2-fluoro-6-isopropyl-4-trifluoromethyl-phenol, 2-fluoro-6-isopropyl-4-(1-methyl-cyclopropyl)-3-trifluoromethoxy-phenol, 3-bromo-2-fluoro-4-pentafluoroethyl-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 3-bromo-2-fluoro-4-pentafluoroethyl-6-(2,2,2-trifluoro-1-methyl-ethyl)-phenol, 3-bromo-2-fluoro-6-isopropyl-4-(2,2,3,3,3-pentafluoro-propyl)-phenol, 3-bromo-2-fluoro-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-6-(1-trifluoromethyl-cyclopropyl)-phenol, 3-bromo-2-

fluoro-4-(1-methyl-cyclopropyl)-6-(1-trifluoromethyl-cyclopropyl)-phenol, 3-bromo-2-fluoro-6-(1-methyl-cyclopropyl)-4-(1-trifluoromethyl-cyclopropyl)-phenol, 3-bromo-2-fluoro-4,6-bis-(1-trifluoromethyl-cyclopropyl)-phenol, 3-bromo-2-fluoro-6-(1-methyl-cyclopropyl)-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-phenol, and 3-bromo-2-fluoro-4-(2,2,2-trifluoro-1,1-dimethyl-ethyl)-6-(1-trifluoromethyl-cyclopropyl)-phenol.

162. A compound or pharmaceutically acceptable salt of the compound, wherein the compound has the structure of Formula (IX):

(IX)



wherein:

R^2 is selected from the group consisting of haloalkyl and cycloalkyl;

R^5 is selected from the group consisting of haloalkyl and cycloalkyl; and

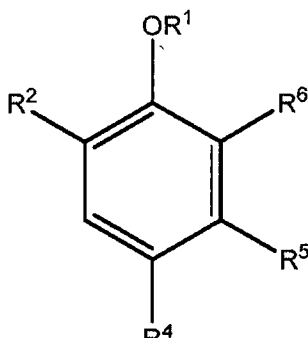
R^6 is halo.

163. The method of any one of Claims 106–124, 126–137, 140–148, 155, 158, or 160, wherein the compound is deuterated.

164. The compound or pharmaceutically acceptable salt of any one of Claims 125, 138, 139, 149–154, or 156–161 wherein the compound is deuterated.

165. A method of treating a neurological or an inflammatory condition comprising administering a therapeutically effective amount of a compound or pharmaceutically acceptable salt of the compound, wherein the compound has a structure of Formula (XII):

(XII)



wherein:

R^1 is selected from the group consisting of an ester, a carbonate, a phosphate, a carbamate, a sulfamate, and an acylmethylester;

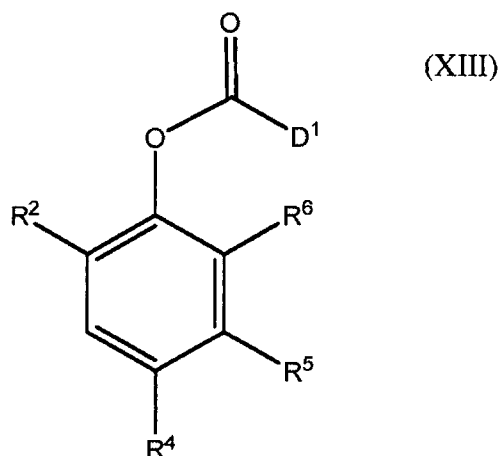
R^2 is selected from the group consisting of alkyl, haloalkyl, and cycloalkyl, wherein the alkyl or haloalkyl is optionally substituted with one or more cycloalkyl substituents;

R^4 is selected from the group consisting of H, halo, alkyl, alkoxy, haloalkyl, haloalkoxy and cycloalkyl, wherein alkyl or haloalkyl is optionally substituted with one or more cycloalkyl substituents, wherein alkoxy alkyl hydrogens may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl and halo, and wherein R^4 is not methyl;

