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(54) Title: MONOTERPENOID/PHENYLPROPANOID-CONTAINING COMPOUNDS AND METHODS OF THEIR MAKING AND USE AS HERBICIDES

(57) Abstract: Disclosed are compounds having a monoterpenoid and/or phenylpropanoid moiety and methods of their making and use as pesticidal compounds, such as herbicides.

MONOTERPENOID/PHENYLPROPANOID-CONTAINING COMPOUNDS AND METHODS OF THEIR MAKING AND USE AS HERBICIDES

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This patent application claims the benefit of US Provisional Patent Application No. 62/378,541, filed August 23, 2016. The entire disclosures of the above-identified prior provisional patent application and all other concurrently filed non-provisional patent applications claiming the benefit from the provisional application are incorporated herein by reference.

BACKGROUND

[0002] The disclosed embodiments relate to compounds having a monoterpenoid and/or phenylpropanoid moiety and methods of their making and use.

[0003] Many plant essential oils contain monoterpene or monoterpenoid compounds, some of which are insecticidal. Their potency is typically less than for conventional synthetic insecticides, but they are just as effective at causing insect mortality or control when a sufficient dose is delivered to the pest.

[0004] Monoterpenoids have been demonstrated to possess various properties that allow them to manipulate various biological systems. These compounds have been demonstrated to be insecticidal, bactericidal, fungicidal, and herbicidal. The utility of select derivatives of monoterpenoids as potential herbicides are disclosed herein. These compounds kill plants via other mechanisms than those described in other patents that describe the utility of monoterpenoids as herbicides. Moreover, these compounds are selective toward dicotyledon species of plants, which makes their utility and value in the current market significant.

[0005] The disclosed embodiments are believed to overcome one or more deficiencies in the art.

SUMMARY

[0006] One aspect of the disclosed embodiments relates to a compound of formula (I):

$$R_1—A$$

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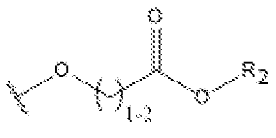

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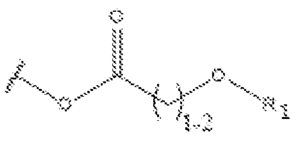


;

[0007] R_1 is a phenylpropanoid or monoterpenoid moiety;

[0008] R2 is a phenylpropanoid or monoterpenoid moiety or is selected from the group consisting of H, M, substituted or unsubstituted C3-C7 unbranched or branched alkyl, substituted or unsubstituted C2-C7 unbranched or branched alkenyl, substituted or unsubstituted C3-C7 unbranched or branched alkynyl, substituted or unsubstituted C3-C7 unbranched or branched cycloalkyl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted C3-C7 unbranched or branched cycloalkenyl; and

[0009] M is a counterion selected from the group consisting of sodium, potassium, calcium, magnesium, iron, zinc, copper, and an amine;

[0010] According to an example embodiment, the principal monoterpenoid and phenylpropanoid molecules employed are thymol, eugenol, isoeugenol, geraniol, menthol, citronellol, geraniol, linalool, cinnamic alcohol, vanillic acid, syringic acid, and carvacrol. 2-(2-formylphenoxy) acetic acid, salicylic acid, methyl salicylate, ferulic acid, p-coumaric acid, umbelliferone, piceol are also relevant starting materials that are considered monoterpenoids in accordance with the disclosed embodiments.

[0011] The disclosed embodiments exhibit toxicity as systemic herbicides for killing or controlling unwanted vegetation, etc. Moreover, these herbicides are selective toward dicotyledon plant species and are effective against a wide variety of pest plant species. These compounds represent herbicidal chemistry that is less residual than currently available herbicides on the market. By utilizing natural compounds for the production of herbicidal compounds, safer pesticidal formulations may be brought to market.

BRIEF DESCRIPTION OF THE DRAWINGS

[0012] FIG. 1 is a graph demonstrating the efficacy of various monoterpenoid-oxyacetic acids to inhibit the germination of corn seeds treated with these compounds at a rate of 1% weight compound/weight seed. Numerous compounds were capable of inhibiting the germination of corn seedlings in this assay.

[0013] FIG. 2 is a graph demonstrating the efficacy of various compounds to inhibit the growth of soybeans coated in 1% weight compound/weight bean. Three compounds, thymyloxyacetic acid, eugenyloxyacetic acid, and carvacryloxyacetic acid, prevented the growth of soybeans in this assay. Vanillyloxyacetic acid is a representative compound that does not produce significant inhibition of plant growth when beans are treated with this compound.

[0014] FIG. 3 is a representation of 1-month old soybean plants that have been exposed to a foliar spray of 1% thymyloxyacetic acid, 14 days after exposure. Treated plants exhibit signs of both significant chlorosis and wilting. It is possible that at higher concentrations of thymyloxyacetic acid, significant mortality could be achieved. There was no apparent differences in wilting and chlorosis between the high-intensity and low-intensity light groups, indicating that thymyloxyacetic acid exerts its phytotoxicity via a different mode of action than other terpenoids. New growth was observed in the low intensity light group. This is most likely due to the lack of light and not a consequence of the treatment. Control plants did not experience any negative effects associated with the high-intensity/low-intensity light environments.

[0015] FIG. 4 Is a representation of wood sorrel treated with 20 sprays of 1% carvacryloxyacetic acid or 1% 2,4-dichlorophenoxyacetic acid from a MAINStays™ ironing spray bottle, observed 2 days after exposure. The 1% carvacryloxyacetic acid caused a more immediate phytotoxic effect than the 2,4-dichlorophenoxyacetic acid. Plants treated with 2,4-dichloroacetic acid at this rate experienced uncontrolled growth and some chlorosis. Carvacryloxyacetic acid caused immediate and widespread chlorosis followed by relatively quick plant death. Plants took much longer to die from 2,4-dichlorophenoxyacetic acid.

[0016] FIG. 5 is a representation of the pre-emergent application of thymyloxyacetic acid and carvacryloxyacetic acid 3-weeks after application. In each picture, the treated pot is featured on the left adjacent to the control (untreated) pot on the right. Both thymyloxyacetic acid and carvacryloxyacetic acid were capable of inhibiting the growth of both corn and soybeans when applied shortly after planting. Of the two formulations, carvacryloxyacetic acid outperformed thymyloxyacetic acid at inhibiting plant growth in both plant types. Soybeans and wood sorrel were completely prevented from growing at the 1% concentration of carvacryloxyacetic acid, suggesting this active ingredient may be an ideal pre-emergent herbicide. Moreover, this formulation caused significant inhibition in corn growth; however, corn plants still emerged and continued growing. Thymyloxyacetic acid caused a major inhibition of growth in both the soybean and wood sorrel at the beginning of the trial. However, treated wood sorrel experienced latent growth after the application, and plants in the treatment group may be larger than the control plants.

[0017] FIG. 6 is a representation of significant chlorosis and subsequent phytotoxicity that was observed in pigweed plants that were treated with 40mL of 5% monoterpenoid derivatives. Both carvacryloxyacetic acid and thymyloxyacetic acid were capable of causing significant chlorosis and phytotoxicity in pigweed plants, 2 days after application.

[0018] FIG. 7 is a representation of significant chlorosis and subsequent phytotoxicity that was observed in velvet leaf plants that were treated with 40mL of 5% monoterpenoid derivatives. Both carvacryloxyacetic acid and thymyloxyacetic acid were capable of causing significant chlorosis and phytotoxicity in velvet leaf plants, 2 days after application.

[0019] FIG. 8 is a representation of significant chlorosis and subsequent phytotoxicity that was observed in dandelions that were treated with 40mL of 5% monoterpenoid derivatives. Both carvacryloxyacetic acid and thymyloxyacetic acid were capable of causing significant chlorosis and phytotoxicity in dandelions, 2 days after application.

[0020] FIG. 9 is a representation of significant chlorosis and subsequent phytotoxicity that was observed in lamb's quarters plants that were treated with 40 mL of 5% monoterpenoid derivatives. Both carvacryloxyacetic acid and thymyloxyacetic acid were capable of causing significant chlorosis and phytotoxicity in lamb's quarters, two days after application.

[0021] FIG. 10 is a representation of significant chlorosis and subsequent phytotoxicity that was observed in giant foxtail plants that were treated with 40mL of 5% monoterpenoid derivatives. Both carvacryloxyacetic acid and thymyloxyacetic acid were capable of causing significant chlorosis and phytotoxicity in giant foxtail, 2 days after application.

DETAILED DESCRIPTION

[0022] The disclosed embodiments relates to compounds having a monoterpenoid and/or phenylpropanoid moiety, and methods use.

[0023] In particular, the disclosed embodiments relate to monoterpenoid and phenylpropanoid compounds derived from biorational sources. As discussed in more detail infra, the monoterpenoid and phenylpropanoid derivative compounds of the embodiments disclosed herein are particularly suited for use as pesticides, including as herbicides.

[0024] Throughout this disclosure, the following terms are provided for clarity.

[0025] As used herein, the term "monoterpenoid" refers to a monoterpene-like substance and is used to refer collectively to monoterpenoid derivatives as well as monoterpenoid analogs. By "monoterpene," it is meant a compound having a 10-carbon skeleton with non-linear branches. A monoterpene technically refers to a compound with two isoprene units connected in a head-to-end manner. Monoterpenoids can therefore include monoterpenes, alcohols, ketones, aldehydes, esters, ethers, acids, hydrocarbons without an oxygen functional group, and so forth. It is common practice to refer to certain phenolic compounds, such as eugenol, thymol, and carvacrol, as monoterpenoids because their function is essentially the same as a monoterpenoid. However, these compounds are not technically "monoterpenoids" (or "monoterpenes") because they are not synthesized by the same isoprene biosynthesis pathway, but rather by production of phenols from tyrosine. However, common practice will be followed herein.

[0026] The term "monoterpenoid alcohol" means any monoterpenoid or phenylpropanoid alcohol or phenol that occurs naturally, including, for example and without limitation: acyclic, unsaturated monoterpenoids, including citronellol, linalool, geraniol, nerol, and lavandulol; cyclic or bicyclic unsaturated monoterpenoids, including carveol, pinocarveol, myrcenol, myrtenol, α-terpineol, 4-terpeniol, verbenol, and perillyl alcohol; cyclic or polycyclic saturated monoterpenoids, including menthol, fenchol, borneol, isoborneol, and myrtanol; isopropyl cresols, including thymol, carvacrol, or 4-isopropyl-3-methylphenol; cycloheptatrienolones, such as any of the isomeric thujaplicins; phenylpropanoid alcohols or phenols, including eugenol, isoeugenol, cinnamyl alcohol, coniferyl alcohol, zingerone, umbelliferone, coumaryl alcohol, and chavicol; or alcohols or phenols produced by the natural plant metabolism of a phenylpropanoid, including vanillin, ethyl vanillin, piperonyl alcohol, or syringaldehyde.

[0027] Moreover, O-alkylated and O-acylated monoterpenoids, for example and without limitation etherified monoterpenoids containing carboxylic acid moieties or ester moieties and oligoesters of monoterpenoids containing carboxylic acid moieties are herein referred to as monoterpenoid derivatives.

[0028] The term “phenylpropanoid” refers to a diverse group of organic compounds that are synthesized by plants from the amino acid phenylalanine. Their name is derived from the six-carbon, aromatic phenyl group and the three-carbon propene tail of cinnamic acid, which is synthesized from phenylalanine in the first step of phenylpropanoid biosynthesis. Phenylpropanoids are found throughout the plant kingdom, where they serve as essential components of a number of structural polymers, provide protection from ultraviolet light, defend against herbivores and pathogens, and mediate plant-pollinator interactions as floral pigments and scent compounds.

[0029] According to one embodiment, the monoterpenoid and/or phenylpropanoid moiety of the compounds of the disclosed embodiments are derived from a biorational source, such as a plant volatile or as a constituent of plant essential oils obtained from the leaf tissue, stem tissue, root tissue, or mixture thereof.

[0030] As used herein, the term “alkyl” means an aliphatic hydrocarbon group which may be straight or branched. When not otherwise restricted, the term refers to an alkyl of from 2 to 7 carbons. Exemplary alkyl groups include, for example and without limitation, ethyl, n-propyl, i-propyl, n-butyl, t-butyl, n-pentyl, 3-pentyl, and the like.

