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(54) Title: PRODUCTION OF FATTY OLEFIN DERIVATIVES VIA OLEFIN METATHESIS

(57) Abstract: The invention provides a method for synthesizing a fatty olefin derivative. In some embodiments, the method includes: a) contacting an unsaturated olefin with an unsaturated fatty acid ester in the presence of a metathesis catalyst under conditions sufficient to form a metathesis product and b) converting the metathesis product to the fatty olefin derivative. In certain embodiments, the metathesis catalyst is a tungsten catalyst or a molybdenum catalyst. In various embodiments, the fatty olefin derivative is an insect pheromone. Pheromone compositions and methods of using them are also described.



## PRODUCTION OF FATTY OLEFIN DERIVATIVES VIA OLEFIN METATHESIS

### 5 CROSS-REFERENCES TO RELATED APPLICATIONS

[0001] The present application claims priority to U.S. Provisional Pat. Appl. No. 62/257,148, filed on Nov. 18, 2015, which application is incorporated herein by reference in its entirety.

### BACKGROUND OF THE INVENTION

10 [0002] Insect infestation is a primary cause of crop loss throughout the United States. A wide variety of chemical pesticides has been relied upon in the past to control insect pests. However, environmental concerns as well as consumer safety concerns have led to the de-registration of many pesticides and a reluctance to use others on agricultural products which are ultimately consumed as food. As a consequence, there is a desire for the development of  
15 alternative biological control agents.

[0003] Pheromones are chemicals which are secreted outside the body of insects can be classified according to the type of behavioral reaction they induce. Pheromone classes include aggregation pheromones, sexual pheromones, trail pheromones, and alarm pheromones. Sex pheromones, for example, are typically secreted by insects to attract  
20 partners for mating.

[0004] When pheromones are dispersed on leaves of a crop plant, or in an orchard environment in small quantities over a continuous period of time, pheromone levels reach thresholds that can modify insect behavior. Maintenance of pheromone levels at or above such thresholds can impact insect reproductive processes and reduce mating. Use of  
25 pheromones in conjunction with conventional insecticides can therefore reduce the quantity of insecticide required for effective control and can specifically target pest insects while preserving beneficial insect populations. These advantages can reduce risks to humans and the environment and lower overall insect control costs.

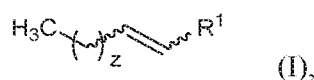
[0005] Despite these advantages, pheromones are not widely used today because of the  
30 high cost of active ingredient (AI). Even though thousands of insect pheromones have been identified, less than about twenty insect pests worldwide are currently controlled using

pheromone strategies, and only 0.05% of global agricultural land employs pheromones. Lepidopteran pheromones, which are naturally occurring compounds, or identical or substantially similar synthetic compounds, are designated by an unbranched aliphatic chain (between 9 and 18 carbons) ending in an alcohol, aldehyde, or acetate functional group and containing up to 3 double bonds in the aliphatic backbone. Improved methods for preparing lepidopteran insect pheromones and structurally related compounds are needed. The present invention meets this and other needs.

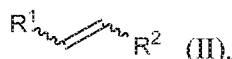
#### BRIEF SUMMARY OF THE INVENTION

[0006] In a first aspect, the invention provides a method for synthesizing a fatty olefin derivative. The method includes:

a) contacting an olefin according to Formula I



with a metathesis reaction partner according to Formula II



in the presence of a metathesis catalyst under conditions sufficient to form a metathesis product; and

b) optionally converting the metathesis product to the fatty olefin derivative; wherein:

$\text{R}^1$  is selected from H,  $\text{C}_{1-18}$  alkyl, and  $\text{C}_{2-18}$  alkenyl;

$\text{R}^2$  is selected from  $-(\text{CH}_2)_x\text{OR}^{2a}$  and  $-(\text{CH}_2)_y\text{COOR}^{2b}$ , wherein  $\text{R}^{2a}$  is an alcohol protecting group and  $\text{R}^{2b}$  is  $\text{C}_{1-8}$  alkyl;

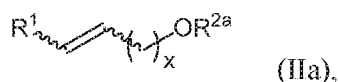
subscript x is an integer ranging from 1 to 18;

subscript y is an integer ranging from 0 to 17; and

subscript z is an integer ranging from 0 to 17.

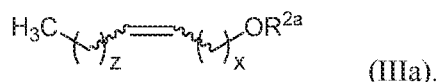
[0007] In some embodiments, the metathesis catalyst is a tungsten metathesis catalyst, a molybdenum metathesis catalyst, or a ruthenium metathesis catalyst. In certain embodiments, the metathesis catalyst is a tungsten catalyst or a molybdenum catalyst.

[0008] In some embodiments, the metathesis reaction partner is a protected alcohol according to Formula IIa:

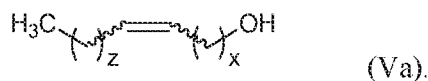


wherein  $R^{2a}$  is an alcohol protecting group,

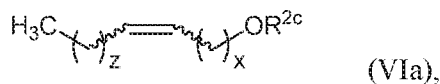
and wherein the metathesis product is a compound according to Formula IIIa:



[0009] In some embodiments, converting the metathesis product to the fatty olefin derivative includes removing  $R^{2a}$  from the compound of Formula IIIa to form an alkenol according to Formula Va:

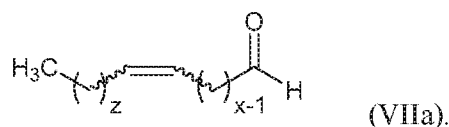


[0010] In some embodiments, the alkenol of Formula Va is the pheromone. In some embodiments, converting the metathesis product to the fatty olefin derivative further includes acylating the alkenol of Formula Va, thereby forming a fatty olefin derivative according to Formula VIa:



wherein  $R^{2c}$  is  $\text{C}_{1-6}$  acyl.

[0011] In some embodiments, converting the metathesis product to the fatty olefin derivative further includes oxidizing the alkenol of Formula Va, thereby forming a fatty olefin derivative according to Formula VIIa:

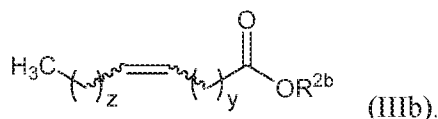


[0012] In some embodiments, the metathesis reaction partner is an ester according to Formula IIb:

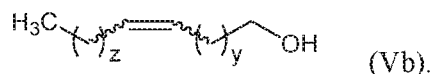


and subscript  $z$  is an integer ranging from 1 to 18; and

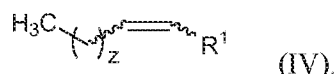
wherein the metathesis product is a compound according to Formula IIIb:



[0013] In some embodiments, converting the metathesis product to the fatty olefin derivative includes reducing the metathesis product of Formula IIIb to form an alkenol according to Formula Vb:



5 [0014] In some embodiments, the metathesis reaction partner is a protected alcohol according to Formula IIIa or Formula IIIb and the metathesis product is a compound according to Formula IV:



[0015] In some embodiments, R<sup>1</sup> in the compound of Formula IV is C<sub>2-18</sub> alkenyl.

10 [0016] A number of pheromones and pheromone precursors, including unsaturated fatty alcohols, unsaturated fatty alcohol acetates, unsaturated fatty aldehydes, unsaturated fatty acid esters, and polyenes, can be synthesized using the methods of the invention.

## DETAILED DESCRIPTION OF THE INVENTION

### I. INTRODUCTION

15 [0017] The present invention provides methods for the synthesis of fatty olefin derivatives (such as straight-chain lepidopteran pheromones; SCLPs) through the cross-metathesis of protected fatty alcohols or fatty acid esters with olefins (*e.g.*,  $\alpha$ -olefins). Through the use of a variety of fatty alcohols, fatty acid alkyl esters and  $\alpha$ -olefin feedstocks in concert with olefin metathesis catalysts (including Group VI Z-selective catalysts), a wide variety of protected  
20 unsaturated fatty alcohol precursors with high Z-olefin content can be obtained. These precursor compounds can be converted to pheromones (*e.g.*, long chain Z-alcohols, Z-aldehydes, Z-acetates, and Z-nitrates) and other useful fatty olefin derivatives as described in detail below. Alternatively, non-selective olefin metathesis catalysts (including Group VI non-selective catalysts) can be used to generate cis/trans mixtures of protected long chain  
25 fatty alcohols. Such mixtures can be refined to provide pure *E*-pheromone precursors and other fatty *E*-olefin derivatives via Z-selective ethenolysis. The methods provide access to valuable products, including SCLPs containing 7-, 9-, or 10-monounsaturation.

### II. DEFINITIONS

[0018] The following definitions and abbreviations are to be used for the interpretation of  
30 the invention. The term “invention” or “present invention” as used herein is a non-limiting

term and is not intended to refer to any single embodiment but encompasses all possible embodiments.

[0019] As used herein, the terms “comprises,” “comprising,” “includes,” “including,” “has,” “having,” “contains,” “containing,” or any other variation thereof, are intended to cover  
5 a non-exclusive inclusion. A composition, mixture, process, method, article, or apparatus that comprises a list of elements is not necessarily limited to only those elements but may include other elements not expressly listed or inherent to such composition, mixture, process, method, article, or apparatus. Further, unless expressly stated to the contrary, “or” refers to an inclusive “or” and not to an exclusive “or.”

10 [0020] The terms “about” and “around,” as used herein to modify a numerical value, indicate a close range surrounding that explicit value. If “X” were the value, “about X” or “around X” would indicate a value from 0.9X to 1.1X, and in certain instances, a value from 0.95X to 1.05X or from 0.98X to 1.02X. Any reference to “about X” or “around X” specifically indicates at least the values X, 0.95X, 0.96X, 0.97X, 0.98X, 0.99X, 1.01X,  
15 1.02X, 1.03X, 1.04X, and 1.05X. Thus, “about X” and “around X” are intended to teach and provide written description support for a claim limitation of, *e.g.*, “0.99X.”

[0021] As used herein, the term “pheromone” refers to a substance, or characteristic mixture of substances, that is secreted and released by an organism and detected by a second organism of the same species or a closely related species. Typically, detection of the  
20 pheromone by the second organism promotes a specific reaction, such as a definite behavioral reaction or a developmental process. Insect pheromones, for example, can influence behaviors such as mating and aggregation. Examples of pheromones include, but are not limited to, compounds produced by Lepidoptera (*i.e.*, moths and butterflies belonging to the *Geometridae*, *Noctuidae*, *Arctiidae*, and *Lymantriidae* families) such as C<sub>10</sub>-C<sub>18</sub> acetates, C<sub>10</sub>-  
25 C<sub>18</sub> alcohols, C<sub>10</sub>-C<sub>18</sub> aldehydes, and C<sub>17</sub>-C<sub>23</sub> polyenes. An “unsaturated pheromone” refers to any pheromone having at least one carbon-carbon double bond.

[0022] As used herein, the term “contacting” refers to the process of bringing into contact at least two distinct species such that they can react. It should be appreciated, however, that the resulting reaction product can be produced directly from a reaction between the added  
30 reagents or from an intermediate from one or more of the added reagents that can be produced in the reaction mixture.

[0023] As used herein, the term “olefin” refers to a straight-chain or branched hydrocarbon compound containing at least one carbon-carbon double bond and derivatives thereof. The olefin can be unsubstituted or substituted with one or more functional groups including alcohol groups, protected alcohol groups, carboxylate groups, and carboxylic acid ester groups. As used herein, the term “olefin” encompasses hydrocarbons having more than one carbon-carbon double bond (e.g., di-olefins, tri-olefins, etc.). Hydrocarbons having more than one carbon-carbon double bond and derivatives thereof are also referred to as “polyenes.” The term “fatty olefin” refers to an olefin having at least four carbon atoms; fatty olefins can have, for example, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, or 28 carbon atoms. A “fatty olefin derivative” refers to a compound obtained from an olefin starting material or a fatty olefin starting material. Examples of fatty olefin derivatives include, but are not limited to, unsaturated fatty alcohols, unsaturated fatty alcohol acetates, unsaturated fatty aldehydes, unsaturated fatty acids, unsaturated fatty acid esters, and polyenes. In certain embodiments, fatty olefins derivatives synthesized according to the methods of the invention have from 8 to 28 carbon atoms.