R^5 is selected from the group consisting of alkyl, haloalkyl, cycloalkyl, halo, and alkoxy, wherein the alkoxy may be optionally substituted with one or more substituents independently selected from the group consisting of alkyl and haloalkyl; and

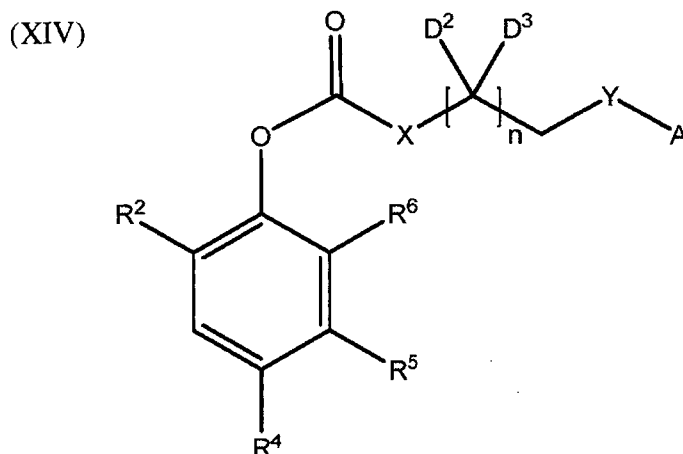
R^6 is halo.

166. The method of Claim 165, wherein the compound has a structure of Formula (XIII):



wherein D^1 is alkyl, aryl, cycloalkyl, heterocycloalkyl, heteroalkyl, heteroaryl, heteroaralkyl, carbonylalkyl, or phosphonoxyalkyl, optionally substituted with one or more substituents selected from the group consisting of alkyl, carboxylate, heteroalkyl, monocyclic ring, bicyclic ring, and hydroxyl moieties.

167. The method of Claim 166, wherein the compound has a structure of Formula (XIV):



wherein:

D^2 and D^3 together with the carbon atom to which they are bonded form a cycloalkyl or cycloheteroalkyl ring, or alternatively D^2 and D^3 are each independently selected from the group consisting of hydrogen, alkyl, and heteroalkyl;

A , Y , and one of D^2 or D^3 together with the atoms to which they are bonded to form a cycloheteroalkyl ring, or alternatively A is selected from the group consisting of hydrogen, phosphono, alkyl, aryl, arylalkyl, heteroalkyl, heteroaryl, and heteroarylalkyl;

X is selected from the group consisting of $—ND^4—$, $—O—$, $—CH_2—$, and $—S—$;

Y is selected from the group consisting of $—O—$ and $—ND^4—$;

n is an integer from 1 to 5; and

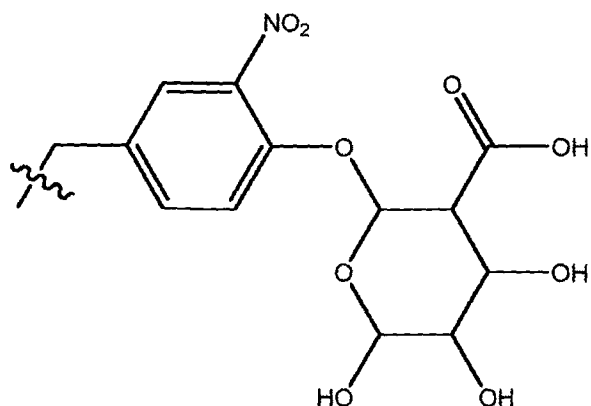
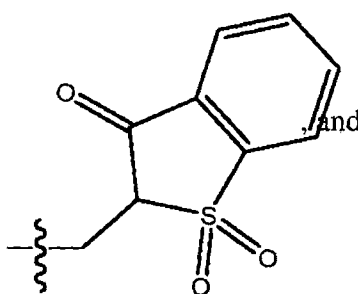
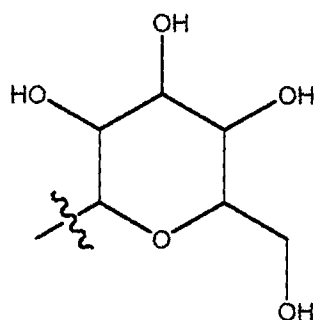
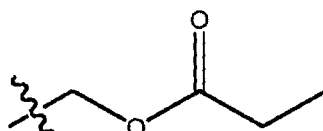
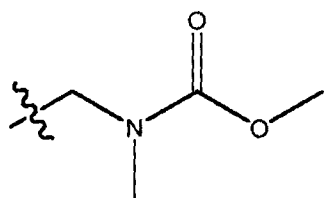
D^4 is selected from the group consisting of hydrogen, alkyl, and arylalkyl.