[0031] The term “alkenyl” means an aliphatic hydrocarbon group containing a carbon—carbon double bond and which may be straight or branched having from 2 to about 7 carbon atoms in the chain. Non-limiting, exemplary alkenyl groups include ethenyl, propenyl, n-butenyl, isoprene, and i-butenyl. The term “alkenyl” may also refer to a hydrocarbon chain having 2 to 7 carbons containing at least one double bond and at least one triple bond.

[0032] The term “alkynyl” means an aliphatic hydrocarbon group containing a carbon—carbon triple bond and which may be straight or branched having about 3 to about 7 carbon atoms in the chain. Non-limiting, exemplary alkynyl groups include propynyl, n-butynyl, 2-butynyl, 3-methylbutynyl, propargyl, and n-pentynyl.

[0033] The term “cycloalkyl” means a non-aromatic, saturated or unsaturated, mono- or multi-cyclic ring system of about 3 to about 7 carbon atoms. Exemplary cycloalkyl groups include, without limitation, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and cycloheptyl.

[0034] The term “cycloalkenyl” means a non-aromatic, unsaturated, mono- or multi-cyclic ring system of about 3 to about 7 carbon atoms. Exemplary cycloalkenyl groups include, without limitation, cyclopropenyl, cyclobutenyl, cyclopentenyl, cyclohexenyl, and cycloheptenyl.

[0035] The term “heteroaryl” means an aromatic monocyclic or multi-cyclic ring system of about 5 to about 19 ring atoms, or about 5 to about 10 ring atoms, in which one or more of the atoms in the ring system is/are element(s) other than carbon, for example, nitrogen, oxygen, or sulfur. In the case of a multi-cyclic ring system, only one of the rings needs to be aromatic for the ring system to be defined as “heteroaryl.” Particular heteroaryls contain about 5 to 6 ring atoms. The prefix aza, oxa, thia, or thio before heteroaryl means that at least a nitrogen, oxygen, or sulfur atom, respectively, is present as a ring atom. A nitrogen, carbon, or sulfur atom in the heteroaryl ring may be optionally oxidized; the nitrogen may optionally be quaternized. Suitable heteroaryls include, without limitation, pyridyl, 2-oxo-pyridinyl, pyrimidinyl, pyridazinyl, pyrazinyl, triazinyl, furanyl, pyrrolyl, thiophenyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, triazolyl, oxadiazolyl, thiadiazolyl, tetrazolyl, indolyl, isoindolyl, benzofuranyl, benzothiophenyl, indolinyl, 2-oxoindolinyl, dihydrobenzofuranyl, dihydrobenzothiophenyl, indazolyl, benzimidazolyl, benzooxazolyl, benzothiazolyl, benzoisoxazolyl, benzoisothiazolyl, benzotriazolyl, benzo[1,3]dioxolyl, quinolinyl, isoquinolinyl, quinazolinyl, cinnolinyl, pthalazinyl, quinoxalinyl, 2,3-dihydro-benzo[1,4]dioxinyl, benzo[1,2,3]triazinyl, benzo[1,2,4]triazinyl, 4*H*-chromenyl, indolizinyl, quinolizinyl, 6*aH*-thieno[2,3-d]imidazolyl, 1*H*-pyrrolo[2,3-*b*]pyridinyl, imidazo[1,2-*a*]pyridinyl, pyrazolo[1,5-*a*]pyridinyl, [1,2,4]triazolo[4,3-*a*]pyridinyl, [1,2,4]triazolo[1,5-*a*]pyridinyl, thieno[2,3-*b*]furanyl, thieno[2,3-*b*]pyridinyl, thieno[3,2-*b*]pyridinyl, furo[2,3-*b*]pyridinyl, furo[3,2-*b*]pyridinyl, thieno[3,2-*d*]pyrimidinyl, furo[3,2-*d*]pyrimidinyl, thieno[2,3-*b*]pyrazinyl, imidazo[1,2-*a*]pyrazinyl, 5,6,7,8-tetrahydroimidazo[1,2-*a*]pyrazinyl, 6,7-dihydro-4*H*-pyrazolo[5,1-*c*][1,4]oxazinyl, 2-oxo-2,3-dihydrobenzo[*d*]oxazolyl, 3,3-dimethyl-2-oxoindolinyl, 2-oxo-2,3-dihydro-1*H*-pyrrolo[2,3-*b*]pyridinyl, benzo[*c*][1,2,5]oxadiazolyl, benzo[*c*][1,2,5]thiadiazolyl, 3,4-dihydro-2H-benzo[*b*][1,4]oxazinyl, 5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-*a*]pyrazinyl, [1,2,4]triazolo[4,3-*a*]pyrazinyl, 3-oxo-[1,2,4]triazolo[4,3-*a*]pyridin-2(3*H*)-yl, and the like.

[0036] The term “monocyclic” used herein indicates a molecular structure having one ring.

[0037] The term “polycyclic” or “multi-cyclic” used herein indicates a molecular structure having two or more rings, including, but not limited to, fused, bridged, or spiro rings.

[0038] The term “substituted” specifically envisions and allows for one or more substitutions that are common in the art. However, it is generally understood by those skilled in the art that the substituents should be selected so as to not adversely affect the useful characteristics of the compound or adversely interfere with its function. Suitable substituents may include, for example, alkyl groups, alkenyl groups, alkynyl groups, hydroxy groups, oxo groups, mercapto groups, alkylthio groups, alkoxy groups, aryl or heteroaryl groups, aryloxy or heteroaryloxy groups, aralkyl or heteroaralkyl groups, aralkoxy or heteroaralkoxy groups, amino groups, alkyl- and dialkylamino groups, carbamoyl groups, alkylcarbonyl groups, carboxyl groups, alkoxycarbonyl groups, alkylaminocarbonyl groups, dialkylamino carbonyl groups, arylcarbonyl groups, aryloxycarbonyl groups, alkylsulfonyl groups, arylsulfonyl groups, cycloalkyl groups, cyano groups, C1-C6 alkylthio groups, arylthio groups, nitro groups, keto groups, acyl groups, boronate or boronyl groups, phosphate or phosphonyl groups, sulfamyl groups, sulfonyl groups, sulfinyl groups, and combinations thereof. In the case of substituted combinations, such as “substituted arylalkyl,” either the aryl or the alkyl group may be substituted, or both the aryl and the alkyl groups may be substituted with one or more substituents. Additionally, in some cases, suitable substituents may combine to form one or more rings as known to those of skill in the art.

[0039] According to one embodiment, the compounds are substituted, meaning a group may have a substituent at a substitutable atom of the group (including more than one substituent on a single atom), provided that the designated atom’s normal valence is not exceeded and the identity of each substituent is independent of the others. For example, up to three H atoms in each residue are replaced with substituents such as alkyl, hydroxy, loweralkoxy, carboxy, carboalkoxy (also referred to as alkoxycarbonyl), carboxamido (also referred to as alkylaminocarbonyl), cyano, carbonyl, nitro, amino, alkylamino, dialkylamino, mercapto, alkylthio, sulfoxide, sulfone, acylamino, amidino, phenyl, benzyl, heteroaryl, phenoxy, benzyloxy, or heteroaryloxy. When a substituent is keto (i.e., =0), then two hydrogens on the atom are replaced. Combinations of substituents and/or variables are permissible only if such combinations result in stable compounds; by “stable compound” it is meant a compound that is sufficiently robust to survive isolation to a useful degree of purity from a reaction mixture, and formulation into an agent intended for a suitable use.

[0040] According to certain embodiments, the compounds are unsubstituted. “Unsubstituted” atoms bear all of the hydrogen atoms dictated by their valence.

[0041] The term “compound,” and equivalent expressions, are meant to embrace compounds as described herein. Also contemplated are salts, oxides, solvates, e.g., hydrates, and inclusion complexes of the compounds, where the context so permits, as well as any stereoisomeric form, or a mixture of any such forms of that compound in any ratio.

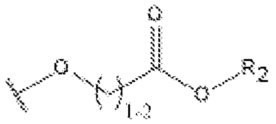
Inclusion complexes are described in Remington, The Science and Practice of Pharmacy, 19th Ed. 1:176-177 (1995), which is hereby incorporated by reference in its entirety. The most commonly employed inclusion complexes are those with cyclodextrins, and all cyclodextrin complexes, natural and synthetic, are specifically encompassed by the compounds disclosed herein.

[0042] Compounds described herein may contain one or more asymmetric centers and may thus give rise to enantiomers, diastereomers, and other stereoisomeric forms. Each chiral center may be defined, in terms of absolute stereochemistry, as (R)- or (S)-. This is meant to include all such possible isomers, as well as mixtures thereof, including racemic and optically pure forms. Optically active (R)- and (S)-, (-)- and (+)-, or (D)- and (L)- isomers may be prepared using chiral synthons or chiral reagents, or resolved using conventional techniques. When the compounds described herein contain olefinic double bonds or other centers of geometric asymmetry, and unless specified otherwise, it is intended that the compounds include both E and Z geometric isomers. Likewise, all tautomeric forms are also intended to be included.

[0043] One aspect of the disclosed embodiments relates to a compound of formula (I):

[0044] R_1—A ,

[0045]



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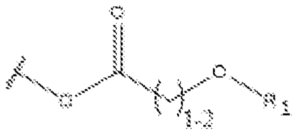

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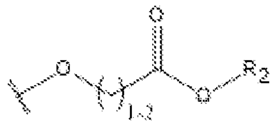
[0046] R1 is a phenylpropanoid or monoterpenoid moiety;

[0047] R2 is a substituted or unsubstituted phenylpropanoid or monoterpenoid moiety or is selected from the group consisting of H, M, substituted or unsubstituted C3-C7 unbranched or branched alkyl, substituted or unsubstituted C2-C7 unbranched or branched alkenyl, substituted or unsubstituted C3-C7 unbranched or branched alkynyl, substituted or unsubstituted C3-C7 unbranched or branched cycloalkyl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted C3-C7 unbranched or branched cycloalkenyl; and

[0048] M is a counterion selected from the group consisting of sodium, potassium, calcium, magnesium, iron, zinc, copper, and an amine;

[0049] In one embodiment of the compound of formula (I), R2 is H.

[0050] In another embodiment of the compound of formula (I), A is



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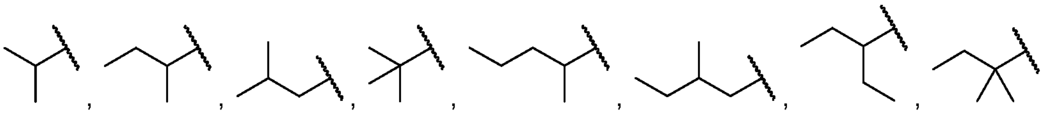
the carbon in the parentheses is 1, and R_2 is H.

[0051] In yet another embodiment of the compound of formula (I), R_2 is C_3-C_7 branched alkyl selected from the group consisting of



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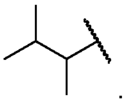

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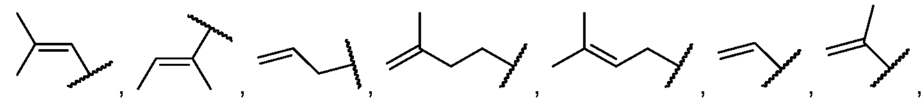
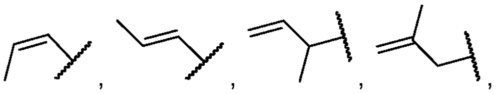
[0052] In another embodiment of the compound of formula (I), R2 is C2-C7 unbranched or branched alkenyl selected from the group consisting of

[0053] 



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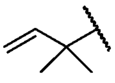

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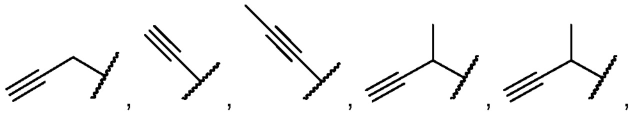
[0054] In another embodiment of the compound of formula (I), R2 is C3-C7 unbranched or branched alkynyl selected form the group consisting of

[0055] 

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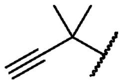
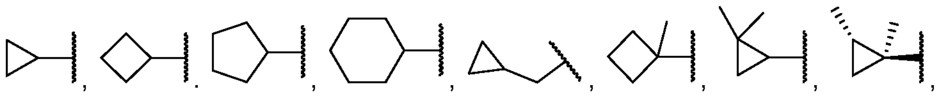
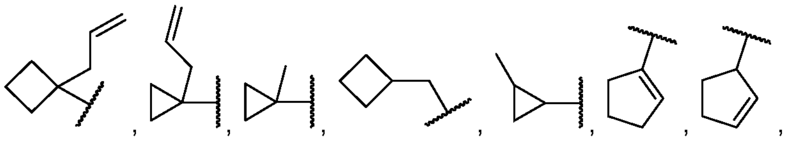


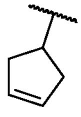
.