[0024] A  $\Delta^9$ -unsaturated olefin refers to an olefin wherein the ninth bond from the end of olefin is a double bond. A  $\Delta^9$ -unsaturated fatty acid refers to an olefinic carboxylic acid wherein the ninth bond from the carboxylic acid group is a double bond. Examples of  $\Delta^9$ -unsaturated fatty acids include, but are not limited to, 9-decenoic acid, oleic acid (*i.e.*, (*Z*)-octadec-9-enoic acid), and elaidic acid (*i.e.*, (*E*)-octadec-9-enoic acid).

[0025] As used herein, the term “metathesis reaction” refers to a catalytic reaction which involves the interchange of alkylidene units (*i.e.*,  $R_2C=$  units) among compounds containing one or more carbon-carbon double bonds (e.g., olefinic compounds) via the formation and cleavage of the carbon-carbon double bonds. Metathesis can occur between two molecules having the same structure (often referred to as self-metathesis) and/or between two molecules having different structures (often referred to as cross-metathesis). The term “metathesis reaction partner” refers to a compound having a carbon-carbon double bond that can react with an olefin in a metathesis reaction to form a new carbon-carbon double bond.

[0026] As used herein, the term “metathesis catalyst” refers to any catalyst or catalyst system that catalyzes a metathesis reaction. One of skill in the art will appreciate that a metathesis catalyst can participate in a metathesis reaction so as to increase the rate of the reaction, but is itself not consumed in the reaction. A “tungsten catalyst” refers to a

metathesis catalyst having one or more tungsten atoms. A "molybdenum catalyst" refers to a metathesis catalyst having one or more molybdenum atoms.

[0027] As used herein, the term "metathesis product" refers to an olefin containing at least one double bond, the bond being formed via a metathesis reaction.

5 [0028] As used herein, the term "converting" refers to reacting a starting material with at least one reagent to form an intermediate species or a product. The converting can also include reacting an intermediate with at least one reagent to form a further intermediate species or a product.

[0029] As used herein, the term "oxidizing" refers to the transfer of electron density from a  
10 substrate compound to an oxidizing agent. The electron density transfer typically occurs via a process including addition of oxygen to the substrate compound or removal of hydrogen from the substrate compound. The term "oxidizing agent" refers to a reagent which can accept electron density from the substrate compound. Examples of oxidizing agents include, but are not limited to, pyridinium chlorochromate, *o*-iodoxybenzoic acid, and 2,2,6,6-  
15 tetramethylpiperidine 1-oxyl.

[0030] As used herein, the term "reducing" refers to the transfer of electron density from a reducing agent to a substrate compound. The electron density transfer typically occurs via a process including addition of hydrogen to the substrate compound. The term "reducing agent" refers to a reagent which can donate electron density to the substrate compound.  
20 Examples of reducing agents include, but are not limited to, sodium borohydride and sodium triacetoxyborohydride.

[0031] As used herein, the term "acylating" refers to converting a alcohol group (-OH), to an ester group (-OC(O)R), where R is an alkyl group as described below.

[0032] The term "aliphatic" or "aliphatic group," as used herein, means a straight-chain  
25 (*i.e.*, unbranched) or branched, substituted or unsubstituted hydrocarbon chain that is completely saturated or that contains one or more units of unsaturation, or a monocyclic hydrocarbon, bicyclic hydrocarbon, or tricyclic hydrocarbon that is completely saturated or that contains one or more units of unsaturation, but which is not aromatic (also referred to herein as "carbocycle" or "cycloaliphatic"), that has a single point of attachment to the rest of  
30 the molecule. Unless otherwise specified, aliphatic groups contain 1-30 aliphatic carbon atoms. In some embodiments, aliphatic groups contain 1-20 aliphatic carbon atoms. In other



embodiments, aliphatic groups contain 1-10 aliphatic carbon atoms. In still other embodiments, aliphatic groups contain 1-5 aliphatic carbon atoms, and in yet other embodiments, aliphatic groups contain 1, 2, 3, or 4 aliphatic carbon atoms. In some embodiments, “cycloaliphatic” (or “carbocycle”) refers to a monocyclic C<sub>3</sub>-C<sub>6</sub> hydrocarbon, or a C<sub>8</sub>-C<sub>10</sub> bicyclic hydrocarbon that is completely saturated or that contains one or more units of unsaturation, but which is not aromatic, that has a single point of attachment to the rest of the molecule. Suitable aliphatic groups include, but are not limited to, linear or branched, substituted or unsubstituted alkyl, alkenyl, alkynyl groups and hybrids thereof such as (cycloalkyl)alkyl, (cycloalkenyl)alkyl, or (cycloalkyl)alkenyl. The term “heteroaliphatic” refers to an aliphatic group wherein at least one carbon atom of the aliphatic group is replaced with a heteroatom (*i.e.*, nitrogen, oxygen, or sulfur, including any oxidized form of nitrogen or sulfur, and any quaternized form of a basic nitrogen).

[0033] As used herein, the term “alkyl” is given its ordinary meaning in the art and includes straight-chain alkyl groups and branched-chain alkyl groups having the number of carbons indicated. In certain embodiments, a straight chain or branched chain alkyl has about 1-30 carbon atoms in its backbone (*e.g.*, C<sub>1</sub>-C<sub>30</sub> for straight chain, C<sub>3</sub>-C<sub>30</sub> for branched chain), and alternatively, about 1-20. In some embodiments, an alkyl group may be a lower alkyl group, wherein a lower alkyl group comprises 1-4 carbon atoms (*e.g.*, C<sub>1</sub>-C<sub>4</sub> for straight chain lower alkyls).

[0034] The term “heteroalkyl” is given its ordinary meaning in the art and refers to alkyl groups as described herein in which one or more carbon atoms is replaced with a heteroatom (*e.g.*, oxygen, nitrogen, sulfur, and the like). Examples of heteroalkyl groups include, but are not limited to, alkoxy, poly(ethylene glycol)-, alkyl-substituted amino, and the like.

[0035] As used herein, the term “acyl” refers to the functional group -C(O)R, wherein R is an alkyl group as described above.

[0036] As used herein, the term “alkoxy” refers to a moiety -OR wherein R is an alkyl group as defined above. The term “silylalkyl” refers to an alkyl group as defined herein wherein at least one carbon atom is replaced with a silicon atom. The term “silyloxy” refers to a moiety -OSiR<sub>3</sub>, wherein each R is independently selected from the group consisting of H, alkyl, substituted alkyl, aryl, and substituted aryl as described herein.

[0037] As used herein, the term “cycloalkyl” refers to a saturated, monocyclic hydrocarbon, bicyclic hydrocarbon, or tricyclic hydrocarbon group that has a single point of

attachment to the rest of the molecule. Cycloalkyl groups include alkyl substituted cycloalkyl groups and cycloalkyl substituted alkyl groups. In some embodiments, cycloalkyl rings have from about 3-10 carbon atoms in their ring structure where such rings are monocyclic or bicyclic, and alternatively about 5, 6 or 7 carbons in the ring structure.

5 [0038] As used herein, the term “alkenyl” refers to an alkyl group, as defined herein, having one or more double bonds. The term “heteroalkenyl” refers to an alkenyl group wherein one or more carbon atoms is replaced with a heteroatom (*i.e.*, nitrogen, oxygen, or sulfur, including any oxidized form of nitrogen or sulfur, and any quaternized form of a basic nitrogen).

10 [0039] As used herein, the term “alkenol” refers to a compound having a formula R-OR' wherein R is an alkenyl group and R' is hydrogen or an alcohol protecting group.

[0040] As used herein, the term “alkynyl” refers to an alkyl group, as defined herein, having one or more triple bonds.

[0041] The term “aryl” used alone or as part of a larger moiety as in “aralkyl,” “aralkoxy,”  
15 or “aryloxyalkyl,” refers to monocyclic or bicyclic ring systems having a total of five to fourteen ring members, wherein at least one ring in the system is aromatic and wherein each ring in the system contains 3 to 7 ring members. The term “aryl” may be used interchangeably with the term “aryl ring.” In certain embodiments of the present invention, “aryl” refers to an aromatic ring system which includes, but is not limited to, phenyl,  
20 biphenyl, naphthyl, anthracyl and the like, which may bear one or more substituents. Also included within the scope of the term “aryl,” as it is used herein, is a group in which an aromatic ring is fused to one or more non-aromatic rings, such as indanyl, phthalimidyl, naphthimidyl, phenanthridinyl, or tetrahydronaphthyl, and the like. The term “aryloxy” refers to a moiety -OR, wherein R is an aryl group as defined above.

25 [0042] The terms “heteroaryl” and “heteroar-,” used alone or as part of a larger moiety, *e.g.*, “heteroaralkyl,” or “heteroaralkoxy,” refer to groups having 5 to 10 ring atoms (*i.e.*, monocyclic or bicyclic), in some embodiments 5, 6, 9, or 10 ring atoms. In some embodiments, such rings have 6, 10, or 14 pi electrons shared in a cyclic arrangement; and having, in addition to carbon atoms, from one to five heteroatoms. The term “heteroatom”  
30 refers to nitrogen, oxygen, or sulfur, and includes any oxidized form of nitrogen or sulfur, and any quaternized form of a basic nitrogen. Heteroaryl groups include, without limitation,

thienyl, furanyl, pyrrolyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, oxazolyl, isoxazolyl, oxadiazolyl, thiazolyl, isothiazolyl, thiadiazolyl, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, indolizinyl, purinyl, naphthyridinyl, and pteridinyl. The terms "heteroaryl" and "heteroar-", as used herein, also include groups in which a heteroaromatic ring is fused to one or more aryl, cycloaliphatic, or heterocyclyl rings, where the radical or point of attachment is on the heteroaromatic ring. Nonlimiting examples include indolyl, isoindolyl, benzothienyl, benzofuranyl, dibenzofuranyl, indazolyl, benzimidazolyl, benzthiazolyl, quinolyl, isoquinolyl, cinnolyl, phthalazinyl, quinazolyl, quinoxalyl, 4H-quinolizyl, carbazolyl, acridinyl, phenazinyl, phenothiazinyl, phenoxazinyl, tetrahydroquinolyl, tetrahydroisoquinolyl, and pyrido[2,3-b]-1,4-oxazin-3(4H)-one. A heteroaryl group may be mono- or bicyclic. The term "heteroaryl" may be used interchangeably with the terms "heteroaryl ring," "heteroaryl group," or "heteroaromatic," any of which terms include rings that are optionally substituted. The term "heteroaralkyl" refers to an alkyl group substituted by a heteroaryl, wherein the alkyl and heteroaryl portions independently are optionally substituted.

**[0043]** Examples of aryl and heteroaryl groups include, but are not limited to, phenyl, pyrrolyl, furanyl, thiophenyl, imidazolyl, oxazolyl, thiazolyl, triazolyl, pyrazolyl, pyridinyl, pyrazinyl, pyridazinyl and pyrimidinyl, and the like. It should be understood that, when aryl and heteroaryl groups are used as ligands coordinating a metal center, the aryl and heteroaryl groups may have sufficient ionic character to coordinate the metal center. For example, when a heteroaryl group such as pyrrole is used as a nitrogen-containing ligand, as described herein, it should be understood that the pyrrole group has sufficient ionic character (*e.g.*, is sufficiently deprotonated to define a pyrrolyl) to coordinate the metal center. In some cases, the aryl or heteroaryl group may comprise at least one functional group that has sufficient ionic character to coordinate the metal center, such as a biphenolate group, for example.