168. The method of Claim 167, wherein D^2 and D^3 are each hydrogen, X is $—CH_2—$, Y is $—O—$, A is phosphono, and $n=1$.

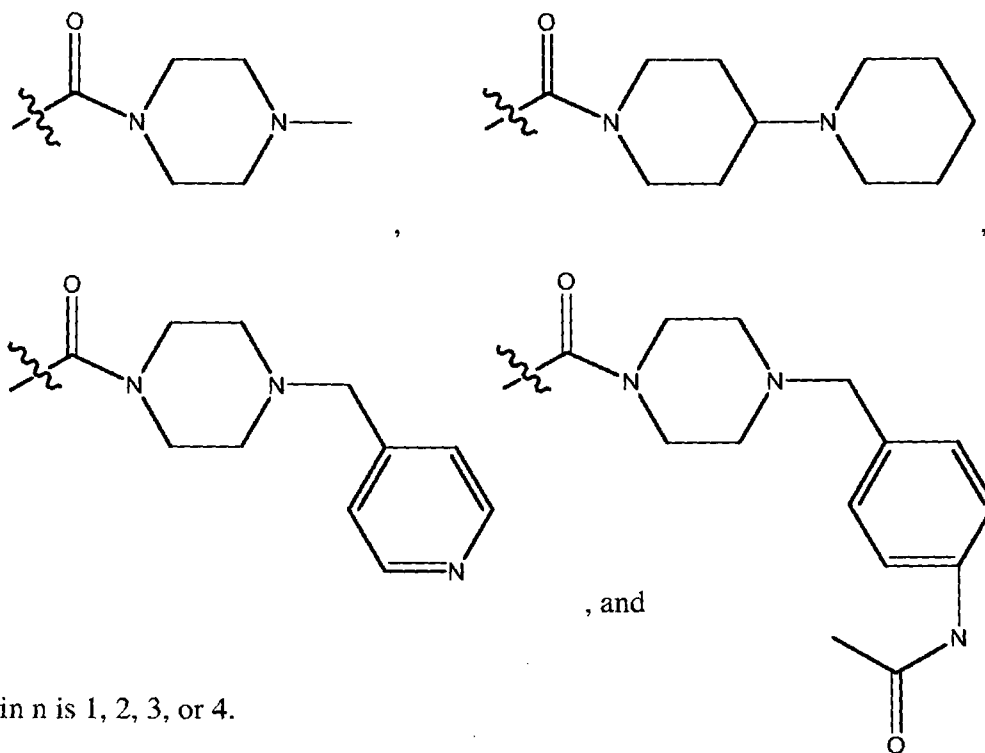
169. The method of Claim 165, wherein R^1 is selected from the group consisting of $-P-(O)(OD^5)_2$, $-CH_2-O-P-(O)(OD^5)_2$, $-(CH_2)_2-O-P-(O)(OD^5)_2$, and $-CH_2-O-P-(O)(OD^5)_2$, and further wherein D^5 is H or a pharmaceutically acceptable cation.

170. The method of Claim 169, wherein the pharmaceutically acceptable cation is selected from the group consisting of Li^+ , Na^+ , and K^+ .

171. The method of Claim 165, wherein R^1 is selected from the group consisting of



172. The method of Claim 165, wherein R^1 is selected from the group consisting of $-\text{CONHCH}_2(\text{CH}_2)_n\text{CH}_3$, $-\text{CON}(\text{CH}_3)_2$, $-\text{CON}(\text{C}_2\text{H}_5)_2$, $-\text{CON}(\text{CH}(\text{CH}_3)_2)_2$, $-\text{CON}(\text{NHCH}_3)_2$, and



wherein n is 1, 2, 3, or 4.