[0056] In another embodiment of the compound of formula (I), R2 is C3-C7 unbranched or branched cycloalkyl selected form the group consisting of

[0057] 

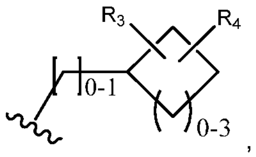


, and



.

[0058] In another embodiment of the compound of formula (I), R2 is:

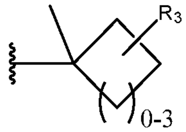
[0059] 

,

[0060] where R3 and R4 are independently selected from the group consisting of H, methyl, ethyl, propyl, isopropyl, vinyl, allyl, and propargyl.

[0061] In more specific embodiments, R3 and R4 are both H; R3 and R4 are both CH3; R3 is CH3 and R4 is H; or R3 is allyl and R4 is H.

[0062] In another embodiment of the compound of formula (I), R2 is:

[0063] 

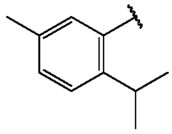
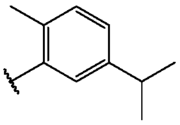
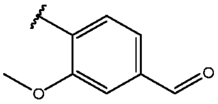
,

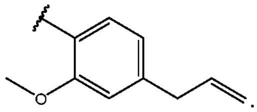
[0064] where R3 is selected from the group consisting of H, methyl, ethyl, propyl, isopropyl, vinyl, allyl, and propargyl.

[0065] In another embodiment of the compound of formula (I), R1 is a phenypropanoid moiety.

[0066] In yet another embodiment of the compound of formula (I), R_1 is a monoterpenoid moiety.

[0067] In a more specific embodiment, the monoterpenoid moiety is selected from the group consisting of

[0068]  ,  , 

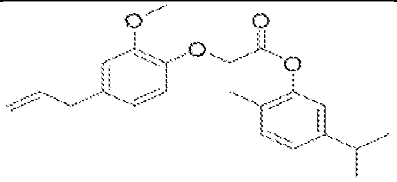
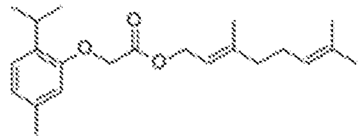
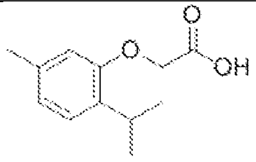
, and 

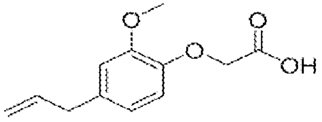
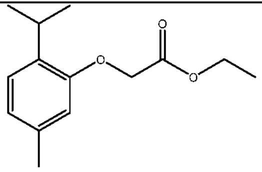
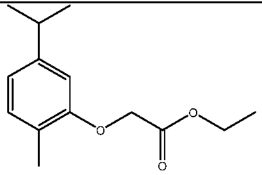
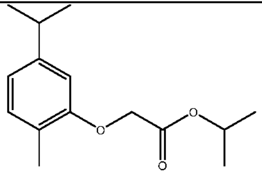
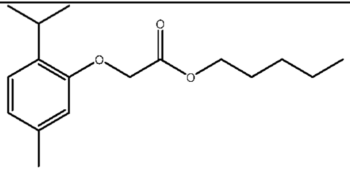
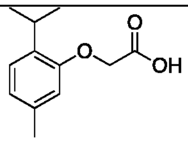
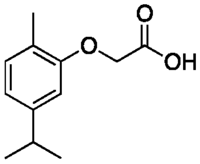
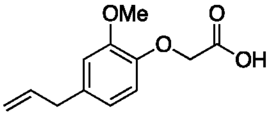
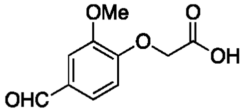
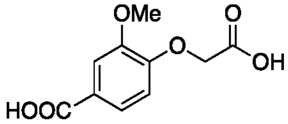
.

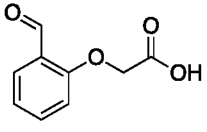
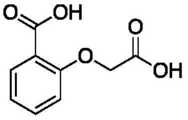
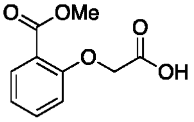
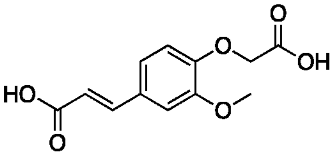
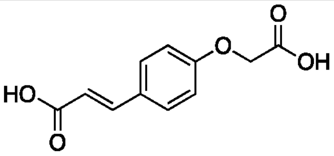
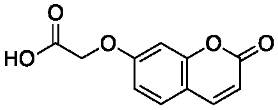
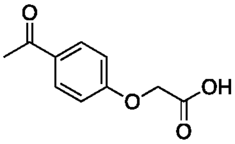
[0069]

[0070] In another embodiment of the compound of formula (I), R2 is selected from the group consisting of methyl, ethyl, isopropyl, propyl, isobutyl, butyl, and tert-butyl.

[0071] Compounds of formula (I) include, without limitation, the specific compounds set forth in the following Table 1.

Compound Name	**Compound Structure**
123B carvacrol eugenyloxyacetate	
2016 geranyl thymyloxyacetate	
106 thymyloxyacetic acid	

Compound Name	**Compound Structure**
109 eugenyloxyacetic acid	
2283 ethyl thymyloxyacetate	
2283 ethyl carvacryloxyacetate	
2288A isopropyl carvacryloxyacetate	
2289 amyl thymyloxyacetate	
Thymyloxyacetic acid (2-(2-isopropyl-5-methylphenoxy)acetic acid)	
Carvacryloxyacetic acid (2-(5-isopropyl-2-methylphenoxy)acetic acid)	
Eugenyloxyacetic acid (2-(4-allyl-2-methoxyphenoxy)acetic acid)	
Vanillyloxyacetic acid (2-(4-formyl-2-methoxyphenoxy)acetic acid)	
Carboxymethylvanillic acid (4-(carboxymethoxy)-3-methoxybenzoic acid) (from vanillic acid)	

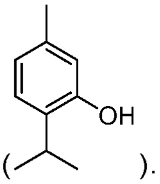
Compound Name	Compound Structure
Salicyloxyacetic acid (2-(2-formylphenoxy)acetic acid)	
Carboxymethylsalicylic acid (2-(carboxymethoxy)benzoic acid) (from salicylic acid)	
2-(2-(methoxycarbonyl)phenoxy)acetic acid (from methyl salicylate)	
3-(4-(carboxymethoxy)-3-methoxyphenyl)acrylic acid (from ferulic acid)	
3-(4-(carboxymethoxy)phenyl)acrylic acid (from *p*-coumaric acid)	
coumarin-7-oxyacetic acid (2-((2-oxo-2*H*-chromen-7-yl)oxy)acetic acid) (from umbelliferone)	
2-(4-acetylphenoxy)acetic acid (from piceol/4'-hydroxyacetophenone)	

[0072] According to one embodiment, compounds of formula (I) that have a free carboxylic acid can have each acid esterified, or the carboxylic acid can be used to form a carboxylate salt.

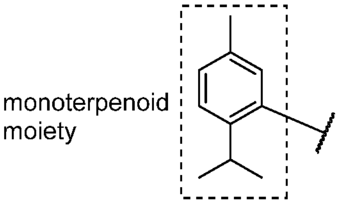
[0073] In one embodiment, compounds of formula (I) include the specific structures identified in Table 3 other than thymyloxyacetic acid, carvacryloxyacetic acid, and eugenyloxyacetic acid.

[0074] As noted supra, the certain example compounds may be derived from a biorational source, such as a plant volatile or as a constituent of plant essential oils obtained from the leaf tissue, stem tissue, root tissue, or mixture thereof.

[0075] As noted supra, certain compounds are derivatives of monoterpenoids or phenylpropanoids. By way of a non-limiting example, a compound of the present disclosure may be a derivative of an alcohol-containing monoterpenoid or phenylpropanoid, such as, e.g., thymol

().

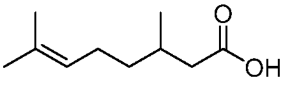
[0076] In one example embodiment, a thymol-derivative has the structure



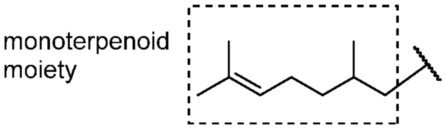
,

[0077] where the 10-carbon skeleton of thymol makes up the monoterpenoid or monoterpenoid moiety (e.g., R1 of formula (I)), and the wavy line, 〰, represents the linkage to the rest of the molecule.

[0078] By way of another non-limiting example, a compound may be a derivative of a carboxylic acid-containing monoterpenoid or phenylpropanoid, such as, *e.g.*, citronellic acid

().

In another example embodiment, a citronellic acid derivative has the structure



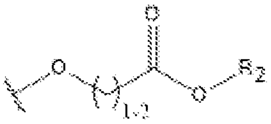
,

[0079] where the 9-carbon skeleton of citronellic acid (excluding the carboxylic acid carbon) makes up the monoterpenoid or monoterpenoid moiety and the wavy line, 〰, represents the linkage to the rest of the molecule

[0080] Thus, the example compounds may be derived from monoterpenoid alcohols (i.e., monoterpenoids containing a hydroxyl group) or from monoterpenoid carboxylic acids (i.e., monoterpenoids containing a carboxylic acid). Alternatively, the compounds may be derived from phenylpropanoid alcohols (i.e., phenylpropanoids containing a hydroxyl group) or from phenylpropanoid carboxylic acids (i.e., phenylpropanoids containing a carboxylic acid).

[0081] A further aspect of the disclosed embodiments relates to an herbicidal composition comprising the compounds of formula (I) and a carrier.

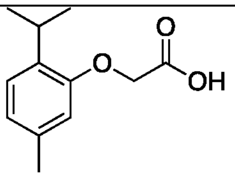
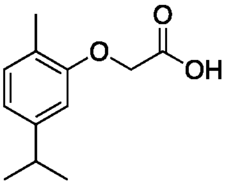
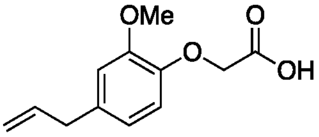
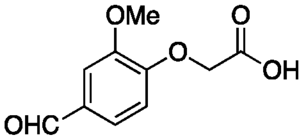
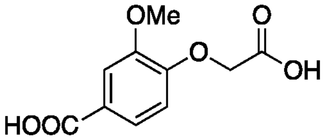
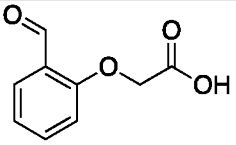
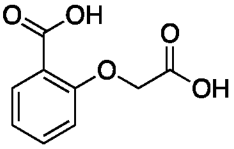
[0082] In one embodiment, the herbicide composition comprises a subsect of compounds of formula (I) and a carrier. For example, and without limitation, the herbicide composition comprises a compound of formula (I), where A is

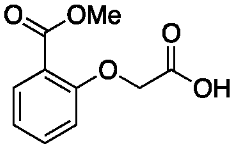
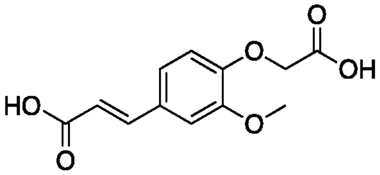
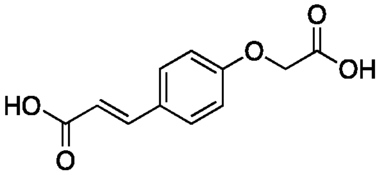
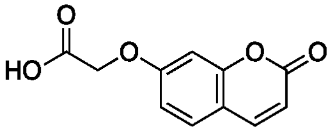
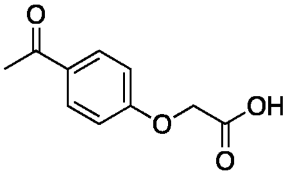
[0083] 

,

[0084] the carbon in the parentheses is 1, and R_2 is H.