**[0044]** As used herein, the terms "heterocycle," "heterocyclyl," "heterocyclic radical," and "heterocyclic ring" are used interchangeably and refer to a stable 5- to 7-membered monocyclic or 7-10-membered bicyclic heterocyclic moiety that is either saturated or partially unsaturated, and having, in addition to carbon atoms, one or more heteroatoms (*e.g.*, one to four heteroatoms), as defined above. When used in reference to a ring atom of a heterocycle, the term "nitrogen" includes a substituted nitrogen. As an example, in a saturated or partially unsaturated ring having 1-3 heteroatoms selected from oxygen, sulfur or nitrogen,

the nitrogen may be N (as in 3,4-dihydro-2*H*-pyrrolyl), NH (as in pyrrolidiny), or <sup>+</sup>NR (as in *N*-substituted pyrrolidiny).

[0045] A heterocyclic ring can be attached to its pendant group at any heteroatom or carbon atom that results in a stable structure and any of the ring atoms can be optionally substituted. Examples of such saturated or partially unsaturated heterocyclic radicals include, without limitation, tetrahydrofuranyl, tetrahydrothiophenyl, pyrrolidiny, piperidiny, pyrroliny, tetrahydroquinoliny, tetrahydroisoquinoliny, decahydroquinoliny, oxazolidiny, piperaziny, dioxanyl, dioxolanyl, diazepiny, oxazepiny, thiazepiny, morpholiny, and quinuclidiny. The terms “heterocycle,” “heterocyclyl,” “heterocyclyl ring,” “heterocyclic group,” “heterocyclic moiety,” and “heterocyclic radical,” are used interchangeably herein, and also include groups in which a heterocyclyl-ring is fused to one or more aryl, heteroaryl, or cycloaliphatic rings, such as indoliny, 3*H*-indolyl, chromanyl, phenanthridiny, or tetrahydroquinoliny. A heterocyclyl group may be mono- or bicyclic. The term “heterocyclylalkyl” refers to an alkyl group substituted by a heterocyclyl, wherein the alkyl and heterocyclyl portions independently are optionally substituted.

[0046] The terms “halogen” and “halo” are used interchangeably to refer to F, Cl, Br, or I.

[0047] As used herein, the term “protecting group” refers to a chemical moiety that renders a functional group unreactive, but is also removable so as to restore the functional group. Examples of “alcohol protecting groups” include, but are not limited to, benzyl; *tert*-butyl; trityl; *tert*-butyldimethylsilyl (TBDMS; TBS); 4,5-dimethoxy-2-nitrobenzyloxycarbonyl (Dmnb); propargyloxycarbonyl (Poc); and the like. Examples of “amine protecting groups” include, but are not limited to, benzyloxycarbonyl; 9-fluorenylmethyloxycarbonyl (Fmoc); *tert*-butyloxycarbonyl (Boc); allyloxycarbonyl (Alloc); *p*-toluene sulfonyl (Tos); 2,2,5,7,8-pentamethylchroman-6-sulfonyl (Pmc); 2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-sulfonyl (Pbf); mesityl-2-sulfonyl (Mts); 4-methoxy-2,3,6-trimethylphenylsulfonyl (Mtr); acetamido; phthalimido; and the like. Other alcohol protecting groups and amine protecting groups are known to those of skill in the art including, for example, those described by Green and Wuts (*Protective Groups in Organic Synthesis*, 4<sup>th</sup> Ed. 2007, Wiley-Interscience, New York).

[0048] As described herein, compounds of the invention may contain “optionally substituted” moieties. In general, the term “substituted,” whether preceded by the term “optionally” or not, means that one or more hydrogens of the designated moiety are replaced

with a suitable substituent. Unless otherwise indicated, an “optionally substituted” group may have a suitable substituent at each substitutable position of the group, and when more than one position in any given structure may be substituted with more than one substituent selected from a specified group, the substituent may be either the same or different at every position. Combinations of substituents envisioned by this invention are generally those that result in the formation of stable or chemically feasible compounds. The term “stable,” as used herein, refers to compounds that are not substantially altered when subjected to conditions to allow for their production, detection, and, in certain embodiments, their recovery, purification, and use for one or more of the purposes disclosed herein.

5

10 [0049] Suitable monovalent substituents on a substitutable carbon atom of an “optionally substituted” group are independently halogen;  $-(\text{CH}_2)_{0-4}\text{R}^a$ ;  $-(\text{CH}_2)_{0-4}\text{OR}^a$ ;  $-\text{O}(\text{CH}_2)_{0-4}\text{R}^a$ ;  $-\text{O}(\text{CH}_2)_{0-4}\text{C}(\text{O})\text{OR}^a$ ;  $-(\text{CH}_2)_{0-4}\text{CH}(\text{OR}^a)_2$ ;  $-(\text{CH}_2)_{0-4}\text{SR}^a$ ;  $-(\text{CH}_2)_{0-4}\text{Ph}$ , which may be substituted with  $\text{R}^a$ ;  $-(\text{CH}_2)_{0-4}\text{O}(\text{CH}_2)_{0-1}\text{Ph}$  which may be substituted with  $\text{R}^a$ ;  $-\text{CH}=\text{CHPh}$ , which may be substituted with  $\text{R}^a$ ;  $-(\text{CH}_2)_{0-4}\text{O}(\text{CH}_2)_{0-1}\text{-pyridyl}$  which may be substituted with

15  $\text{R}^a$ ;  $-\text{NO}_2$ ;  $-\text{CN}$ ;  $-\text{N}_3$ ;  $-(\text{CH}_2)_{0-4}\text{N}(\text{R}^a)_2$ ;  $-(\text{CH}_2)_{0-4}\text{N}(\text{R}^a)\text{C}(\text{O})\text{R}^a$ ;  $-\text{N}(\text{R}^a)\text{C}(\text{S})\text{R}^a$ ;  $-(\text{CH}_2)_{0-4}\text{N}(\text{R}^a)\text{C}(\text{O})\text{NR}^a_2$ ;  $-\text{N}(\text{R}^a)\text{C}(\text{S})\text{NR}^a_2$ ;  $-(\text{CH}_2)_{0-4}\text{N}(\text{R}^a)\text{C}(\text{O})\text{OR}^a$ ;  $-\text{N}(\text{R}^a)\text{N}(\text{R}^a)\text{C}(\text{O})\text{R}^a$ ;  $-\text{N}(\text{R}^a)\text{N}(\text{R}^a)\text{C}(\text{O})\text{NR}^a_2$ ;  $-\text{N}(\text{R}^a)\text{N}(\text{R}^a)\text{C}(\text{O})\text{OR}^a$ ;  $-(\text{CH}_2)_{0-4}\text{C}(\text{O})\text{R}^a$ ;  $-\text{C}(\text{S})\text{R}^a$ ;  $-(\text{CH}_2)_{0-4}\text{C}(\text{O})\text{OR}^a$ ;  $-(\text{CH}_2)_{0-4}\text{C}(\text{O})\text{SR}^a$ ;  $-(\text{CH}_2)_{0-4}\text{C}(\text{O})\text{OSiR}^a_3$ ;  $-(\text{CH}_2)_{0-4}\text{OC}(\text{O})\text{R}^a$ ;  $-\text{OC}(\text{O})(\text{CH}_2)_{0-4}\text{SR}-\text{SC}(\text{S})\text{SR}^a$ ;  $-(\text{CH}_2)_{0-4}\text{SC}(\text{O})\text{R}^a$ ;  $-(\text{CH}_2)_{0-4}\text{C}(\text{O})\text{NR}^a_2$ ;  $-\text{C}(\text{S})\text{NR}^a_2$ ;

20  $-\text{C}(\text{S})\text{SR}^a$ ;  $-\text{SC}(\text{S})\text{SR}^a$ ;  $-(\text{CH}_2)_{0-4}\text{OC}(\text{O})\text{NR}^a_2$ ;  $-\text{C}(\text{O})\text{N}(\text{OR}^a)\text{R}^a$ ;  $-\text{C}(\text{O})\text{C}(\text{O})\text{R}^a$ ;  $-\text{C}(\text{O})\text{CH}_2\text{C}(\text{O})\text{R}^a$ ;  $-\text{C}(\text{NOR}^a)\text{R}^a$ ;  $-(\text{CH}_2)_{0-4}\text{SSR}^a$ ;  $-(\text{CH}_2)_{0-4}\text{S}(\text{O})_2\text{R}^a$ ;  $-(\text{CH}_2)_{0-4}\text{S}(\text{O})_2\text{OR}^a$ ;  $-(\text{CH}_2)_{0-4}\text{OS}(\text{O})_2\text{R}^a$ ;  $-\text{S}(\text{O})_2\text{NR}^a_2$ ;  $-(\text{CH}_2)_{0-4}\text{S}(\text{O})\text{R}^a$ ;  $-\text{N}(\text{R}^a)\text{S}(\text{O})_2\text{NR}^a_2$ ;  $-\text{N}(\text{R}^a)\text{S}(\text{O})_2\text{R}^a$ ;  $-\text{N}(\text{OR}^a)\text{R}^a$ ;  $-\text{C}(\text{NH})\text{NR}^a_2$ ;  $-\text{P}(\text{O})_2\text{R}^a$ ;  $-\text{P}(\text{O})\text{R}^a_2$ ;  $-\text{OP}(\text{O})\text{R}^a_2$ ;  $-\text{OP}(\text{O})(\text{OR}^a)_2$ ;  $\text{SiR}^a_3$ ;

25  $-(\text{C}_{1-4}$  straight or branched)alkylene)O-N( $\text{R}^a$ ) $_2$ ; or  $-(\text{C}_{1-4}$  straight or branched)alkylene)C(O)O-N( $\text{R}^a$ ) $_2$ , wherein each  $\text{R}^a$  may be substituted as defined below and is independently hydrogen,  $\text{C}_{1-6}$  aliphatic,  $-\text{CH}_2\text{Ph}$ ,  $-\text{O}(\text{CH}_2)_{0-1}\text{Ph}$ ,  $-\text{CH}_2$ -(5-6 membered heteroaryl ring), or a 5-6-membered saturated, partially unsaturated, or aromatic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or, notwithstanding the definition above, two independent occurrences of  $\text{R}^a$ , taken together with

30 their intervening atom(s), form a 3-12-membered saturated, partially unsaturated, or aromatic mono- or bi-cyclic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, which may be substituted as defined below.

[0050] Suitable monovalent substituents on  $R^a$  (or the ring formed by taking two independent occurrences of  $R^a$  together with their intervening atoms), are independently halogen,  $-(CH_2)_{0-2}R^b$ ,  $-(haloR^b)$ ,  $-(CH_2)_{0-2}OH$ ,  $-(CH_2)_{0-2}OR^b$ ,  $-(CH_2)_{0-2}CH(OR^b)_2$ ,  $-O(haloR^b)$ ,  $-CN$ ,  $-N_3$ ,  $-(CH_2)_{0-2}C(O)R^b$ ,  $-(CH_2)_{0-2}C(O)OH$ ,  $-(CH_2)_{0-2}C(O)OR^b$ ,  $-(CH_2)_{0-2}SR^b$ ,  
 5  $-(CH_2)_{0-2}SH$ ,  $-(CH_2)_{0-2}NH_2$ ,  $-(CH_2)_{0-2}NHR^b$ ,  $-(CH_2)_{0-2}NR^b_2$ ,  $-NO_2$ ,  $SiR^b_3$ ,  $-OSiR^b_3$ ,  $-C(O)SR^b$ ,  $-(C_{1-4}$  straight or branched alkylene) $C(O)OR^b$ , or  $-SSR^b$ ; wherein each  $R^b$  is unsubstituted or where preceded by "halo" is substituted only with one or more halogens, and is independently selected from  $C_{1-4}$  aliphatic,  $-CH_2Ph$ ,  $-O(CH_2)_{0-1}Ph$ , or a 5-6-membered saturated, partially unsaturated, or aromatic ring having 0-4 heteroatoms  
 10 independently selected from nitrogen, oxygen, and sulfur. Suitable divalent substituents on a saturated carbon atom of  $R^a$  include  $=O$  and  $=S$ .