173. The method of Claim 165, wherein R^1 is $-\text{SO}_2\text{NH}_2$.

174. The method of any one of the previous claims wherein:

alkyl is selected from the group consisting of methyl, ethyl, propyl, isopropyl, butyl, isobutyl, *tert*-butyl, *sec*-butyl, pentanyl, isopentanyl, and neopentanyl;

haloalkyl is selected from the group consisting of fluoromethyl, 1-fluoroethyl, 2-fluoroethyl, 1-fluoropropyl, 2-fluoropropyl, 3-fluoropropyl, chloromethyl, 1-chloroethyl, 2-chloroethyl, 1-chloropropyl, 2-chloropropyl, 3-chloropropyl, bromomethyl, 1-bromoethyl, 2-bromoethyl, 1-bromopropyl, 2-bromopropyl, and 3-bromopropyl; and

cycloalkyl is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 15/32876

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61K 31/05; C07C 39/04 (2015.01)

CPC - C07C 39/04; A61K 31/05

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(8): A61K 31/05; C07C 39/04 (2015.01)

CPC: C07C 39/04; A61K 31/05

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC: 568/700Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
PatBase; Keyword limited: phenols, neurological, inflammatory, disease/disorder/condition, anticonvulsant/anti-convulsant, epilepsy

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- Y -- A	US 2003/0176513 A1 (BAKER, MT et al.) 18 September 2003 (18.09.2003), entire document, especially: para [0011]; para [0012]; para [0101]; para [0116]; para [0131]; para [0155].	1-3, 5-7, 13-21, 24-25, 40-42, 44-52, 55-58, 59-60, 62-63, 73-75, 77-86, 91, 94, 106-108, 110-119, 125-131, 134-139, 143-154, 156-157, 162-164 ----- 4, 8-12, 22-23, 26-27, 29, 43, 76, 109, 124, 140-142, 155 ----- 30-38, 53-54, 64-71, 87-90, 92-93, 96-104, 120-123, 132-133, 158-161, 165-173 ----- 17 -----
X -- A	PubChem-CID-21531491, Create Date: 2007-12-05 (05.12.2007), pg 3, Fig	30-38, 53-54, 64-71, 87-90, 92-93, 96-104, 120-123, 132-133, 158-161, 165-173

☒ Further documents are listed in the continuation of Box C.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

22 October 2015 (22.10.2015)

Date of mailing of the international search report

27 NOV 2015

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents
P.O. Box 1450, Alexandria, Virginia 22313-1450

Facsimile No. 571-273-8300

Authorized officer:

Lee W. Young

PCT Helpdesk: 571-272-4300
PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 15/32876

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

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

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

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

3. ☒ Claims Nos.: 28, 39, 72, 105 and 174
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

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

This International Searching Authority found multiple inventions in this international application, as follows:
--Please see attached sheet--

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

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

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☒ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 15/32876