[0085] In a more specific embodiment, compounds useful in the herbicidal composition include, without limitation, any one or more of the exemplary compounds set forth in the following Table 2.

Compound Name	Compound Structure
Thymyloxyacetic acid (2-(2-isopropyl-5-methylphenoxy)acetic acid)	
Carvacryloxyacetic acid (2-(5-isopropyl-2-methylphenoxy)acetic acid)	
Eugenyloxyacetic acid (2-(4-allyl-2-methoxyphenoxy)acetic acid)	
Vanillyloxyacetic acid (2-(4-formyl-2-methoxyphenoxy)acetic acid)	
Carboxymethylvanillic acid (4-(carboxymethoxy)-3-methoxybenzoic acid) (from vanillic acid)	
Salicyloxyacetic acid (2-(2-formylphenoxy)acetic acid)	
Carboxymethylsalicylic acid (2-(carboxymethoxy)benzoic acid) (from salicylic acid)	

Compound Name	Compound Structure
2-(2-(methoxycarbonyl)phenoxy)acetic acid (from methyl salicylate)	
3-(4-(carboxymethoxy)-3-methoxyphenyl)acrylic acid (from ferulic acid)	
3-(4-(carboxymethoxy)phenyl)acrylic acid (from *p*-coumaric acid)	
coumarin-7-oxyacetic acid (2-((2-oxo-2*H*-chromen-7-yl)oxy)acetic acid) (from umbelliferone)	
2-(4-acetylphenoxy)acetic acid (from piceol/4'-hydroxyacetophenone)	

[0086] The herbicide compounds identified in Table 2 are indicated as free carboxylic acids. However, each acid can be esterified or used to form a carboxylate salt.

[0087] In a specific embodiment, suitable esters include, without limitation, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, sec-butyl, tert-butyl, amyl esters.

[0088] In another specific embodiment, suitable carboxylate salts include, without limitation, metal salts, including sodium, potassium, calcium, and magnesium.

[0089] In yet another specific embodiment, suitable herbicide compounds are diacids, including diesters and divalent anionic salts.

[0090] Herbicidal compositions (phytotoxic and/or systemic) may be applied as a pre- or post-emergent application to herbs, such as weeds, to control their growth.

[0091] As used herein, the term "phytotoxic" or "phytotoxicant" or "phytotoxicity" denotes materials that (1) effectively control all plants in a given locus or (2) selectively control the growth of one or more plant species in the presence of other plants. These interchangeable terms are also used to identify the overall and selective control activity of certain compounds and compositions disclosed herein.

[0092] As used herein, the term “systemic” denotes herbicidal compounds or compositions that are assimilated by susceptible vegetation and are then translocated to parts of the plant other than those contacted. A systemic herbicide generally, if not always, depends on a translocation mode of action for their herbicidal activity. For instance, when applied to plant foliage, the systemic herbicides disclosed herein will be assimilated during transpiration, or otherwise, and transported throughout the entire plant so that it eliminates the undesired vegetation, roots, and all.

[0093] Contact herbicidal activity provides immediate vegetation control while the systemic herbicidal mode of action may more desirably reduce treatment cost, improve vegetation control, reduce both immediate and residual toxic effects to humans and animals, and reduce the possibility of herbicide residue on harvested food crops. Immediate vegetation control is defined as phytotoxicity that occurs within the first few hours or days (e.g. 1-3 days) after treating the plant tissue. This is markedly different from the relatively slower activity of 2,4-dichlorophenoxyacetic acid.

[0094] The term “control” as used herein is inclusive of the actions of (l) killing, (2) inhibiting growth, reproduction or proliferation, and (3) removing, destroying or otherwise diminishing the occurrence and activity of plants and is applicable to any of the stated actions, or any combination thereof.

[0095] The herbicidal compositions and methods disclosed herein may exhibit accentuated pre- and post-emergent, systemic herbicidal activity with the result that significantly smaller dosages of a given herbicide may be applied to achieve the same degree of vegetation control or, alternatively, a higher degree of vegetation control is achieved with the same application rate. These herbicidal compositions and methods may also provide contact herbicidal properties and, at the same time, provide nitrogen and sulfur nutrients for the desireable plants. They may also enable the use of systemic herbicides in combination with other conventional herbicidal compounds.

[0096] Application of the herbicidal compositions of the disclosed embodiments may be carried out by foliar spray, soil drench (pre- and post-emergence), powder application, and granule application with and without substrate, for both broadleaf weeds and grasses. An effective amount for phytotoxic or systemic control is that amount necessary for overall or selective control, i.e., a phytotoxic or herbicidal amount. A person of ordinary skill in the art can readily determine from the teachings of this specification, including the examples, suitable approximate application rate(s).

[0097] It will be understood by all readers of this written description that the example embodiments described herein and claimed hereafter may be suitably practiced in the absence of any recited feature, element or step that is, or is not, specifically disclosed herein. For instance, references in this written description to "one embodiment," "an embodiment," "an example embodiment," and the like, indicate that the embodiment described can include a particular feature, structure, or characteristic, but every embodiment may not necessarily include the particular feature, structure, or characteristic. Moreover, such phrases are not necessarily referring to the same embodiment. Further, when a particular feature, structure, or characteristic is described in connection with an embodiment, it is submitted that it is within the knowledge of one of ordinary skill in the art to affect such feature, structure, or characteristic in connection with other embodiments whether or not explicitly described.

[0098] All publications and references cited herein, including those in the Background section, are expressly incorporated herein by reference in their entirety. However, if there are any differences between any similar or identical terms found an incorporated publication or reference and those explicitly put forth or defined in this written description, then those terms definitions or meanings explicitly put forth in this written description shall control in all respects. Further, any reference to prior art in this specification is not, and should not be taken as, an acknowledgment or any form of suggestion that such prior art forms part of the common general knowledge in any country.

[0099]

EXAMPLES

[00100] The following examples are provided to illustrate embodiments but they are by no means intended to limit its scope.

Example 1 - Germination Assays

Materials and methods

Soybeans

[00101] Soybeans originally obtained were untreated and did not contain any form of pesticide coating. Soybeans were susceptible to *Aphis glycines* infestation and were not determined to be a biotype that was resistant to infestation, which could confide results. Germination typically occurred between 3-5 days after moistening.

Corn Seeds

[00102] Corn seeds obtained were untreated and did not contain any form of pesticide coating. Corn seeds used were a non-transgenic type strain of corn in order to prevent confounding results. Germination typically occurred between 2-4 days after moistening.

Germination Assessment

Seed Coating (Solid Compounds)

[00103] Seed coating was accomplished by placing 20 g of corn seeds or soybeans into a container with approximately 1 mL of a 1:5 Elmer's Glue®:water solution (or a different adhesive:water mixture) with a small amount of Triton-X 100™ (present 100 µL/5 mL). For solid compounds, 0.25 g of compound was subsequently introduced into the container. This mixture of seeds, Elmer's Glue/water/Triton-X 100™ solution, and active compound was mixed thoroughly until seeds were coated with the active ingredient.

Seed Coating (Liquid Compounds)

[00104] For each treatment, 0.25 g of liquid compound was dissolved in 5 mL of hexane. 0.25 g of Hi-Sil 233 Silica gel was introduced into this mixture of hexane and active ingredient. The solvent was removed using a rotary evaporator, allowing for the compound to adsorb to the silica gel. This 0.5 g of silca gel:active ingredient was then used as the solid material used for coating the seeds. The seeds were then coated with the same method used for solid compound.

Germination Assays

[00105] Ten soybeans or corn seeds were introduced into 1-pint regular mouth mason jars (Kerr®) surrounded by paper towels that were coated with 10 mL of water (minimum amount necessary to drench the paper towel). Soybeans or corn seeds were grouped together and paper towels were folded twice to allow for continual exposure to moisture. After the introduction of soybeans or corn seeds, mason jars were sealed with Mason jar lids for the entirety of the experiment to prevent desiccation and to provide a continually moist environment for soybeans and corn seeds. Germination was defined as the extrusion of the radicle from the seed coat. Plants were grown at ambient room temperature and in a 12 hr:12 hr light:dark cycle. Beans/seeds were removed periodically throughout the experiment in order to observe the number of radicles clearly visible at 3, 5, and 7 days after the introduction of beans/seeds. After each observation, seeds/beans were reintroduced into the moist paper towel and mason jar which was then sealed. Each treatment was replicated twice, and the average percentage germination and standard error was reported for each time point and treatment.

Results

[00106] All compounds tested caused inhibition of seed/bean germination at 3, 5, and 7-days after introducing seeds/beans into the moist paper towel. These data suggest the potential of these components as herbicides, particularly herbicides applied prior to emergence. Moreover, monocots seemed to be less susceptible to the inhibitory effects on germination caused by these compounds than dicots (corn vs. soybean). It is possible that these compounds may exert their effects in a selective manner, with dicots being more susceptible than monocots

[00107] Corn seed germination was significantly inhibited by all compounds screened except for vanillyloxyacetic acid and vanillic acid-oxyacetic acid (FIG. 9). Of the compounds that produced significant inhibition of seed germination, eugenyloxyacetic acid methyl ester was the most capable of inhibiting the growth of corn seeds. This may indicate the increased potential of this compound to be used in future herbicidal formulations. The other compounds were capable of significantly reducing the number of seeds germinating and also delayed the germination of seeds in some instances. Thymyloxyacetic acid was capable of causing the second most significant inhibition compared to eugenyloxyacetate methyl ester and prevented any germination at day 3. Both eugenyloxyacetic acid and carvacryloxy acetic acid were capable of some level of germination at day 3. All compounds caused significant inhibition compared to the control and all prevented germination below an average percentage germination of 35%. The control by contrast caused 100% germination by day 7 in this assay.

[00108] Soybeans did not sprout in the presence of all of the active ingredients tested in this exploration, except for vanillyloxyacetic acid which produced little to no inhibitory effect (FIG. 10). Moreover, the inhibition of soybean seed germination was more pronounced than the inhibitory effect observed in the corn seedling exploration. This partial selectivity in controlling dicots to a higher degree than monocots may indicate its similarity to currently used herbicides on the market today. This selectivity may be utilized for the control of various weeds in gardens or in agricultural fields without harming various monocot plants (grass and corn).

Example 2 - Soil Drench

Materials and Methods

Soybeans

[00109] Soybean plants were planted under 1 cm of potting soil and watered every 2-3 days as necessary. Plants were grown in pots (6” wide x 4.5” deep) with approximately 800 mL of soil for each plant. Seeds germinated approximately 3-5 days after being planted. Plants were grown in a greenhouse under a constant temperature and light environment (25 ± 5°C, 12 hr:12 hr light:dark cycle). Plants were grown until reaching 1-2 weeks old and 3-4 weeks old; these plants served as the “young” and “old” plants in this study, respectively.

Corn Plants

[00110] Corn plants were planted under ½" of potting soil and watered every 2-3 days as necessary. Plants were grown in potting plants (6" wide x 4.5" deep) with approximately 800 mL of soil for each plant. Seeds germinated approximately 4-7 days after being planted. Plants were grown in a greenhouse under a constant temperature and light environment (25 ± 5°C, 12 hr:12 hr light:dark cycle). Plants were grown until reaching 1-2 weeks old and 3-4 weeks old; these plants served as the "young" and "old" plants in this study, respectively.

Soil Drench Assay

[00111] Formulations of the various active ingredients were created using the monoterpenoid derivatives, potassium hydroxide, and Triton-X 100^{TM} to aid in the solvation of the active ingredient. Formulations consisted of 0.5%-1% active ingredient by weight (0.5-1 g/100 mL water), with a 1:1 molar ratio of potassium hydroxide used to aid in the solvation (135-269 mg/100 mL for both thymyloxyacetic acid and carvacryloxyacetic acid). Triton-X 100^{TM} was introduced into the formulation to aid in solubility at a final concentration of 0.25%. 40 mL of formulation (either 0.5% or 1% active ingredient) was applied to each plant at different stages in the plant life cycle. Formulations were applied to the soil next to the base of the stem of the plant to avoid foliar contact. Observations were performed 2 days and 3 weeks after soil drench to determine the effects of the treatments on the various types and stages of plants. Qualitative data is provided in the table below demonstrating the effects of each concentration of compound on different plants and plant life stages.