[0051] Suitable divalent substituents on a saturated carbon atom of an "optionally substituted" group include the following:  $=O$ ;  $=S$ ;  $=NNR^y_2$ ;  $=NNHC(O)R^y$ ;  $=NNHC(O)OR^y$ ;  $=NNHS(O)_2R^y$ ;  $=NR^y$ ;  $=NOR^y$ ;  $-O(C(R^y_2))_{2-3}O-$ ; or  $-S(C(R^y_2))_{2-3}S-$ ; wherein each independent  
 15 occurrence of  $R^y$  is selected from hydrogen,  $C_{1-6}$  aliphatic which may be substituted as defined below, or an unsubstituted 5-6-membered saturated, partially unsaturated, or aromatic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur. Suitable divalent substituents that are bound to vicinal substitutable carbons of an "optionally substituted" group include:  $-O(CR^b_2)_{2-3}O-$ , wherein each independent occurrence of  $R^b$  is  
 20 selected from hydrogen,  $C_{1-6}$  aliphatic which may be substituted as defined below, or an unsubstituted 5-6-membered saturated, partially unsaturated, or aromatic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur.

[0052] Suitable substituents on the aliphatic group of  $R^y$  include halogen,  $-R^{\delta}$ ,  $-(haloR^{\delta})$ ,  $-OH$ ,  $-OR^{\delta}$ ,  $-O(haloR^{\delta})$ ,  $-CN$ ,  $-C(O)OH$ ,  $-C(O)OR^{\delta}$ ,  $-NH_2$ ,  $-NHR^{\delta}$ ,  $-N$   
 25  $R^{\delta}_2$ , or  $-NO_2$ , wherein each  $R^{\delta}$  is unsubstituted or where preceded by "halo" is substituted only with one or more halogens, and is independently  $C_{1-4}$  aliphatic,  $-CH_2Ph$ ,  $-O(CH_2)_{0-1}Ph$ , or a 5-6-membered saturated, partially unsaturated, or aromatic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur.

[0053] Suitable substituents on a substitutable nitrogen of an "optionally substituted" group  
 30 include  $-R^e$ ,  $-NR^e_2$ ,  $-C(O)R^e$ ,  $-C(O)OR^e$ ,  $-C(O)C(O)R^e$ ,  $-C(O)CH_2C(O)R^e$ ,  $-S(O)_2R^e$ ,  $-S(O)_2NR^e_2$ ,  $-C(S)NR^e_2$ ,  $-C(NH)NR^e_2$ , or  $-N(R^e)S(O)_2R^e$ ; wherein each  $R^e$  is independently hydrogen,  $C_{1-6}$  aliphatic which may be substituted as defined below, unsubstituted  $-OPh$ , or

an unsubstituted 5-6-membered saturated, partially unsaturated, or aromatic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur, or, notwithstanding the definition above, two independent occurrences of  $R^e$ , taken together with their intervening atom(s) form an unsubstituted 3-12-membered saturated, partially unsaturated, or aromatic mono- or bicyclic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur.

[0054] Suitable substituents on the aliphatic group of  $R^e$  are independently halogen,  $-R^\delta$ ,  $-(\text{halo}R^\delta)$ ,  $-\text{OH}$ ,  $-\text{OR}^\delta$ ,  $-\text{CN}$ ,  $-\text{C}(\text{O})\text{OH}$ ,  $-\text{C}(\text{O})\text{OR}^\delta$ ,  $-\text{NH}_2$ ,  $-\text{NHR}^\delta$ ,  $-\text{NR}^\delta_2$ , or  $-\text{NO}_2$ , wherein each  $R^\delta$  is unsubstituted or where preceded by "halo" is substituted only with one or more halogens, and is independently  $\text{C}_{1-4}$  aliphatic,  $-\text{CH}_2\text{Ph}$ ,  $-\text{O}(\text{CH}_2)_{0-1}\text{Ph}$ , or a 5-6-membered saturated, partially unsaturated, or aromatic ring having 0-4 heteroatoms independently selected from nitrogen, oxygen, and sulfur.

[0055] In some embodiments, the term "substituted" is contemplated to include all permissible substituents of organic compounds, "permissible" being in the context of the chemical rules of valence known to those of ordinary skill in the art. In some cases, "substituted" may generally refer to replacement of a hydrogen atom with a substituent as described herein. However, "substituted," as used herein, does not encompass replacement and/or alteration of a key functional group by which a molecule is identified, *e.g.*, such that the "substituted" functional group becomes, through substitution, a different functional group. For example, a "substituted phenyl" group must still comprise the phenyl moiety and cannot be modified by substitution, in this definition, to become, *e.g.*, a cyclohexyl group. In a broad aspect, permissible substituents include acyclic and cyclic, branched and unbranched, carbocyclic and heterocyclic, aromatic and nonaromatic substituents of organic compounds. Illustrative substituents include, for example, those described herein. Permissible substituents can be one or more and the same or different for appropriate organic compounds. For example, a substituted alkyl group may be  $\text{CF}_3$ . For purposes of this invention, the heteroatoms such as nitrogen may have hydrogen substituents and/or any permissible substituents of organic compounds described herein which satisfy the valencies of the heteroatoms. This invention is not intended to be limited in any manner by the permissible substituents of organic compounds.

[0056] Examples of substituents include, but are not limited to, alkyl, aryl, arylalkyl, cyclic alkyl, heterocycloalkyl, hydroxy, alkoxy, aryloxy, perhaloalkoxy, arylalkoxy, heteroaryl,

heteroaryloxy, heteroarylalkyl, heteroarylalkoxy, azido, amino, halogen, alkylthio, oxo, acylalkyl, carboxy esters, carboxyl, carboxamido, nitro, acyloxy, aminoalkyl, alkylaminoaryl, alkylaryl, alkylaminoalkyl, alkoxyaryl, arylamino, arylalkylamino, alkylsulfonyl, carboxamidoalkylaryl, carboxamidoaryl, hydroxyalkyl, haloalkyl, alkylaminoalkylcarboxy, aminocarboxamidoalkyl, cyano, alkoxyalkyl, perhaloalkyl, arylalkyloxyalkyl, and the like.

[0057] As used herein, the term “natural oil” refers to an oil derived from a plant or animal source. The term “natural oil” includes natural oil derivatives, unless otherwise indicated. The plant or animal sources can be modified plant or animal sources (*e.g.*, genetically modified plant or animal sources), unless indicated otherwise. Examples of natural oils include, but are not limited to, vegetable oils, algae oils, fish oils, animal fats, tall oils, derivatives of these oils, combinations of any of these oils, and the like. Representative non-limiting examples of vegetable oils include canola oil, rapeseed oil, coconut oil, corn oil, cottonseed oil, olive oil, palm oil, peanut oil, safflower oil, sesame oil, soybean oil, sunflower oil, linseed oil, palm kernel oil, tung oil, jatropha oil, mustard oil, pennycress oil, camelina oil, and castor oil. Representative non-limiting examples of animal fats include lard, tallow, poultry fat, yellow grease, and fish oil. Tall oils are by-products of wood pulp manufacture.

[0058] “Natural oil derivatives” refer to compounds (or mixtures of compounds) derived from natural oils using any one or combination of methods known in the art. Such methods include but are not limited to saponification, fat splitting, transesterification, esterification, hydrogenation (partial or full), isomerization, oxidation, reduction, and metathesis. Representative non-limiting examples of natural oil derivatives include gums, phospholipids, soapstock, acidulated soapstock, distillate or distillate sludge, fatty acids, and fatty acid alkyl esters (*e.g.*, non-limiting examples such as 2-ethylhexyl ester), and hydroxy substituted variations thereof. For example, the natural oil derivative may be a fatty acid methyl ester (“FAME”) derived from the glyceride of the natural oil.

[0059] The term “contaminant” refers broadly and without limitation to any impurity, regardless of the amount in which it is present, admixed with a substrate to be used in olefin metathesis. A “catalyst poisoning contaminant” refers to a contaminant having the potential to adversely affect the performance of a metathesis catalyst. Examples of catalyst poisoning contaminants include, but are not limited to, water, peroxides, and hydroperoxides.

[0060] As used herein, the term “metal alkyl compound” refers to a compound having the formula  $MR_m$  wherein, M is a metal (*e.g.*, a Group II metal or a Group IIIA metal), each R is



independently an alkyl radical of 1 to about 20 carbon atoms, and subscript m corresponds to the valence of M. Examples of metal alkyl compounds include  $Mg(CH_3)_2$ ,  $Zn(CH_3)_2$ ,  $Al(CH_3)_3$ , and the like. Metal alkyl compounds also include substances having one or more halogen or hydride groups, such as Grignard reagents, diisobutylaluminum hydride, and the like.

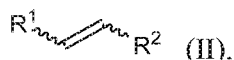
### III. DESCRIPTION OF THE EMBODIMENTS

[0061] In one aspect, the invention provides a method for synthesizing a fatty olefin derivative. The method includes:

a) contacting an olefin according to Formula I



with a metathesis reaction partner according to Formula II



in the presence of a metathesis catalyst under conditions sufficient to form a metathesis product; and

15 b) optionally converting the metathesis product to the fatty olefin derivative; wherein:

$R^1$  is selected from H,  $C_{1-18}$  alkyl, and  $C_{2-18}$  alkenyl;

$R^2$  is selected from  $-(CH_2)_xOR^{2a}$  and  $-(CH_2)_yCOOR^{2b}$ , wherein  $R^{2a}$  is an alcohol protecting group and  $R^{2b}$  is  $C_{1-8}$  alkyl;

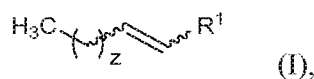
20 subscript x is an integer ranging from 1 to 18;

subscript y is an integer ranging from 0 to 17; and

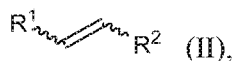
subscript z is an integer ranging from 0 to 17.

[0062] In some embodiments, the invention provides a method for synthesizing a fatty olefin derivative including:

25 a) contacting an olefin according to Formula I



with a metathesis reaction partner according to Formula II



30 in the presence of a metathesis catalyst under conditions sufficient to form a metathesis product; and

b) optionally converting the metathesis product to the fatty olefin derivative;  
 wherein:

$R^1$  is selected from H,  $C_{1-18}$  alkyl, and  $C_{2-18}$  alkenyl;

$R^2$  is selected from  $-(CH_2)_xOR^{2a}$  and  $-(CH_2)_yCOOR^{2b}$ , wherein  $R^{2a}$  is an  
 5 alcohol protecting group and  $R^{2b}$  is  $C_{1-8}$  alkyl;

subscript x is an integer ranging from 1 to 18;

subscript y is an integer ranging from 0 to 17; and

subscript z is an integer ranging from 0 to 17;

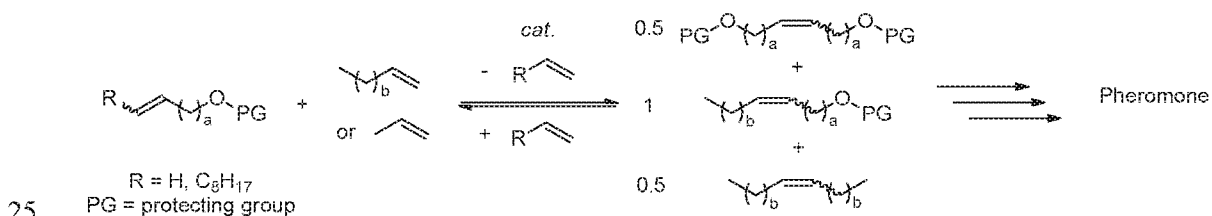
wherein the metathesis catalyst is a tungsten catalyst or a molybdenum  
 10 catalyst.

[0063] In the methods of the invention, olefins can be reacted with a variety of metathesis reaction partners to obtain pheromones, pheromone precursors, and other useful fatty olefin derivatives.