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X -- A	✓ PubChem-CID-82266122, Create Date: 2014-10-20 (20.10.2014), pg 3, Fig	18 ----- 30-38, 53-54, 64-71, 87-90, 92-93, 96-104, 120-123, 132-133, 158-161, 165-173
X -- A	✓ PubChem-CID-57426115, Create Date: 2012-08-08 (08.08.2012), pg 3, Fig	19-20 ----- 30-38, 53-54, 64-71, 87-90, 92-93, 96-104, 120-123, 132-133, 158-161, 165-173
X -- A	✓ PubChem-CID-68855429, Create Date: 2012-11-30 (30.11.2012), pg 3, Fig	21 ----- 30-38, 53-54, 64-71, 87-90, 92-93, 96-104, 120-123, 132-133, 158-161, 165-173
X -- A	✓ PubChem-CID-21446494, Create Date: 2007-12-05 (05.12.2007), pg 3, Fig	59 ----- 30-38, 53-54, 64-71, 87-90, 92-93, 96-104, 120-123, 132-133, 158-161, 165-173
X -- A	✓ PubChem-CID-10364, Create Date: 2005-03-26 (26.03.2005), pg 3, Fig	60, 61, 91, 95, 125 ----- 30-38, 53-54, 64-71, 87-90, 92-93, 96-104, 120-123, 132-133, 158-161, 165-173
Y -- A	US 2007/0141113 A1 (BEZWADA, RS et al.) 21 Jun 2007 (21.06.2007), entire document, especially: para [0003]; para [0068]; para [0169]	4,43,76,109, 155 ----- 30-38, 53-54, 64-71, 87-90, 92-93, 96-104, 120-123, 132-133, 158-161, 165-173
Y -- A	US 6,358,995 B1 (TAGAMI, K et al.) 19 March 2002 (19.03.2002), entire document, especially: col 13, ln 1-30; col 29, ln 1-10, 4-fluoro-2,5-dimethylphenol; col 31, ln 6-18, 2,5-diethyl-4-fluorophenol	8-12, 22-23, 26-27, 29, 124, 140-142 ----- 30-38, 53-54, 64-71, 87-90, 92-93, 96-104, 120-123, 132-133, 158-161, 165-173
A	✓ PubChem-CID-47199322, Deposit Date: 2008-02-08 (08.02.2008), pg 3, Fig	30-38, 53-54, 64-71, 87-90, 92-93, 96-104, 120-123, 132-133, 158-161, 165-173

Attachment to Box.No.III:

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

Group I: Claims 1-7 (in part), 8-18, 22-27, 29-38, 40-70, 70a, 71, 73-104 and 162 directed to a method of treating a neurological or an inflammatory disease comprising administering a therapeutically effective amount of a tetra-substituted phenol compound, and to said tetra-substituted phenol compounds, where the phenyl ring contains four substituents including the phenolic OH.

Group II: Claims 1-7 (in part) and 19-21, directed to a method of treating a neurological or an inflammatory disease comprising administering a therapeutically effective amount of a tri-substituted phenol compound, and to said tri-substituted phenol compound, where the phenyl ring contains three substituents including the phenolic OH.

Group III: Claims 106-161, 163-173, directed to a method of treating a neurological or an inflammatory disease comprising administering a therapeutically effective amount of a penta-substituted phenol compound, and to said penta-substituted phenol compounds, where the phenyl ring contains five substituents including the phenolic OH.

The groups of inventions listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Special Technical Features:

Group I includes the technical feature of a tetra-substituted phenol compound, which is not required in groups II and III.

Group II includes the technical feature of a tri-substituted phenol compound, not required in Groups I and III.

Group III includes the technical feature of a penta-substituted phenol compound, not required by Groups I and II.

Common technical features:

The inventions of Groups I-III share the technical feature of a poly-substituted phenol compound.

Groups I -III further share the technical feature of a method of treating a neurological or an inflammatory disease comprising administering a therapeutically effective amount of a poly-substituted phenol compound,

These shared technical features do not provide a contribution over the prior art as being anticipated by US 2003/0176513 A1 to Baker et al. (hereinafter 'Baker') which discloses a method of treating a neurological or an inflammatory condition (para [0011], [0116]) comprising administering a therapeutically effective amount of a compound wherein the compound has the structure of Formula (I) wherein R2 is alkyl and R4 is H; and R5 is haloalkyl (para [0155]).

As said method and poly-substituted phenol compound were known in the art at the time of the invention, these cannot be considered special technical features, that would otherwise unify the inventions of Group I-III.

The inventions of Group I-III, therefore, lack unity under PCT Rule 13.

Note reg. Item 4: Claims 28, 39, 72, 105 and 174 are unsearchable because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a). These claims are, therefore, not included in the above analysis.

Note: The claim following Claim 70 has been marked in the application as claim 40. For the purposes of this analysis the claim following claim 70 and preceding claim 71 is numbered claim 70a.