Results

[00112] Compounds tested via a soil application protocol successfully inhibited the growth of plants at various stages throughout the experiment. A majority of the compounds tested significantly inhibited the growth of both young and old corn and soybean plants or caused significant phytotoxicity at 3 weeks. Control solution comprised of the formulation without the active ingredient (monoterpenoid-oxyacetic acids) did not produce a significant phytotoxic response.

[00113] When applied to soybean plants, thymyloxyacetic acid caused significant immediate effects on both young and old plants (Table 1). Young plants were susceptible to both the 0.5% and 1% concentration. 2 days after exposure to thymyoloxyacetic acid, soybean plants were significantly inhibited. Minor inhibition was observed in plants exposed to the 0.5% whereas major inhibition was observed in plants exposed to the 1% concentration. This was defined as significant chlorosis and wilting of leaves. Eventually, leaves completely dried out and the plants died. At 3 weeks after exposure, young plants experienced 100% mortality and plants treated as old plants experienced mortality when exposed to the 1% concentration. The old plant treated with 0.5% thymyloxyacetic acid experienced significant wilting and chlorosis. Regrowth of dead plants was not observed 1 month after the treatment. The methyl ester of thymyloxyacetic acid, also significantly inhibited the growth of soybeans and its effect was more pronounced than both carvacryloxyacetic acid and thymyloxyacetic acid. Interestingly, the vanillyloxyacetic acid and vanillic acid-oxyacetic acid did not cause phytotoxic effects against soybean plants

[00114] Corn plants reacted similarly to these concentrations of both thymyloxyacetic acid and carvacryloxyacetic acid (Table 1). At 2 days after exposure, young plants did not show any significant effects to both concentrations of both thymyloxyacetic acid and carvacryloxyacetic acid. This was markedly different than the reaction of soybeans, which exhibited significant effects at 2 days after exposure. At 3 weeks however, plants experienced significant inhibition of growth or phytotoxicity. Both thymyloxyacetic acid and carvacryloxyacetic acid caused phytotoxicity at 3 weeks after exposure. Interestingly, the 1% carvacryloxyacetic acid did not cause mortality at 3 weeks, whereas the 0.5% concentration did. This may simply be an artifact of only one replication within this study. Thymyloxyacetic acid seemed to be more phytotoxic to corn plants in this assay. At 2 days after treatment, both the 0.5% and 1% concentration was capable of causing significant phytotoxic effects against older plants. This was not the case for 0.5% carvacryloxyacetic acid, which did not cause any significant effects at 2-days. Again, it was observed that the methyl ester of thymyloxyacetic acid was the most phytotoxic to corn and both vanillyloxyacetic acid and vanillic acid-oxyacetic acid did not produce significant phytotoxic symptoms. In general, corn plants were seen to be less susceptible to these compounds compared to soybeans. This further indicates the potential of these compounds to be used as selective herbicides, with greater toxicity against dicots compared to monocots.

Soil Drench Summary Table

Treatment	Soybean								Corn							
	2-days after treatment				3-weeks after treatment				2-days after treatment				3-weeks after treatment			
	Young Plants		Old Plants		Young Plants		Old Plants		Young Plants		Old Plants		Young Plants		Old Plants	
	0.50%	1%	0.50%	1%	0.50%	1%	0.50%	1%	0.50%	1%	0.50%	1%	0.50%	1%	0.50%	1%
vanillyloxyacetic acid	NOE	NOE	NOE	NOE	NOE	NOE	NOE	NOE	NOE	NOE	NOE	NOE	NOE	NOE	NOE	NOE
vanillic acid - oxyacetic acid	NOE	NOE	NOE	NOE	NOE	NOE	NOE	NOE	NOE	NOE	NOE	NOE	NOE	NOE	NOE	NOE
eugenyloxy acetic acid	-	- -	-	-	-	XXX	XXX	-	NOE	NOE	NOE	-	-	- -	-	- -
Thymyloxyacetic acid	- -	- - -	-	-	XXX	XXX	-	XXX	-	-	- -	- - -	XXX	XXX	XXX	XXX
Carvacryloxyacetic acid	- - -	- - - -	- -	- - -	XXX	XXX	XXX	XXX	-	-	-	- -	XXX	- -	XXX	XXX
thymyloxyacetate methyl ester	- - -	- - - -	- - -	- - - -	XXX	XXX	XXX	XXX	- -	- -	- -	- -	XXX	XXX	XXX	XXX

Table 1. The efficacy of various oxyacetic acid and esters of the oxyacetic acids derived from monoterpenoid sources. The phytotoxicity of each compound is listed in qualitative terms from “No Observable Effect” (NOE), indicating no herbicidal effect noted to “Dead” (XXX), indicating the plant was dead at the designated time points of observation. The symbols, “-,” “- -,“ “- - -,” and “- - - -“ were used to indicate phytotoxicity that did not result in death, with “-“ being the lowest phytotoxic effect and “- - - -“ being the highest.

Example 3 - Foliar Spray

Materials and Methods

Soybeans

[00115] Soybean plants were planted under 1 cm of potting soil and watered every 2-3 days as necessary. Plants were grown in pots (6” wide x 4.5” deep) with approximately 800 mL of soil for each plant. Plants germinated approximately 3-5 days after being planted. Plants were grown in a greenhouse under a constant temperature and light environment (25 ± 5°C, 12 hr:12 hr light:dark cycle). Plants were grown until reaching 4 weeks old and were then used for the foliar spray experiment.

Foliar Spray Assay

[00116] Formulations were made to include 1% thymyloxyacetic acid, 0.269% potassium hydroxide, and 0.25% Triton-X 100^{TM}. Soybean plants were sprayed with 10 mists from a MAINStays™ Ironing Spray bottle set to the mist setting. This corresponded to the minimum amount necessary to cause dripping from the leaves of the plants. Observations of phytotoxicity or inhibition of growth was observed at 3, 5, 7, and 14 days after exposure to the formulation. Plants were placed under high intensity light (directly below greenhouse lamps) and low intensity light (not under lamp/ ambient light environment). Light intensity was chosen as a factor for this experimental design. Many terpenoids have been demonstrated to be phytotoxic under high intensity light conditions. This effect is greatly diminished under low intensity light conditions. If thymyloxyacetic acid is causing phytotoxicity in the same mechanism of action as other plant terpenoids, there should be a drastic difference in the phytotoxicity among these different levels of light intensity.

[00117] Wood sorrel on the ground of the greenhouse was also treated with active ingredient in order to better assess the effects of foliar treatments on multiple plant species. A patch of wood sorrel was (approximately 4’ x 3’) was treated with 20 sprays (mist setting) from a MAINStays ironing spray bottle. Effects of the spray were recorded 2 days after exposure.

Results

[00118] Thymyloxyacetic acid was capable of causing significant phytotoxic effects when applied topically to 1-month soybean plants. These effects were predominantly characterized by chlorosis of the plant leaves that were sprayed with the formulation containing 1%

thymyloxyacetic acid. Significant wilting also occurred followed by leaf death in each of the plants exposed to the active ingredient.

[00119] No differences were observed among the different light levels. This result indicates that thymyloxyacetic acid most likely exerts its phytotoxicity via a different mode of action from other phytotoxic terpenoids. Moreover, it is possible that these compounds may exert their activity via a similar mode of action to 2,4-dichlorophenoxyacetic acid.

[00120] Wood sorrel treatments demonstrated interesting differences between active ingredients featured in this disclosure compared to 2,4-dichlorophenoxyacetic acid, a commercial comparison. First, the effects of carvacryloxyacetic acid treatment were immediate and apparent compared to the 2,4-dichlorophenoxyacetic acid treatment. Moreover, chlorosis was far more prominent in the carvacryloxyacetic acid treatment. Death followed quickly after 2 days post-exposure in the carvacryloxyacetic acid treatment. For the 2,4-dichloroacetic acid treated plants, plant death was not observed until much later. This immediate herbicidal character is a component of all of the oxyacetic acid monoterpenoids and esters thereof described.

[00121] Table 2 is a tabular representation of the data shown in FIGs. 11 and 12. Significant leaf death and chlorosis was observed in both light levels. No major differences were observed between light levels. This indicates that these compounds exert their toxicity in a way that is unique to parent monoterpenoids applied to plant tissue in the presence of light to cause significant burndown.

Table 2. Summary of the Major Effects on Soybean Plants

Treatment	Low intensity light		High intensity light	
	chlorosis	leaf death	chlorosis	leaf death
thymyloxyacetic acid	✓	✓	✓	✓

Example 4 - Pre-Emergence

Materials and Methods

Soybeans

[00122] Soybean plants were planted under 1 cm of potting soil and watered every 2-3 days as necessary. Plants were grown in pots (6” wide x 4.5” deep) with approximately 800 mL of soil for each plant. Plants germinated approximately 3-5 days after being planted. Plants were grown in a greenhouse under a constant temperature and light environment (25 ± 5°C, 12 hr:12 hr light:dark cycle).

Corn Seeds

[00123] Corn plants were planted under ½” of potting soil and watered every 2-3 days as necessary. Plants were grown in potting plants (6” wide x 4.5” deep) with approximately 800 mL of soil for each plant. Plants germinated approximately 4-7 days after being planted. Plants were grown in a greenhouse under a constant temperature and light environment (25 ± 5°C, 12 hr:12 hr light:dark cycle).

Pre-Emergence Assay

[00124] 1-day after seeds/beans were planted, soil was drenched with 40 mL of formulation with 1% active ingredient. This was done to assess germination inhibition in the soil. Plants were observed at multiple time points throughout the experimental interval. Table 8 and FIGs. 13-18 featured in this disclosure demonstrate the activity of the compounds 3 weeks after application of compounds to the soil. Qualitative growth assessment was made by comparing the treated plants to the untreated controls. Observations included enhanced growth (+), minor inhibition of growth (-), major inhibition of growth (- -), plant death (XXX), and no observable effects (No effect).

Table 3. Effects of Compounds on Plants Before Germination

Pre-emergence Tests - Soil Treated with 40ml of 1% solution - 1 day after planting			
Treatment	**Corn**	**Soy**	**Sorrel**
thymyloxyacetic acid	-	- -	-
carvacryloxyacetic acid	- -	XXX	- -
control	No effect	No effect	No effect

[00125] Both thymyloxyacetic acid and carvacryloxyacetic acid had significant phytotoxic effects on all plants that were exposed to the active ingredients. Of the plants exposed, soybeans were the most susceptible. Carvacryloxyacetic acid prevented the emergence of soybean plants entirely and significantly inhibited the growth of both corn and wood sorrel. Soybean plants were also the most susceptible to thymyloxyacetic acid. However, both corn and wood sorrel growth were significantly inhibited by this compound as well. In pre-emergent applications, carvacryloxyacetic acid was the most phytotoxic of the two treatments. Moreover, dicotyledons (soybeans and wood sorrel) were more susceptible to both active ingredients than monocotyledons (corn).

Example 5 - Weed Treatments

Materials and Methods

Pigweed (Amaranthus palmeri)

[00126] Pigweed plants were obtained from the wild in prairie fields in Iowa. Plants were carefully transplanted into pots (6” wide x 4.5” deep) with approximately 800 mL of soil for each plant. Plants were maintained in a greenhouse under a constant temperature and light environment (25 ± 5°C, 12 hr:12 hr light:dark cycle). Plants were watered every 2-3 days as needed. Plants that did not survive transplanting were not used for this study.

Velvetleaf (Abutilon theophrasti)

[00127] Velvetleaf plants were obtained from the wild in prairie fields in Iowa. Plants were carefully transplanted into pots (6” wide x 4.5” deep) with approximately 800 mL of soil for each plant. Plants were maintained in a greenhouse under a constant temperature and light environment (25 ± 5°C, 12 hr:12 hr light:dark cycle). Plants were watered every 2-3 days as needed. Plants that did not survive transplanting were not used for this study.

Dandelion (Taraxacum officinale)

[00128] Dandelion seeds were obtained from native prairie fields in Ames, IA. Individual seeds were sown for each pot (6” wide x 4.5” deep) with approximately 800 mL of soil for each plant. Only plants that germinated were used for the study. Plants were treated 1-2 weeks post emergence. Plants were watered every 2-3 days as needed.