**Metathesis of Fatty Alcohols**

15 [0064] Certain embodiments of the method are summarized in Scheme 1. A fatty alcohol containing an appropriate protecting group is reacted with an  $\alpha$ -olefin in the presence of a group VI olefin metathesis catalyst (e.g., a Z-selective Group VI metathesis catalyst) to produce a statistical mixture of the desired cross-metathesis product and the self-metathesis co-products. The ratio of the feedstocks can be adjusted to vary the ratio of products. For  
 20 example, feeding the reactants in a 1.5:1 molar ratio of  $\alpha$ -olefin to protected fatty alcohol can result in a 3:2.25:1 ratio of the internal olefin, metathesis product, and protected diol products. This process condition results in the efficient utilization of the more costly protected fatty alcohol.

**Scheme 1**



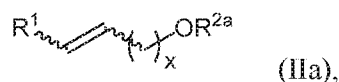
[0065] Products obtained from metathesis of protected fatty alcohols can be converted to a number of pheromones, as set forth in Table 1.

Table 1. Pheromones accessible from fatty alcohol metathesis products.

Olefin	Metathesis Reaction Partner	Metathesis Product	Exemplary Pheromone	Pheromone CAS #
propylene	oleyl alcohol	protected (Z)-9-undecenol	(Z)-9-undecenyl acetate	85576-13-2
1-butene	oleyl alcohol	protected (Z)-9-dodecenol	(Z)-9-dodecenal	56219-03-5
1-butene	oleyl alcohol	protected (Z)-9-dodecenol	(Z)-9-dodecenyl acetate	16974-11-1
1-pentene	oleyl alcohol	protected (Z)-9-tridecenol	(Z)-9-tridecenyl acetate	35835-78-0
1-hexene	oleyl alcohol	protected (Z)-9-tetradecenol	(Z)-9-tetradecenal	53939-27-8
1-hexene	oleyl alcohol	protected (Z)-9-tetradecenol	(Z)-9-tetradecenyl acetate	16725-53-4
1-hexene	oleyl alcohol	protected (Z)-9-tetradecenol	(Z)-9-tetradecenyl formate	56776-10-4
1-hexene	oleyl alcohol	protected (Z)-9-tetradecenol	(Z)-9-tetradecenyl nitrate	143816-21-1
1-heptene	oleyl alcohol	protected (Z)-9-pentadecenol	(Z)-9-pentadecenyl acetate	64437-41-8
1-octene	oleyl alcohol	protected (Z)-9-hexadecenol	(Z)-9-hexadecenal	56219-04-6
1-octene	oleyl alcohol	protected (Z)-9-hexadecenol	(Z)-9-hexadecenyl acetate	34010-20-3
propylene	9-decen-1-ol	protected (Z)-9-undecenol	(Z)-9-undecenyl acetate	85576-13-2
1-butene	9-decen-1-ol	protected (Z)-9-dodecenol	(Z)-9-dodecenal	56219-03-5
1-butene	9-decen-1-ol	protected (Z)-9-dodecenol	(Z)-9-dodecenyl acetate	16974-11-1
1-pentene	9-decen-1-ol	protected (Z)-9-tridecenol	(Z)-9-tridecenyl acetate	35835-78-0
1-hexene	9-decen-1-ol	protected (Z)-9-tetradecenol	(Z)-9-tetradecenal	53939-27-8
1-hexene	9-decen-1-ol	protected (Z)-9-tetradecenol	(Z)-9-tetradecenyl acetate	16725-53-4
1-hexene	9-decen-1-ol	protected (Z)-9-tetradecenol	(Z)-9-tetradecenyl formate	56776-10-4
1-hexene	9-decen-1-ol	protected (Z)-9-tetradecenol	(Z)-9-tetradecenyl nitrate	143816-21-1
1-heptene	9-decen-1-ol	protected (Z)-9-pentadecenol	(Z)-9-pentadecenyl acetate	64437-41-8
1-octene	9-decen-1-ol	protected (Z)-9-hexadecenol	(Z)-9-hexadecenal	56219-04-6
1-octene	9-decen-1-ol	protected (Z)-9-hexadecenol	(Z)-9-hexadecenyl acetate	34010-20-3
propylene	10-undecen-1-ol	protected (Z)-10-dodecenol	(Z)-10-dodecenyl acetate	35148-20-0
1-butene	10-undecen-1-ol	protected (Z)-10-tridecenol	(Z)-10-tridecenyl acetate	64437-24-7
1-pentene	10-undecen-1-ol	protected (Z)-10-tetradecenol	(Z)-10-tetradecenyl acetate	35153-16-3
1-hexene	10-undecen-1-ol	protected (Z)-10-pentadecenol	(Z)-10-pentadecenal	60671-80-9
1-hexene	10-undecen-1-ol	protected (Z)-10-pentadecenol	(Z)-10-pentadecenyl acetate	64437-43-0

Olefin	Metathesis Reaction Partner	Metathesis Product	Exemplary Pheromone	Pheromone CAS #
1-heptene	10-undecen-1-ol	protected (Z)-10-hexadecenol	(Z)-10-hexadecenyl acetate	56218-71-4
1-butene	8-octen-1-ol	protected (Z)-7-decenol	(Z)-7-decenyl acetate	13857-03-9
1-pentene	8-octen-1-ol	protected (Z)-7-undecenol	(Z)-7-undecenyl acetate	-
1-hexene	8-octen-1-ol	protected (Z)-7-dodecenol	(E)-7-dodecenal	60671-75-2
1-hexene	8-octen-1-ol	protected (Z)-7-dodecenol	(Z)-7-dodecenyl acetate	14959-86-5
1-octene	8-octen-1-ol	protected (Z)-7-tetradecenol	(Z)-7-tetradecenal	65128-96-3
1-octene	8-octen-1-ol	protected (Z)-7-tetradecenol	(Z)-7-tetradecenyl acetate	16974-10-0
1-decene	8-octen-1-ol	protected (Z)-7-hexadecenol	(Z)-7-hexadecenal	56797-40-1
1-decene	8-octen-1-ol	protected (Z)-7-hexadecenol	(Z)-7-hexadecenyl acetate	23192-42-9

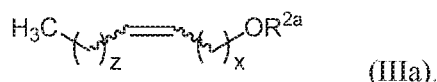
[0066] Accordingly, some embodiments of the invention provide a method wherein the metathesis reaction partner is a protected alcohol according to Formula IIa:



5

wherein R<sup>2a</sup> is an alcohol protecting group,

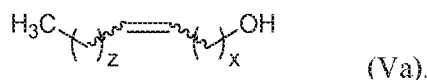
and wherein the metathesis product is a compound according to Formula IIIa:



[0067] Any protecting group R<sup>2a</sup> that is stable under the metathesis reaction conditions can be used in the methods of the invention. Examples of suitable protecting groups include, but are not limited to, silyl, *tert*-butyl, benzyl, and acetyl. In some embodiments, R<sup>2a</sup> is acetyl.

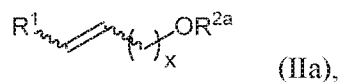
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[0068] In some embodiments, converting the metathesis product to the fatty olefin derivative includes removing R<sup>2a</sup> from the compound of Formula IIIa to form an alkenol according to Formula Va:



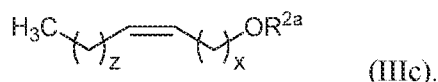
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[0069] In some embodiments, the metathesis reaction partner is a protected alcohol according to Formula IIa:

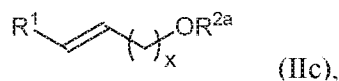


wherein R<sup>2a</sup> is an alcohol protecting group,

and the metathesis product is a compound according to Formula IIIc:

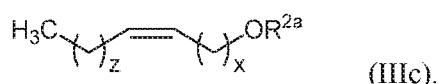


[0070] In some embodiments, the metathesis reaction partner is a protected alcohol  
5 according to Formula IIc:



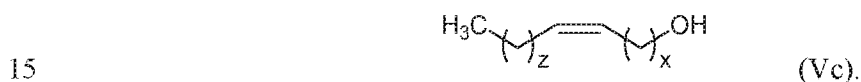
wherein R<sup>2a</sup> is an alcohol protecting group,

and the metathesis product is a compound according to Formula IIIc:



10 [0071] Metathesis products of Formula IIIc can be prepared using Z-selective metathesis catalysts.

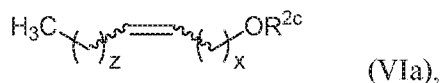
[0072] In some embodiments, converting the metathesis product to the fatty olefin derivative includes removing R<sup>2a</sup> from the compound of Formula IIIc to form an alkenol according to Formula Vc:



### Conversion of Fatty Alcohol Metathesis Products to Fatty Olefin Derivatives

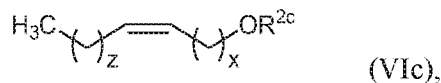
[0073] In some embodiments, the alkenol is the fatty olefin derivative. In some  
embodiments, an alkenol is converted to a desired fatty olefin derivative product via one or  
more chemical or biochemical transformations. In some such embodiments, the fatty olefin  
20 derivative is a pheromone.

[0074] In some embodiments, converting the metathesis product to the fatty olefin  
derivative further includes acylating the alkenol of Formula Va, thereby forming a fatty olefin  
derivative according to Formula VIa:



25 wherein R<sup>2c</sup> is C<sub>1-6</sub> acyl.

[0075] In some embodiments, converting the metathesis product to the fatty olefin derivative further includes acylating the alkenol of Formula Vc, thereby forming a fatty olefin derivative according to Formula VIc:



5 wherein R<sup>2c</sup> is C<sub>1-6</sub> acyl.

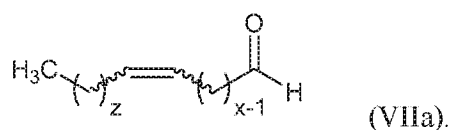
[0076] Any acylating agent suitable for forming the fatty olefin derivative of Formula VIa or Formula VIc can be used in the method of the invention. Examples of suitable acylating agents include acid anhydrides (*e.g.*, acetic anhydride), acid chlorides (*e.g.*, acetyl chloride), activated esters (*e.g.*, pentafluorophenyl esters of carboxylic acids), and carboxylic acids used with coupling agents such as dicyclohexylcarbodiimide or carbonyl diimidazole. Typically, 10 1-10 molar equivalents of the acylating agent with respect to the alkenol will be used. For example, 1-5 molar equivalents of the acylating agent or 1-2 molar equivalents of the acylating agent can be used. In some embodiments, around 1.0, 1.1, 1.2, 1.3, 1.4, or 1.5 molar equivalents of the acylating agent (*e.g.*, acetic anhydride) with respect to the alkenol is used to form the fatty olefin derivative of Formula VIa or Formula VIc.

[0077] A base can be used to promote acylation of the alkenol by the acylating agent. Examples of suitable bases include potassium carbonate, sodium carbonate, sodium acetate, Huenig's base (*i.e.*, *N,N*-diisopropylethylamine), lutidines including 2,6-lutidine (*i.e.*, 2,6-dimethylpyridine), triethylamine, tributylamine, pyridine, 2,6-di-*tert*-butylpyridine, 1,8-diazabicycloundec-7-ene (DBU), quinuclidine, and the collidines. Combinations of two or more bases can be used. Typically, less than one molar equivalent of base with respect to the alkenol will be employed in the methods of the invention. For example, 0.05-0.9 molar equivalents or 0.1-0.5 molar equivalents of the base can be used. In some embodiments, around 0.05, 0.1, 0.15, or 0.2 molar equivalents of the base (*e.g.*, sodium acetate) with respect to the alkenol is used in conjunction with the acylating agent (*e.g.*, acetic anhydride) to form the fatty olefin derivative of Formula VIa or Formula VIc.

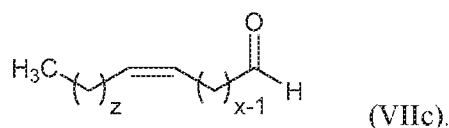
[0078] Any suitable solvent can be used for acylating the alkenol. Suitable solvents include, but are not limited to, toluene, methylene chloride, ethyl acetate, acetonitrile, tetrahydrofuran, benzene, chloroform, diethyl ether, dimethyl formamide, dimethyl sulfoxide, petroleum ether, and mixtures thereof. Alternatively, an alkenol such as 7-octen-1-ol can be combined with an acylating agent such as acetic anhydride and a base such as sodium acetate without an additional solvent. The acylation reaction is typically conducted at temperatures

ranging from around 25°C to about 100°C for a period of time sufficient to form the fatty olefin derivative of Formula VIa or Formula VIc. The reaction can be conducted for a period of time ranging from a few minutes to several hours or longer, depending on the particular alkenol and acylating agent used in the reaction. For example, the reaction can be conducted  
 5 for around 10 minutes, or around 30 minutes, or around 1 hour, or around 2 hours, or around 4 hours, or around 8 hours, or around 12 hours at around 40°C, or around 50°C, or around 60°C, or around 70°C, or around 80°C.

[0079] In some embodiments, converting the metathesis product to the fatty olefin derivative further includes oxidizing the alkenol of Formula Va, thereby forming a fatty  
 10 olefin derivative according to Formula VIIa:



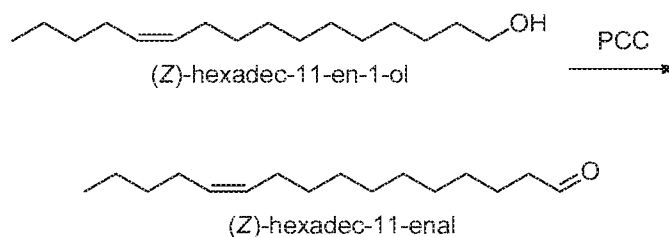
[0080] Many insect pheromones are fatty aldehydes or comprise a fatty aldehyde component. As such, synthesis of certain pheromones includes the conversion of alkenols prepared according to the methods of the invention to fatty aldehydes. In some embodiments,  
 15 converting the metathesis product to the fatty olefin derivative further includes oxidizing the alkenol of Formula Vc, thereby forming a fatty olefin derivative according to Formula VIIc:



[0081] Any oxidizing agent suitable for converting the alkenol Formula Va to the fatty olefin derivative of Formula VIIa or Formula VIIc can be used in the methods of the  
 20 invention. Examples of suitable oxidizing agents include, but are not limited to, chromium-based reagents (*e.g.*, chromic acid; Jones reagent—chromium trioxide in aqueous sulfuric acid; Collins reagent—chromium trioxide pyridine complex; pyridinium dichromate; pyridinium chlorochromate and the like); dimethyl sulfoxide (DMSO)-based reagents (*e.g.*, DMSO/oxalyl chloride; DMSO/dicyclohexyl-carbodiimide; DMSO/acetic anhydride;  
 25 DMSO/phosphorous pentoxide; DMSO/trifluoroacetic anhydride; and the like); hypervalent iodine compounds (*e.g.*, Dess-Martin periodinane; *o*-iodoxybenzoic acid; and the like); ruthenium-based reagents (*e.g.*, ruthenium tetroxide; tetra-*n*-propylammonium perruthenate; and the like); and nitroxyl-based reagents (*e.g.*, TEMPO—2,2,6,6-tetramethylpiperidine 1-oxyl—employed with sodium hypochlorite, bromine, or the like).

[0082] Oxidation of fatty alcohols is often achieved, for example, via selective oxidation via pyridinium chlorochromate (PCC) (Scheme 2).

Scheme 2



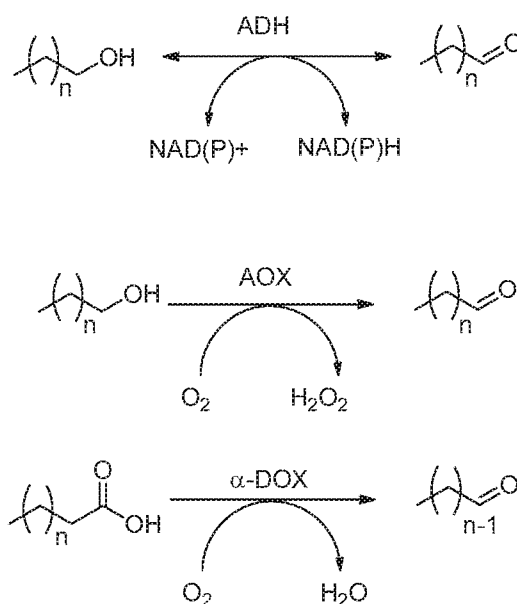
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[0083] Alternatively, TEMPO (TEMPO=2,2,6,6-tetramethylpiperidiny1-N-oxyl) and related catalyst systems can be used to selectively oxidize alcohols to aldehydes. These methods are described in Ryland and Stahl (2014), herein incorporated by reference in its entirety.

#### 10 Bio-oxidation of Terminal Alcohols

[0084] The conversion of a fatty alcohol to a fatty aldehyde is known to be catalyzed by alcohol dehydrogenases (ADH) and alcohol oxidases (AOX). Additionally, the conversion of a length  $C_n$  fatty acid to a  $C_{n-1}$  fatty aldehyde is catalyzed by plant  $\alpha$ -dioxygenases ( $\alpha$ -DOX) (Scheme 3).

15 Scheme 3





[0085] In some embodiments, an alcohol oxidase (AOX) is used to catalyze the conversion of a fatty alcohol to a fatty aldehyde. Alcohol oxidases catalyze the conversion of alcohols into corresponding aldehydes (or ketones) with electron transfer via the use of molecular oxygen to form hydrogen peroxide as a by-product. AOX enzymes utilize flavin adenine dinucleotide (FAD) as an essential cofactor and regenerate with the help of oxygen in the reaction medium. Catalase enzymes may be coupled with the AOX to avoid accumulation of the hydrogen peroxide via catalytic conversion into water and oxygen.

[0086] Based on the substrate specificities, AOXs may be categorized into four groups: (a) short chain alcohol oxidase, (b) long chain alcohol oxidase, (c) aromatic alcohol oxidase, and (d) secondary alcohol oxidase (Goswami *et al.* 2013). Depending on the chain length of the desired substrate, some member of these four groups are better suited for use in the methods of the invention than others.

[0087] Short chain alcohol oxidases (including but not limited to those currently classified as EC 1.1.3.13, Table 2) catalyze the oxidation of lower chain length alcohol substrates in the range of C1-C8 carbons (van der Klei *et al.* 1991) (Ozimek *et al.* 2005). Aliphatic alcohol oxidases from methylotrophic yeasts such as *Candida boidinii* and *Komagataella pastoris* (formerly *Pichia pastoris*) catalyze the oxidation of primary alkanols to the corresponding aldehydes with a preference for unbranched short-chain aliphatic alcohols. The most broad substrate specificity is found for alcohol oxidase from the *Pichia pastoris* including propargyl alcohol, 2-chloroethanol, 2-cyanoethanol (Dienys *et al.* 2003). The major challenge encountered in alcohol oxidation is the high reactivity of the aldehyde product. Utilization of a two liquid phase system (water/solvent) can provide in-situ removal of the aldehyde product from the reaction phase before it is further converted to the acid. For example, hexanal production from hexanol using *Pichia pastoris* alcohol oxidase coupled with bovine liver catalase was achieved in a bi-phasic system by taking advantage of the presence of a stable alcohol oxidase in aqueous phase (Karra-Chaabouni *et al.* 2003). For example, alcohol oxidase from *Pichia pastoris* was able to oxidize aliphatic alcohols of C6 to C11 when used biphasic organic reaction system (Murray and Duff 1990). Methods for using alcohol oxidases in a biphasic system according to (Karra-Chaabouni *et al.* 2003) and (Murray and Duff 1990) are incorporated by reference in their entirety.

[0088] Long chain alcohol oxidases (including but not limited to those currently classified as EC 1.1.3.20; Table 3) include fatty alcohol oxidases, long chain fatty acid oxidases, and

long chain fatty alcohol oxidases that oxidize alcohol substrates with carbon chain length of greater than six (Goswami *et al.* 2013). Banthorpe *et al.* reported a long chain alcohol oxidase purified from the leaves of *Tanacetum vulgare* that was able to oxidize saturated and unsaturated long chain alcohol substrates including hex-trans-2-en-1-ol and octan-1-ol (Banthorpe 1976) (Cardemil 1978). Other plant species, including *Simmondsia chinensis* (Moreau, R.A., Huang 1979), *Arabidopsis thaliana* (Cheng *et al.* 2004), and *Lotus japonicas* (Zhao *et al.* 2008) have also been reported as sources of long chain alcohol oxidases. Fatty alcohol oxidases are mostly reported from yeast species (Hommel and Ratledge 1990) (Vanhanen *et al.* 2000) (Hommel *et al.* 1994) (Kemp *et al.* 1990) and these enzymes play an important role in long chain fatty acid metabolism (Cheng *et al.* 2005). Fatty alcohol oxidases from yeast species that degrade and grow on long chain alkanes and fatty acid catalyze the oxidation of fatty alcohols. Fatty alcohol oxidase from *Candida tropicalis* has been isolated as microsomal cell fractions and characterized for a range of substrates (Eirich *et al.* 2004) (Kemp *et al.* 1988) (Kemp *et al.* 1991) (Mauersberger *et al.* 1992). Significant activity is observed for primary alcohols of length C<sub>8</sub> to C<sub>16</sub> with reported K<sub>M</sub> in the 10-50 μM range (Eirich *et al.* 2004). Alcohol oxidases described may be used for the conversion of medium chain aliphatic alcohols to aldehydes as described, for example, for whole-cells *Candida boidinii* (Gabelman and Luzio 1997), and *Pichia pastoris* (Duff and Murray 1988) (Murray and Duff 1990). Long chain alcohol oxidases from filamentous fungi were produced during growth on hydrocarbon substrates (Kumar and Goswami 2006) (Savitha and Ratledge 1991). The long chain fatty alcohol oxidase (LjFAO1) from *Lotus japonicas* has been heterologously expressed in *E. coli* and exhibited broad substrate specificity for alcohol oxidation including 1-dodecanol and 1-hexadecanol (Zhao *et al.* 2008).

Table 2. Alcohol oxidase enzymes capable of oxidizing short chain alcohols (EC 1.1.3.13).