Lamb’s Quarters (Chenopodium album)

[00129] Lamb’s quarters seeds were obtained from the Department of Agronomy at Iowa State University. Individual seeds were sown for each pot (6” wide x 4.5” deep) with approximately 800 mL of soil for each plant. Only plants that germinated were used for the study. Plants were treated 1-2 weeks post emergence. Plants were watered every 2-3 days as needed.

Giant Foxtail (Setaria faberi)

[00130] Giant foxtail seeds were obtained from the Department of Agronomy at Iowa State University. Three seeds were sown for each pot (6” wide x 4.5” deep) with approximately 800 mL of soil for each plant. Only plants that germinated were used for the study. Plants were treated 1-2 weeks post emergence. Plants were watered every 2-3 days as needed.

Soil Drench Assay

[00131] Formulations of the various active ingredients were created using the monoterpenoid derivatives, potassium hydroxide, and Triton-X 100^{TM} to aid in the solvation of the active ingredient. Formulations included 5% active ingredient by weight (0.5-1 g/100 mL water), with a 1:1 molar ratio of potassium hydroxide used to aid in the solvation (135-269 mg/100 mL for both thymyloxyacetic acid and carvacryloxyacetic acid). Triton-X 100^{TM} was introduced into the formulation to aid in solubility at a final concentration of 0.25%. 40 mL of formulation (either 5% active ingredient) was applied to each plant at 1-2 weeks after emergence. Observations were performed 2 days and 3 weeks after soil drench to determine the effects of the treatments on the various types and stages of plants. Phytotoxicity is reported as percentage of total plants treated compared to a control treatment that was exposed to a similar formulation (without the active monoterpenoid derivatives).

[00132] Both thymyloxyacetic acid and carvacryloxyacetic acid were capable of killing 100% of the treated weeds that were treated from each species (Table 4). This phytotoxicity was observed relatively quickly at two days after the initial treatment.

Table 4. Percentage mortalities of various weed species that were exposed to 40mL of 5% solution in soil drench assays

Treatment	Soil Drench Mortality of Weed Species									
	2-days after treatment					3-weeks after treatment				
	Percentage mortality					Percentage mortality				
	Pigweed	Velvet Leaf	Dandelions	Lamb's quarters	Giant Foxtail	Pigweed	Velvet Leaf	Dandelions	Lamb's quarters	Giant Foxtail
Thymyloxyacetic acid	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
Carvacryloxyacetic acid	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%

Example 6 – Selectivity Assessment and Residual Character in Soil

Materials and Methods

Palmer Amaranth (Amaranthus palmeri)

[00133] Palmer amaranth seeds were obtained from the Department of Agronomy at Iowa State University. Individual seeds were sown for each pot (1.5” wide x 3” deep) with approximately 7.5 g of soil for each plot. Five seeds/plot were sown into numerous plots. After one month of germination, germinated plants were counted in each plot and this number was used for the total number of plants challenged per plot in the toxicity assessment

Cocklebur (Xanthium spp.)

[00134] Cocklebur burs were obtained from the Department of Agronomy at Iowa State University. Individual seeds were sown for each pot (1.5” wide x 3” deep) with approximately 7.5 g of soil for each plot. One bur/plot was sown into numerous plots. After one month of germination, germinated plants were counted in each plot and this number was used for the total number of plants challenged per plot in the toxicity assessment.

Waterhemp (Amaranthus tuberculatus)

[00135] Waterhemp seeds were obtained from the Department of Agronomy at Iowa State University. Individual seeds were sown for each pot (1.5” wide x 3” deep) with approximately 7.5 g of soil for each plot. Five seeds/plot was sown into numerous plots. After one month of germination, germinated plants were counted in each plot and this number was used for the total number of plants challenged per plot in the toxicity assessment.

Bluegrass (Poa pretensis)

[00136] Kentucky bluegrass seeds were purchased in a bag under the commercial name of . Individual seeds were sown for each pot (1.5” wide x 3” deep) with approximately 7.5 g of soil for each plot. 10 seeds/plot was sown into numerous plots. After one month of germination, germinated plants were counted in each plot and this number was used for the total number of plants challenged per plot in the toxicity assessment.

Toxicity Assay

[00137] The total number of plants were counted in each plot in 24 x 6 hexagonal small plot planter tray. The number of germinated seeds in each plot was enumerated after one month, and for each plot this number was recorded and used as the total for each plot. Differing concentrations of thymyloxyacetic acid was applied in 5% Triton-X 100 and 1:1 molar ratio potassium hydroxide: thymyloxyacetic acid to aid in the solubility of the compound in water. Ten mL of solution was applied to each plot, and the mortality of the plants was assessed at 3 days and 2 weeks post application (for some treatments). Mortality at these time points were enumerated out of the total plants germinated in each plot at the beginning of the assay. At both time points, the total number of dead plants and total number of plants at the beginning of the assay were recorded for each observation. A Probit model was used to calculate the LC_{50} values for each of the compounds explored in this assay. A formulation control (with no active ingredient) was screened against a number of plants and factored into the final probit model. This formulation control had little-to-no effect by itself.

Results

[00138] All compounds screened in this exploration were phytotoxic to the plant species in question. The toxicity of each compound was compared to 2,4-dichlorophenoxyacetic acid (2,4-D) as a commercially available herbicide for comparison. Technical 2,4-D was purchased from Sigma Aldrich and incorporated into the formulations in the same manner as the insecticidal active ingredients described herein. The results of the toxicity of thymyloxyacetic acid compared to 2,4-D against palmer amaranth is presented in Table 4. 2,4-D was marginally more phytotoxic than thymyloxyacetic acid; however, the 95% confidence intervals significantly overlapped suggested no difference in the toxicities of both these compounds against palmer amaranth. Moreover, at two weeks after application, a significantly lower LC_{50} value was observed for 2,4-D than at three days after application. This was not the case for thymyloxyacetic acid, with the LC_{50} similar to one observed at three days after application. This suggests that 2,4-D is much more residual in soil than the herbicidal compounds derived from natural monoterpenoids, and is capable of exerting its effects far into the future. It is likely that thymyloxyacetic acid rapidly exerts its toxicity within the plant and quickly degrades in the soil, as suggested by this data.

[00139] The selectivity of these herbicides compared to bluegrass was also explored. If these compounds are to be used in home and garden, as well as agricultural applications, it is paramount that they act selectively against dicot weed species. Table 5 demonstrates that thymyloxyacetic acid is selective against various dicot weed species. The selectivity ratio compared to a blue grass species ranged between 2.06-5 fold for various weed species. The selectivity ratios for 2,4-D on these same weed species were 2.56-5.97 fold. Overall, the selectivity ratios for thymyloxyacetic acid were very similar compared to 2,4-D, a widely recognized selective herbicide, applied in both home and garden and agricultural field scenarios. Pictures demonstrating the phytotoxic effect against all the weed species described are presented in the accompanying figures.

[00140] To the extent necessary to provide descriptive support, it shall be understood that the subject matter and/or text of any appended claims are incorporated herein by reference in their entirety.

[00141] It will be understood by all readers of this written description that the example embodiments described herein may be suitably practiced in the absence of any recited feature, element or step that is, or is not, specifically disclosed herein.

Table 5. Comparison of Thymyloxyacetic Acid and 2,4-D on Palmer Amaranth

Palmer Amaranth	3-day post application				2-week post application			
Compound	N	Slope (SE)	LC50 value (ppm)	95% CI	N	Slope (SE)	LC50 value (ppm)	95% CI
2,4-D	41	2.66 (0.99)	1300	700-4000	41	2.72 (1.3)	465.04	7-949
thymyloxyacetic acid	91	5.14 (1.4)	1700	1300-2400	91	19.9 (3.7)	1350	820-1930

Table 6. Comparison of the Selectivity of Thymyloxyacetic Acid Toward Dicot Weed Species Compared to 2,4-D

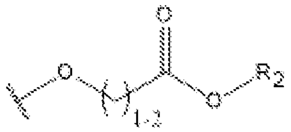
Compounds	thymyloxyacetic acid		2,4-D	
	LC_{50} Value (ppm)	Selective Toxicity Compared to Bluegrass	LC_{50} Value (ppm)	Selective Toxicity Compared to Bluegrass
Waterhemp	700	5	1800	2.56
Palmer Amaranth	1700	2.06	1300	3.54
Cocklebur	1530	2.29	770	5.97

WHAT IS CLAIMED IS:

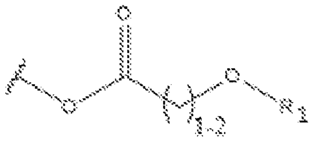
1. A composition comprising:
a carrier and a compound of formula (I):

R_1-A

,



, or



;

wherein

R_1 is an unsubstituted phenylpropanoid or monoterpenoid moiety;

R_2 is an unsubstituted phenylpropanoid or monoterpenoid moiety or is selected from the group consisting of H, M, substituted or unsubstituted C_3-C_7 unbranched or branched alkyl, substituted or unsubstituted C_2-C_7 unbranched or branched alkenyl, substituted or unsubstituted C_3-C_7 unbranched or branched alkynyl, substituted or unsubstituted C_3-C_7 unbranched or branched cycloalkyl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted C_3-C_7 unbranched or branched cycloalkenyl; and

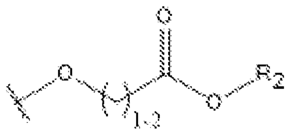
M is a counterion selected from the group consisting of sodium, potassium, calcium, magnesium, iron, zinc, copper, and an amine.

2. The composition of claim 1 as an herbicide having a phytotoxic and/or systemic mode of action.

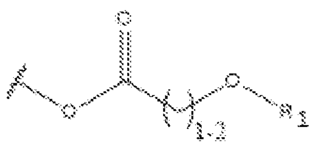
3. A method for controlling pest plant species by applying an effective amount of an herbicidal compound shown by the formula:

R_1-A

,



, or



;

R_1 is a unsubstituted phenylpropanoid or monoterpenoid moiety;
R2 is an unsubstituted phenylpropanoid or monoterpenoid moiety or is selected from the group consisting of H, M, substituted or unsubstituted C3-C7 unbranched or branched alkyl, substituted or unsubstituted C2-C7 unbranched or branched alkenyl, substituted or unsubstituted C3-C7 unbranched or branched alkynyl, substituted or unsubstituted C3-C7 unbranched or branched cycloalkyl, substituted or unsubstituted heteroaryl, and substituted or unsubstituted C3-C7 unbranched or branched cycloalkenyl; and
M is a counterion selected from the group consisting of sodium, potassium, calcium, magnesium, iron, zinc, copper, and an amine;

4. A method for controlling pest plant species by applying the composition defined in claim 1 to the soil adjacent to the pest plant species.

5. A method for controlling pest plant species by applying the composition defined in claim 1 in a granule formulation which is subsequently applied to the soil around a pest plant species.

6. A method for controlling pest plant species by applying the composition defined in claim 1 directly to the leaves of a pest plant species.

7. An herbicidal composition comprised of a carrier and an effective amount of thymyloxyacetic acid, carvacryloxyacetic acid, eugenyloxyacetic acid, umelliferonyloxyacetic acid, and piceyloxyacetic acid and/or esters of the previously mentioned compounds and any mixture thereof.
8. The example embodiment(s) substantially as described in the above written description, claims and accompanying figures/drawings.