Organism	Gene names	Accession No.
Komagataella pastoris (strain ATCC 76273 / CBS 7435 / CECT 11047 / NRRL Y-11430 / Wegner 21-1) (Yeast) ( <i>Pichia pastoris</i> )	AOX1 PP7435_Chr4-0130	F2QY27
Komagataella pastoris (strain GS115 / ATCC 20864) (Yeast) ( <i>Pichia pastoris</i> )	AOX1 PAS_chr4_0821	P04842
Komagataella pastoris (strain ATCC 76273 / CBS 7435 / CECT 11047 / NRRL Y-11430 / Wegner 21-1) (Yeast) ( <i>Pichia pastoris</i> )	AOX2 PP7435_Chr4-0863	F2R038

Organism	Gene names	Accession No.
Komagataella pastoris (strain GS115 / ATCC 20864) (Yeast) ( <i>Pichia pastoris</i> )	AOX2 PAS_chr4_0152	C4R702
<i>Candida boidinii</i> (Yeast)	AOD1	Q00922
<i>Pichia angusta</i> (Yeast) ( <i>Hansenula polymorpha</i> )	MOX	P04841
<i>Thanatephorus cucumeris</i> (strain AG1-IB / isolate 7/3/14) (Lettuce bottom rot fungus) ( <i>Rhizoctonia solani</i> )	AOD1 BN14_10802	M5CC52
<i>Thanatephorus cucumeris</i> (strain AG1-IB / isolate 7/3/14) (Lettuce bottom rot fungus) ( <i>Rhizoctonia solani</i> )	MOX BN14_12214	M5CF32
<i>Thanatephorus cucumeris</i> (strain AG1-IB / isolate 7/3/14) (Lettuce bottom rot fungus) ( <i>Rhizoctonia solani</i> )	AOD1 BN14_10691	M5CAV1
<i>Thanatephorus cucumeris</i> (strain AG1-IB / isolate 7/3/14) (Lettuce bottom rot fungus) ( <i>Rhizoctonia solani</i> )	AOD1 BN14_09479	M5C7F4
<i>Thanatephorus cucumeris</i> (strain AG1-IB / isolate 7/3/14) (Lettuce bottom rot fungus) ( <i>Rhizoctonia solani</i> )	AOD1 BN14_10803	M5CB66
<i>Thanatephorus cucumeris</i> (strain AG1-IB / isolate 7/3/14) (Lettuce bottom rot fungus) ( <i>Rhizoctonia solani</i> )	AOD1 BN14_09900	M5C9N9
<i>Thanatephorus cucumeris</i> (strain AG1-IB / isolate 7/3/14) (Lettuce bottom rot fungus) ( <i>Rhizoctonia solani</i> )	AOD1 BN14_08302	M5C2L8
<i>Thanatephorus cucumeris</i> (strain AG1-IB / isolate 7/3/14) (Lettuce bottom rot fungus) ( <i>Rhizoctonia solani</i> )	MOX BN14_09408	M5C784
<i>Thanatephorus cucumeris</i> (strain AG1-IB / isolate 7/3/14) (Lettuce bottom rot fungus) ( <i>Rhizoctonia solani</i> )	MOX BN14_09478	M5C8F8
<i>Thanatephorus cucumeris</i> (strain AG1-IB / isolate 7/3/14) (Lettuce bottom rot fungus) ( <i>Rhizoctonia solani</i> )	AOD1 BN14_11356	M5CH40
<i>Ogataea henricii</i>	AOD1	A5LGF0
<i>Candida methanosorbosa</i>	AOD1	A5LGE5
<i>Candida methanolovescens</i>	AOD1	A5LGE4
<i>Candida succiphila</i>	AOD1	A5LGE6
<i>Aspergillus niger</i> (strain CBS 513.88 / FGSC A1513)	An15g02200	A2R501
<i>Aspergillus niger</i> (strain CBS 513.88 / FGSC A1513)	An18g05480	A2RB46
<i>Moniliophthora perniciosa</i> (Witches'-broom disease fungus) ( <i>Marasmius pernicius</i> )		I7CMK2
<i>Candida cariosilignicola</i>	AOD1	A5LGE3

Organism	Gene names	Accession No.
<i>Candida pignaliae</i>	AOD1	A5LGE1
<i>Candida pignaliae</i>	AOD2	A5LGE2
<i>Candida sonorensis</i>	AOD1	A5LGD9
<i>Candida sonorensis</i>	AOD2	A5LGE0
<i>Pichia naganishii</i>	AOD1	A5LGF2
<i>Ogataea minuta</i>	AOD1	A5LGF1
<i>Ogataea philodendri</i>	AOD1	A5LGF3
<i>Ogataea wickerhamii</i>	AOD1	A5LGE8
<i>Kuraishia capsulata</i>	AOD1	A5LGE7
<i>Talaromyces stipitatus</i> (strain ATCC 10500 / CBS 375.48 / QM 6759 / NRRL 1006) ( <i>Penicillium stipitatum</i> )	TSTA_021940	B8MHF8
<i>Talaromyces stipitatus</i> (strain ATCC 10500 / CBS 375.48 / QM 6759 / NRRL 1006) ( <i>Penicillium stipitatum</i> )	TSTA_065150	B8LTH7
<i>Talaromyces stipitatus</i> (strain ATCC 10500 / CBS 375.48 / QM 6759 / NRRL 1006) ( <i>Penicillium stipitatum</i> )	TSTA_065150	B8LTH8
<i>Talaromyces stipitatus</i> (strain ATCC 10500 / CBS 375.48 / QM 6759 / NRRL 1006) ( <i>Penicillium stipitatum</i> )	TSTA_000410	B8MSB1
<i>Ogataea glucozymia</i>	AOD1	A5LGE9
<i>Ogataea parapolyomorpha</i> (strain DL-1 / ATCC 26012 / NRRL Y-7560) (Yeast) ( <i>Hansenula polymorpha</i> )	HPODL_03886	W1QCJ3
<i>Gloeophyllum trabeum</i> (Brown rot fungus)	AOX	A8DPS4
<i>Pichia angusta</i> (Yeast) ( <i>Hansenula polymorpha</i> )	mox1	A6PZG8
<i>Pichia trehalophila</i>	AOD1	A5LGF4
<i>Pichia angusta</i> (Yeast) ( <i>Hansenula polymorpha</i> )	mox1	A6PZG9
<i>Pichia angusta</i> (Yeast) ( <i>Hansenula polymorpha</i> )	mox1	A6PZG7
<i>Ixodes scapularis</i> (Black-legged tick) (Deer tick)	IscW_ISCW017898	B7PIZ7

Table 3. Alcohol oxidase enzymes capable of oxidizing long chain alcohols including fatty alcohols (EC 1.1.3.20).

Organism	Gene names	Accession No.
<i>Lotus japonicus</i> ( <i>Lotus corniculatus</i> var. <i>japonicus</i> )	FAO1	B5WWZ8
<i>Arabidopsis thaliana</i> (Mouse-ear cress)	FAO1 At1g03990 F21M11.7	Q9ZWB9
<i>Lotus japonicus</i> ( <i>Lotus corniculatus</i> var. <i>japonicus</i> )	FAO2	B5WWZ9
<i>Arabidopsis thaliana</i> (Mouse-ear cress)	FAO3 At3g23410 MLM24.14 MLM24.23	Q9LW56

Organism	Gene names	Accession No.
<i>Arabidopsis thaliana</i> (Mouse-ear cress)	FAO4A At4g19380 T5K18.160	O65709
<i>Arabidopsis thaliana</i> (Mouse-ear cress)	FAO4B At4g28570 T5F17.20	Q94BP3
<i>Microbotryum violaceum</i> (strain p1A1 Lamole) (Anther smut fungus) ( <i>Ustilago violacea</i> )	MVLG_06864	U5HIL4
<i>Ajellomyces dermatitidis</i> ATCC 26199	BDFG_03507	T5BNQ0
<i>Gibberella zeae</i> (strain PH-1 / ATCC MYA-4620 / FGSC 9075 / NRRL 31084) (Wheat head blight fungus) ( <i>Fusarium graminearum</i> )	FG06918.1 FGSG_06918	IIRS14
<i>Pichia sorbitophila</i> (strain ATCC MYA-4447 / BCRC 22081 / CBS 7064 / NBRC 10061 / NRRL Y-12695) (Hybrid yeast)	Piso0_004410 GNLVRS01_PISO0K16268g GNLVRS01_PISO0L16269g	G8Y5E1
<i>Emmericella nidulans</i> (strain FGSC A4 / ATCC 38163 / CBS 112.46 / NRRL 194 / M139) ( <i>Aspergillus nidulans</i> )	AN0623.2 ANIA_00623	Q5BFQ7
<i>Pyrenophora tritici-repentis</i> (strain Pt-1C-BFP) (Wheat tan spot fungus) ( <i>Drechslera tritici-repentis</i> )	PTRG_10154	B2WJW5
<i>Paracoccidioides lutzii</i> (strain ATCC MYA-826 / Pb01) ( <i>Paracoccidioides brasiliensis</i> )	PAAG_09117	CIHEC6
<i>Candida parapsilosis</i> (strain CDC 317 / ATCC MYA-4646) (Yeast) ( <i>Monilia parapsilosis</i> )	CPAR2_204420	G8BG15
<i>Pseudozyma brasiliensis</i> (strain GHG001) (Yeast)	PSEUBRA_SCAF2g03010	V5GPS6
<i>Candida parapsilosis</i> (strain CDC 317 / ATCC MYA-4646) (Yeast) ( <i>Monilia parapsilosis</i> )	CPAR2_204430	G8BG16
<i>Sclerotinia borealis</i> F-4157	SBOR_5750	W9CDE2
<i>Sordaria macrospora</i> (strain ATCC MYA-333 / DSM 997 / K(L.3346) / K-hell)	SMAC_06361	F7W6K4
<i>Sordaria macrospora</i> (strain ATCC MYA-333 / DSM 997 / K(L.3346) / K-hell)	SMAC_01933	F7VSA1
<i>Meyerozyma guilliermondii</i> (strain ATCC 6260 / CBS 566 / DSM 6381 / JCM 1539 / NBRC 10279 / NRRL Y-324) (Yeast) ( <i>Candida guilliermondii</i> )	PGUG_03467	A5DJL6
<i>Trichophyton rubrum</i> CBS 202.88	H107_00669	A0A023ATC5
<i>Arthrobotrys oligospora</i> (strain ATCC 24927 / CBS 115.81 / DSM 1491) (Nematode-trapping fungus) ( <i>Didymozophaga oligospora</i> )	AOL_s00097g516	G1XJI9
<i>Scheffersomyces stipitis</i> (strain ATCC 58785 / CBS 6054 / NBRC 10063 / NRRL Y-11545) (Yeast) ( <i>Pichia stipitis</i> )	FAO1 PICST_90828	A3LYX9

Organism	Gene names	Accession No.
Scheffersomyces stipitis (strain ATCC 58785 / CBS 6054 / NBRC 10063 / NRRL Y-11545) (Yeast) (Pichia stipitis)	FAO2 PICST_32359	A3LW61
Aspergillus oryzae (strain 3.042) (Yellow koji mold)	Ao3042_09114	I8TL25
Fusarium oxysporum (strain Fo5176) (Fusarium vascular wilt)	FOXB_17532	F9GFU8
Rhizopus delemar (strain RA 99-880 / ATCC MYA-4621 / FGSC 9543 / NRRL 43880) (Mucormycosis agent) (Rhizopus arrhizus var. delemar)	RO3G_08271	I1C536
Rhizopus delemar (strain RA 99-880 / ATCC MYA-4621 / FGSC 9543 / NRRL 43880) (Mucormycosis agent) (Rhizopus arrhizus var. delemar)	RO3G_00154	I1BGX0
Fusarium oxysporum (strain Fo5176) (Fusarium vascular wilt)	FOXB_07532	F9FMA2
Penicillium roqueforti	PROQFM164_S02g001772	W6QPY1
Aspergillus clavatus (strain ATCC 1007 / CBS 513.65 / DSM 816 / NCTC 3887 / NRRL 1)	ACLA_018400	A1CNB5
Arthroderma otae (strain ATCC MYA-4605 / CBS 113480) (Microsporium canis)	MCYG_08732	C5G1B0
Trichophyton tonsurans (strain CBS 112818) (Scalp ringworm fungus)	TESG_07214	F2S8I2
Colletotrichum higginsianum (strain IMI 349063) (Crucifer anthracnose fungus)	CH063_13441	H1VUE7
Ajellomyces capsulatus (strain H143) (Darling's disease fungus) (Histoplasma capsulatum)	HCDG_07658	C6HN77
Trichophyton rubrum (strain ATCC MYA-4607 / CBS 118892) (Athlete's foot fungus)	TERG_08235	F2T096
Cochliobolus heterostrophus (strain C5 / ATCC 48332 / race O) (Southern corn leaf blight fungus) (Bipolaris maydis)	COCHEDRAFT_1201414	M2UMT9
Candida orthopsilosis (strain 90-125) (Yeast)	CORT_0D04510	H8X643
Candida orthopsilosis (strain 90-125) (Yeast)	CORT_0D04520	H8X644
Candida orthopsilosis (strain 90-125) (Yeast)	CORT_0D04530	H8X645
Pseudozyma aphidis DSM 70725	PaG_03027	W3VP49
Coccidioides posadasii (strain C735) (Valley fever fungus)	CPC735_000380	C5P005
Magnaporthe oryzae (strain P131) (Rice blast fungus) (Pyricularia oryzae)	OOW_P131scaffold01214g15	L7IZ92
Neurospora tetrasperma (strain FGSC 2508 / ATCC MYA-4615 / P0657)	NEUTEIDRAFT_82541	F8MKD1
Hypocrea virens (strain Gv29-8 / FGSC 10586) (Gliocladium virens) (Trichoderma virens)	TRIVIDRAFT_54537	G9MMY7