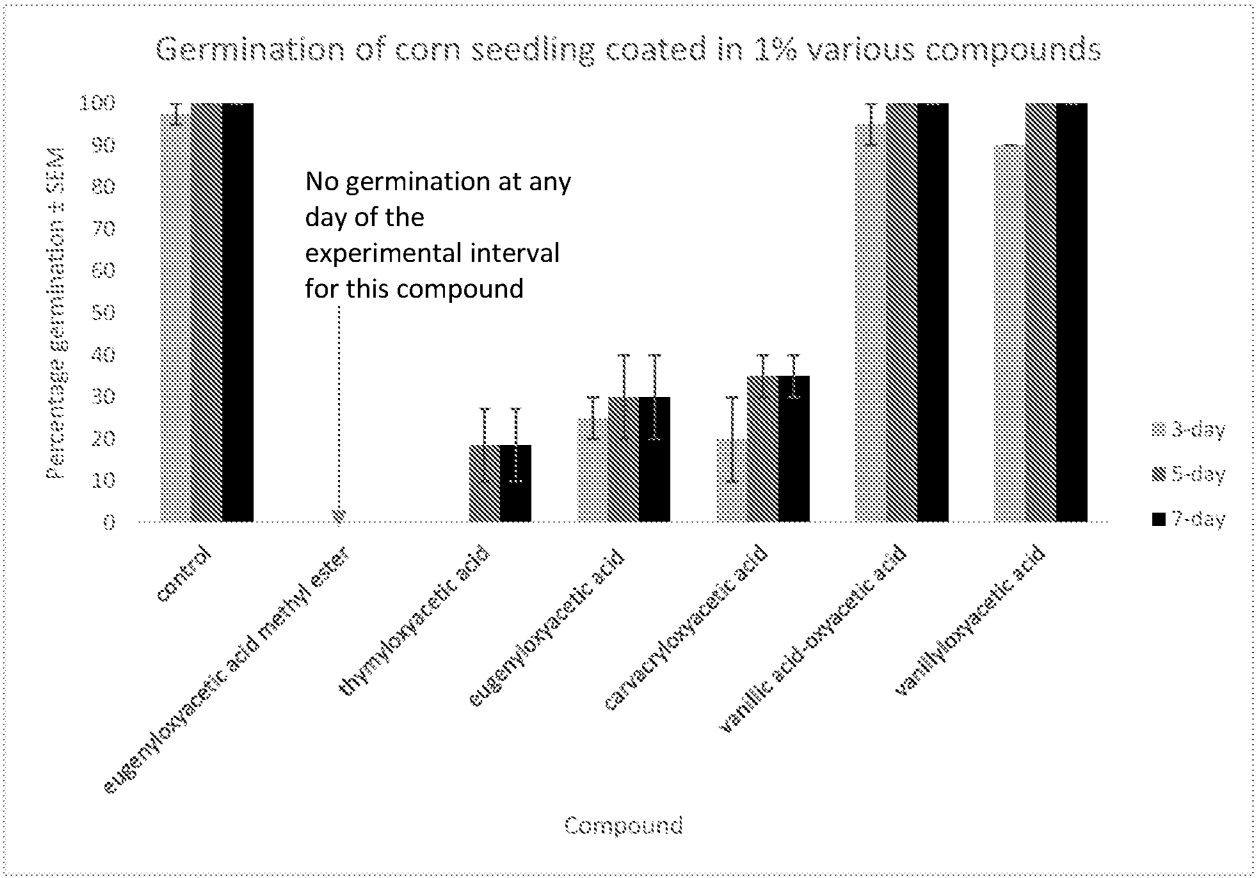

Germination of corn seedling coated in 1% various compounds
Percentage germination ± SEM
100
90
80
70
60
50
40
30
20
10
0
No germination at any day of the experimental interval for this compound
control
eugenyloxyacetic acid methyl ester
thymyloxyacetic acid
eugenyloxyacetic acid
carvacryloxyacetic acid
vanillic acid-oxyacetic acid
vanillyloxyacetic acid
Compound
3-day
5-day
7-day

FIG. 1

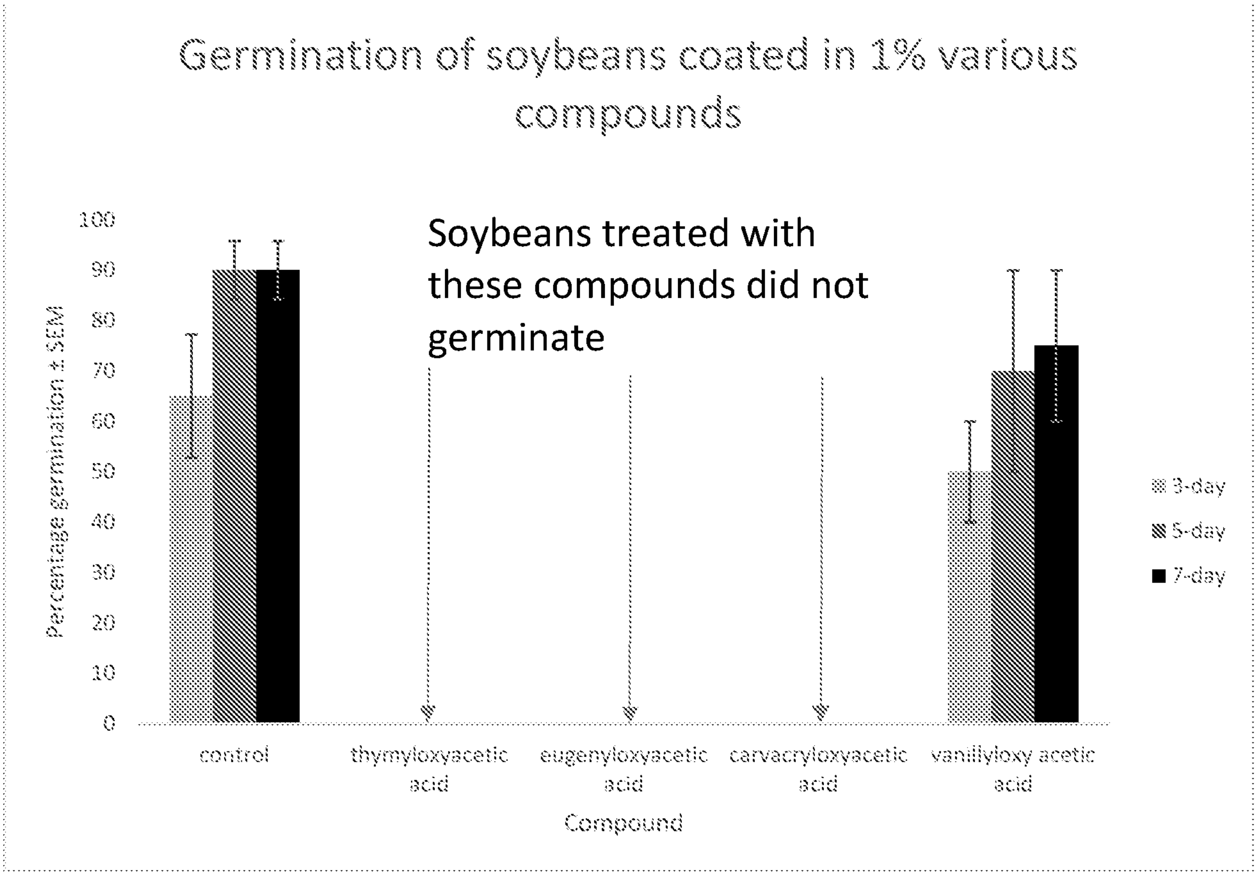
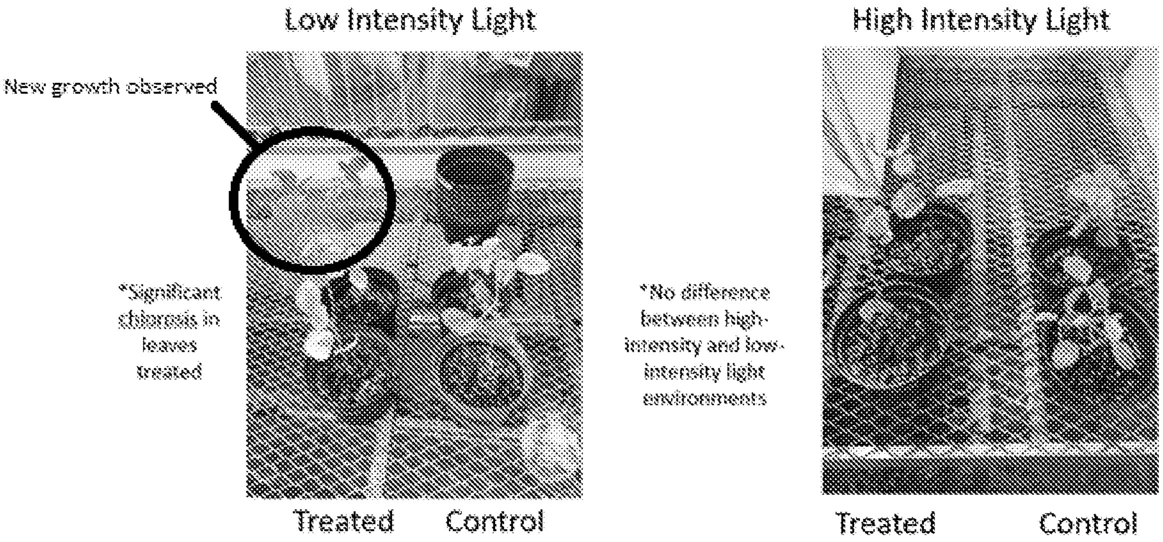

Germination of soybeans coated in 1% various compounds
Soybeans treated with these compounds did not germinate
Percentage germination ± SEM
100
90
80
70
60
50
40
30
20
10
0
control
thymyloxyacetic acid
eugenyloxyacetic acid
carvacryloxyacetic acid
vanillyloxy acetic acid
Compound
3-day
5-day
7-day

FIG. 2



Low Intensity Light

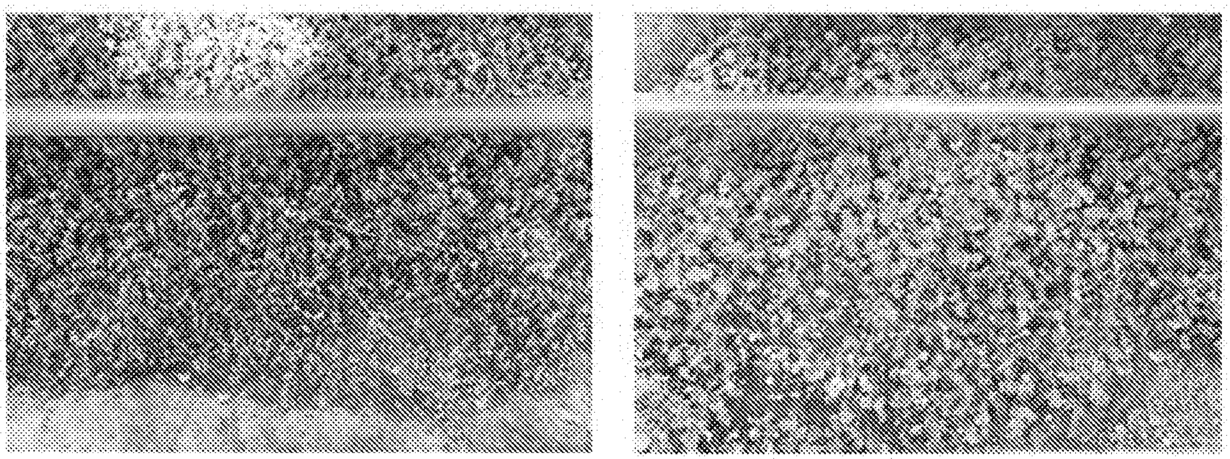
High Intensity Light

New growth observed

*Significant chlorosis in leaves treated

*No difference between high-intensity and low-intensity light environments

FIG. 3



1% carvacryloxyacetic acid

1% 2,4-dichlorophenoxyacetic acid

FIG. 4

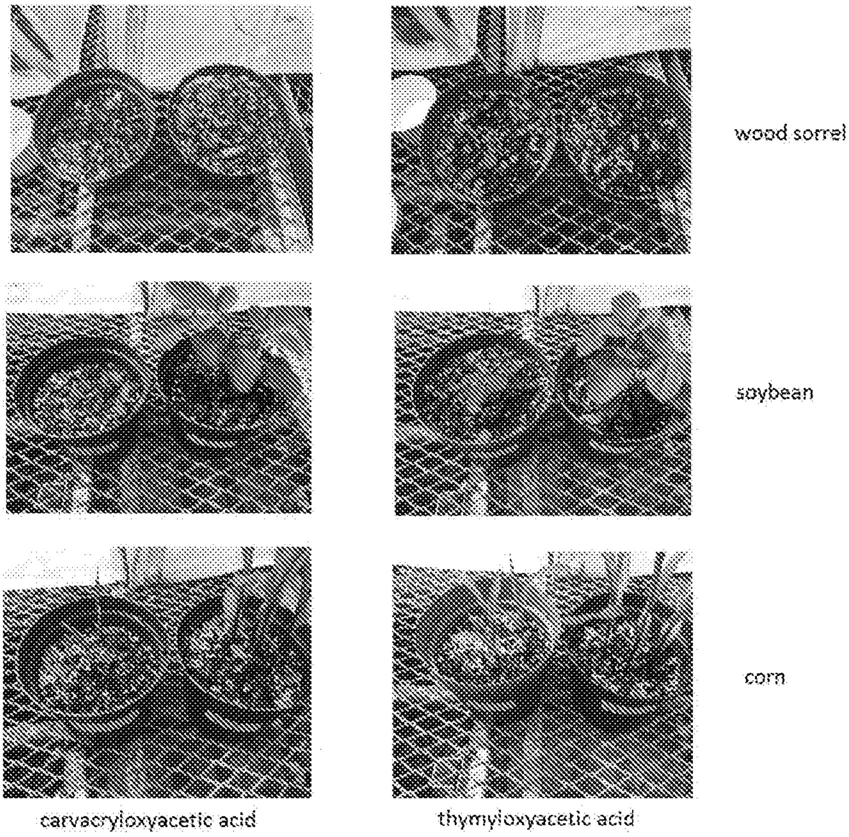

wood sorrel
soybean
corn
carvacryloxyacetic acid
thymyloxyacetic acid

FIG. 5

5% carvacryloxyacetic acid 5% thymyloxyacetic acid control

FIG. 6

5% carvacryloxyacetic acid 5% thymyloxyacetic acid control

FIG 7

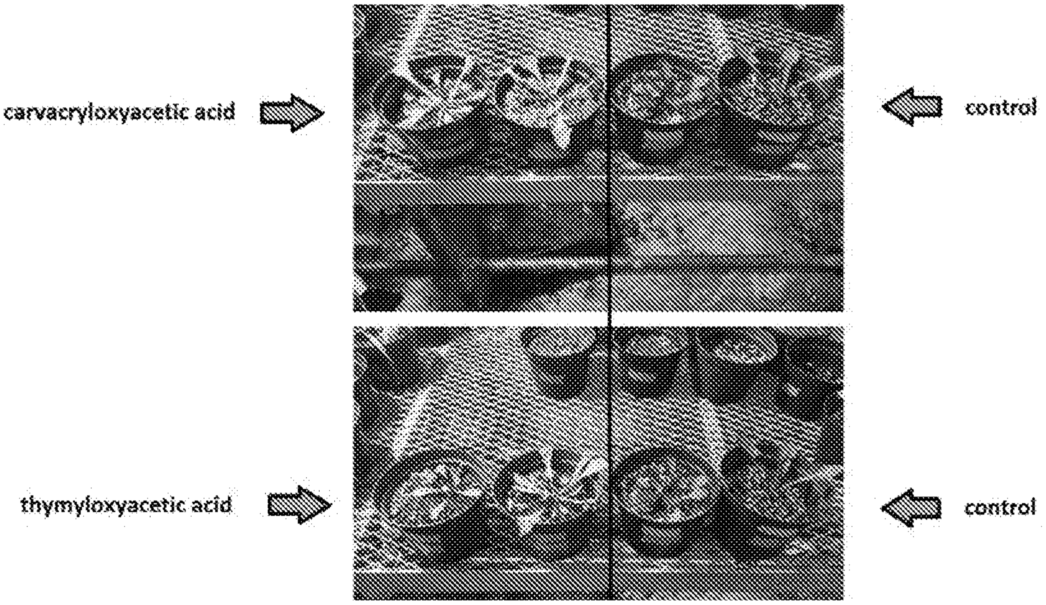


FIG. 8

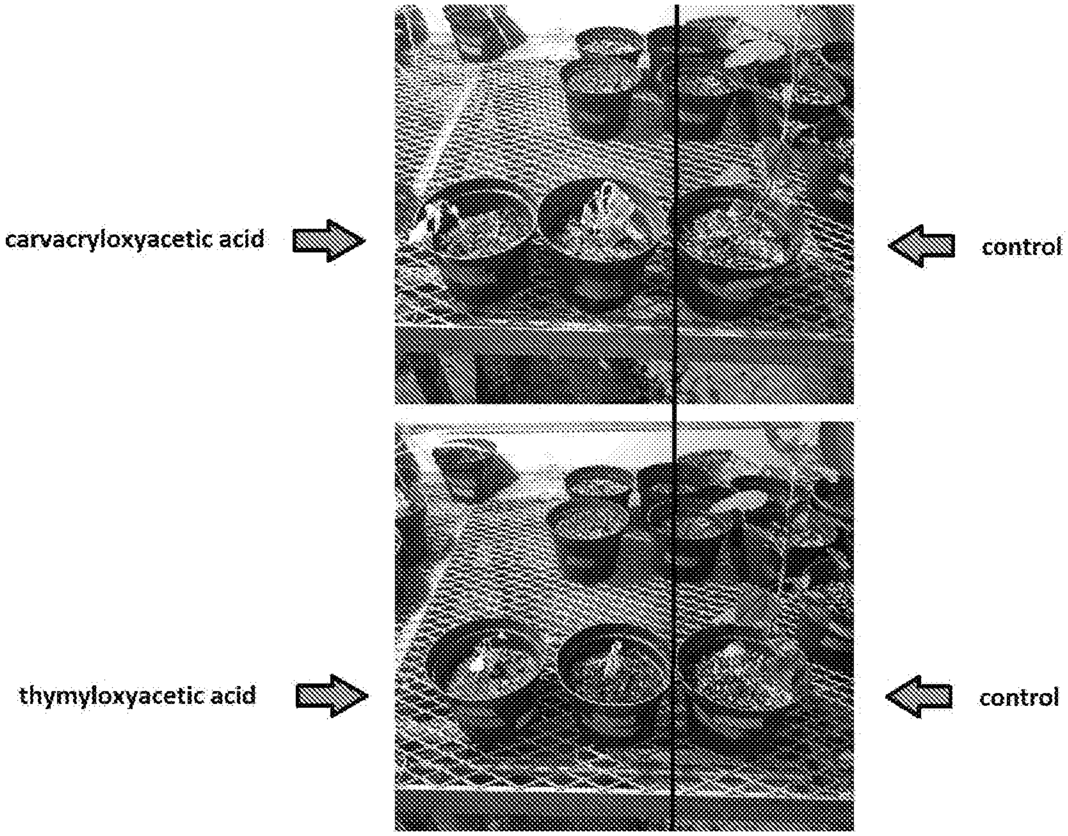

carvacryloxyacetic acid
control
thymyloxyacetic acid
control

FIG. 9

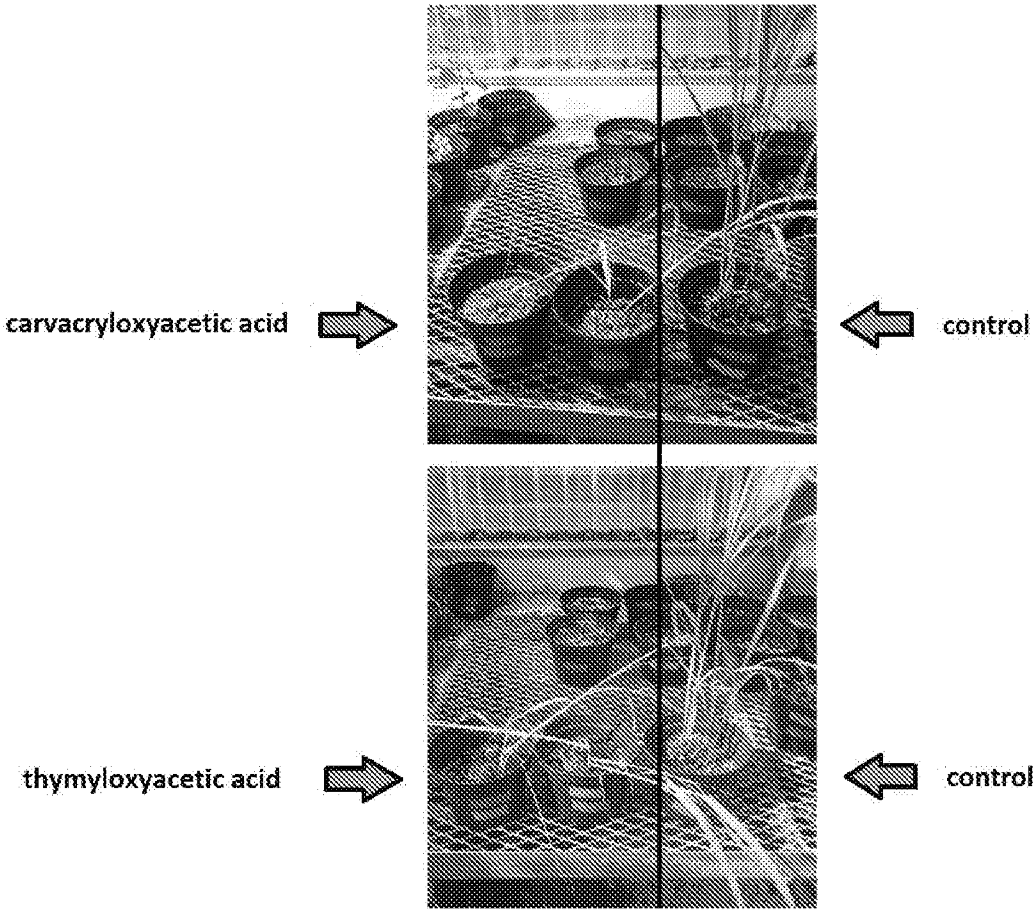

carvacryloxyacetic acid
control
thymyloxyacetic acid
control

FIG. 10

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2017/048290

A. CLASSIFICATION OF SUBJECT MATTER

A01N 31/02(2006.01)i, A01N 25/12(2006.01)i, C07C 59/13(2006.01)i

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)
A01N 31/02; A01N 25/12; C07C 59/13

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Korean utility models and applications for utility models
Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
eKOMPASS(Kipo internal), STN (Registry, Caplus) & Keywords: herbicide, thymyloxyacetic acid, carvacryloxyacetic acid, eugenyloxyacetic acid, umelliferonyloxyacetic acid

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	NIKUMBH, V. P. et al., "Eco-friendly pest management using monoterpenoids-III: Antibacterial efficacy of carvacrol derivatives", Journal of Scientific & Industrial Research, 2003, Vol. 62, pp. 1086-1089 See abstract; pages 1086, 1087; and table 1.	1-7
X	GOWING, D. P. et al., "Uncommon plant growth regulators for the control of nutgrass and oxalis", Weeds, 1960, Vol. 8, No. 2, pp. 279-283 See pages 279, 280; and table 1.	1-7
X	KUMBHAR, P. P. et al., "Eco-friendly pest management using monoterpenoids. I. Antifungal efficacy of thymol derivatives", Journal of Scientific & Industrial Research, 2001, Vol. 60, pp. 645-648 See abstract; page 645; figure 1; and table 1.	1-7
X	MORE, D. H. et al., "Microwave-assisted sinthesis of thymyl ethers and esters in aqueous medium", Russian Journal of General Chemistry, 2004, Vol. 74, No. 2, pp. 217-218 See abstract; page 217; and scheme 1.	1-7

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

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

Date of the actual completion of the international search 04 December 2017 (04.12.2017)	Date of mailing of the international search report **05 December 2017 (05.12.2017)**
Name and mailing address of the ISA/KR International Application Division Korean Intellectual Property Office 189 Cheongsa-ro, Seo-gu, Daejeon, 35208, Republic of Korea Facsimile No. +82-42-481-8578	Authorized officer LEE, Dong Wook Telephone No. +82-42-481-8163

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2017/048290

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	NARKHEDE, H. P. et al., “Solid-supported synthesis of bio-active carvacrol compounds using microwaves” , Synthetic Communications, 2008, Vol. 38, No. 14, pp. 2413-2418 See abstract; page 2417; scheme 1; and table 1.	1-7

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2017/048290

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.: 8
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:
Claim 8 is contrary to PCT Rule 6.2(a), because it relies on unnecessary reference to the description and drawings.

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

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

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

1. ☐ As all required addtional 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 an additional fees, this Authority did not invite payment of any 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

Information on patent family members

International application No.

PCT/US2017/048290

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
None			

Form PCT/ISA/210 (patent family annex) (January 2015)