Organism	Gene names	Accession No.
Hypocrea virens (strain Gv29-8 / FGSC 10586) (Gliocladium virens) (Trichoderma virens)	TRIVIDRAFT_53801	G9MT89
Aspergillus niger (strain CBS 513.88 / FGSC A1513)	An01g09620	A2Q9Z3
Verticillium dahliae (strain VdLs.17 / ATCC MYA-4575 / FGSC 10137) (Verticillium wilt)	VDAG_05780	G2X6J8
Ustilago maydis (strain 521 / FGSC 9021) (Corn smut fungus)	UM02023.1	Q4PCZ0
Fusarium oxysporum f. sp. lycopersici MN25	FOWG_13006	W9LNI9
Fusarium oxysporum f. sp. lycopersici MN25	FOWG_02542	W9N9Z1
Candida tropicalis (Yeast)	FAO1	Q6QIR6
Magnaporthe oryzae (strain 70-15 / ATCC MYA-4617 / FGSC 8958) (Rice blast fungus) (Pyricularia oryzae)	MGG_11317	G4MVK1
Candida tropicalis (Yeast)	faot	Q9P8D9
Candida tropicalis (Yeast)	FAO2a	Q6QIR5
Phaeosphaeria nodorum (strain SN15 / ATCC MYA-4574 / FGSC 10173) (Glume blotch fungus) (Septoria nodorum)	SNOG_02371	Q0V0U3
Candida tropicalis (Yeast)	FAO2b	Q6QIR4
Pestalotiopsis fici W106-1	PFICI_11209	W3WU04
Magnaporthe oryzae (strain Y34) (Rice blast fungus) (Pyricularia oryzae)	OOU_Y34scaffold00240g57	L7IFT5
Pseudogymnoascus destructans (strain ATCC MYA-4855 / 20631-21) (Bat white-nose syndrome fungus) (Geomyces destructans)	GMDG_01756	L8G0G6
Pseudogymnoascus destructans (strain ATCC MYA-4855 / 20631-21) (Bat white-nose syndrome fungus) (Geomyces destructans)	GMDG_04950	L8GCY2
Mycosphaerella fijiensis (strain CIRAD86) (Black leaf streak disease fungus) (Pseudocercospora fijiensis)	MYCFIDRAFT_52380	M2Z831
Bipolaris oryzae ATCC 44560	COCMIDRAFT_84580	W7A0I8
Cladophialophora psammophila CBS 110553	A1O5_08147	W9WTM9
Fusarium oxysporum f. sp. melonis 26406	FOMG_05173	X0AEE6
Fusarium oxysporum f. sp. melonis 26406	FOMG_17829	W9ZBB7
Cyphellophora europaea CBS 101466	HMPREF1541_02174	W2S2S5
Aspergillus kawachii (strain NBRC 4308) (White koji mold) (Aspergillus awamori var. kawachi)	AKAW_00147	G7X626
Aspergillus terreus (strain NIH 2624 / FGSC A1156)	ATEG_05086	Q0CMJ8
Coccidioides immitis (strain RS) (Valley fever fungus)	CIMG_02987	J3KA18

Organism	Gene names	Accession No.
<i>Ajellomyces dermatitidis</i> (strain ER-3 / ATCC MYA-2586) ( <i>Blastomyces dermatitidis</i> )	BDCG_04701	C5GLS5
<i>Fusarium oxysporum</i> f. sp. <i>cubense</i> (strain race 1) (Panama disease fungus)	FOC1_g10013865	N4U732
<i>Rhodotorula glutinis</i> (strain ATCC 204091 / IIP 30 / MTCC 1151) (Yeast)	RTG_00643	G0SVU8
<i>Aspergillus niger</i> (strain ATCC 1015 / CBS 113.46 / FGSC A1144 / LSHB Ac4 / NCTC 3858a / NRRL 328 / USDA 3528.7)	ASPNIDRAFT_35778	G3XTM6
<i>Candida cloacae</i>	fao1	Q9P8D8
<i>Candida cloacae</i>	fao2	Q9P8D7
<i>Fusarium oxysporum</i> f. sp. <i>cubense</i> (strain race 1) (Panama disease fungus)	FOC1_g10006358	N4TUH3
<i>Candida albicans</i> (strain SC5314 / ATCC MYA-2876) (Yeast)	FAO1 CaO19.13562 orf19.13562	Q59RS8
<i>Candida albicans</i> (strain SC5314 / ATCC MYA-2876) (Yeast)	FAO1 CaO19.6143 orf19.6143	Q59RP0
<i>Chaetonium thermophilum</i> (strain DSM 1495 / CBS 144.50 / IMI 039719)	CTHT_0018560	G0S2U9
<i>Mucor circinelloides</i> f. <i>circinelloides</i> (strain 1006PhL) (Mucormycosis agent) ( <i>Calyptromyces circinelloides</i> )	HMPREF1544_05296	S2JDN0
<i>Mucor circinelloides</i> f. <i>circinelloides</i> (strain 1006PhL) (Mucormycosis agent) ( <i>Calyptromyces circinelloides</i> )	HMPREF1544_05295	S2JYP5
<i>Mucor circinelloides</i> f. <i>circinelloides</i> (strain 1006PhL) (Mucormycosis agent) ( <i>Calyptromyces circinelloides</i> )	HMPREF1544_06348	S2JVK9
<i>Botryotinia fuckeliana</i> (strain BcDW1) (Noble rot fungus) ( <i>Botrytis cinerea</i> )	BcDW1_6807	M7UD26
<i>Podospira anserina</i> (strain S / ATCC MYA-4624 / DSM 980 / FGSC 10383) (Pleurage anserina)	PODANS_5_13040	B2AFD8
<i>Neosartorya fumigata</i> (strain ATCC MYA-4609 / Af293 / CBS 101355 / FGSC A1100) ( <i>Aspergillus fumigatus</i> )	AFUA_1G17110	Q4WR91
<i>Fusarium oxysporum</i> f. sp. <i>vasinfectum</i> 25433	FOTG_00686	X0MEE6
<i>Fusarium oxysporum</i> f. sp. <i>vasinfectum</i> 25433	FOTG_12485	X0LE98
<i>Trichophyton interdigitale</i> H6	H101_06625	A0A022U717
<i>Beauveria bassiana</i> (strain ARSEF 2860) (White muscardine disease fungus) ( <i>Tritirachium shioteae</i> )	BBA_04100	J4JUNY3
<i>Fusarium oxysporum</i> f. sp. <i>radicis-lycopersici</i> 26381	FOCG_00843	X0GQ62



Organism	Gene names	Accession No.
<i>Fusarium oxysporum</i> f. sp. <i>radicis-lycopersici</i> 26381	FOCG_15170	X0F4T1
<i>Neurospora tetrasperma</i> (strain FGSC 2509 / P0656)	NEUTE2DRAFT_88670	G4UNN6
<i>Pseudozyma hubeiensis</i> (strain SY62) (Yeast)	PHSY_000086	R9NVU1
<i>Lodderomyces elongisporus</i> (strain ATCC 11503 / CBS 2605 / JCM 1781 / NBRC 1676 / NRRL YB-4239) (Yeast) ( <i>Saccharomyces elongisporus</i> )	LELG_03289	A5E102
<i>Malassezia globosa</i> (strain ATCC MYA-4612 / CBS 7966) (Dandruff-associated fungus)	MGL_3855	A8QAY8
<i>Byssoschlamys spectabilis</i> (strain No. 5 / NBRC 109023) ( <i>Paecilomyces variotii</i> )	PVAR5_7014	V5GBL6
<i>Ajellomyces capsulatus</i> (strain H88) (Darling's disease fungus) ( <i>Histoplasma capsulatum</i> )	HCEG_03274	F0UF47
<i>Trichosporon asahii</i> var. <i>asahii</i> (strain ATCC 90039 / CBS 2479 / JCM 2466 / KCTC 7840 / NCYC 2677 / UAMH 7654) (Yeast)	A1Q1_03669	J6FBP4
<i>Penicillium oxalicum</i> (strain 114-2 / CGMCC 5302) ( <i>Penicillium decumbens</i> )	PDE_00027	S7Z8U8
<i>Fusarium oxysporum</i> f. sp. <i>conglutinans</i> race 2 54008	FOPG_02304	X0IBE3
<i>Fusarium oxysporum</i> f. sp. <i>conglutinans</i> race 2 54008	FOPG_13066	X0H540
<i>Fusarium oxysporum</i> f. sp. <i>raphani</i> 54005	FOQG_00704	X0D1G8
<i>Fusarium oxysporum</i> f. sp. <i>raphani</i> 54005	FOQG_10402	X0C482
<i>Metarhizium acridum</i> (strain CQMa 102)	MAC_03115	E9DZR7
<i>Arthroderma benhamiae</i> (strain ATCC MYA-4681 / CBS 112371) ( <i>Trichophyton mentagrophytes</i> )	ARB_02250	D4B1C1
<i>Fusarium oxysporum</i> f. sp. <i>cubense</i> tropical race 4 54006	FOIG_12161	X0JF16
<i>Fusarium oxysporum</i> f. sp. <i>cubense</i> tropical race 4 54006	FOIG_12751	X0JDU5
<i>Cochliobolus heterostrophus</i> (strain C4 / ATCC 48331 / race T) (Southern corn leaf blight fungus) ( <i>Bipolaris maydis</i> )	COCC4DRAFT_52836	N4WZZ0
<i>Trichosporon asahii</i> var. <i>asahii</i> (strain CBS 8904) (Yeast)	A1Q2_00631	K1VZW1
<i>Mycosphaerella graminicola</i> (strain CBS 115943 / IPO323) (Speckled leaf blotch fungus) ( <i>Septoria tritici</i> )	MYCGRDRAFT_37086	F9X375
<i>Botryotinia fuckeliana</i> (strain T4) (Noble rot fungus) ( <i>Botrytis cinerea</i> )	BofuT4_P072020.1	G2XQ18
<i>Metarhizium anisopliae</i> (strain ARSEF 23 / ATCC MYA-3075)	MAA_05783	E9F014

Organism	Gene names	Accession No.
<i>Cladophialophora carrionii</i> CBS 160.54	G647_05801	V9DAR1
<i>Coccidioides posadasii</i> (strain RMSCC 757 / Silveira) (Valley fever fungus)	CPSG_09174	E9DH75
<i>Rhodosporidium toruloides</i> (strain NP11) (Yeast) ( <i>Rhodotorula gracilis</i> )	RHTO_06879	M7X159
<i>Puccinia graminis</i> f. sp. <i>tritici</i> (strain CRL 75-36-700-3 / race SCCL) (Black stem rust fungus)	PGTG_10521	E3KIL8
<i>Trichophyton rubrum</i> CBS 288.86	H103_00624	A0A022WG28
<i>Colletotrichum fioriniae</i> PJ7	CFIO01_08202	A0A010RKZ4
<i>Trichophyton rubrum</i> CBS 289.86	H104_00611	A0A022XB46
<i>Cladophialophora yegresii</i> CBS 114405	A1O7_02579	W9WC55
<i>Colletotrichum orbiculare</i> (strain 104-T / ATCC 96160 / CBS 514.97 / LARS 414 / MAFF 240422) (Cucumber anthracnose fungus) ( <i>Colletotrichum lagenarium</i> )	Cob_10151	N4VFP3
<i>Drechslerella stenobrocha</i> 248	DRE_03459	W7IDL6
<i>Neosartorya fumigata</i> (strain CEA10 / CBS 144.89 / FGSC A1163) ( <i>Aspergillus fumigatus</i> )	AFUB_016500	B0XP90
<i>Thielavia terrestris</i> (strain ATCC 38088 / NRRL 8126) ( <i>Acremonium alabamense</i> )	THITE_2117674	G2R8H9
<i>Gibberella fujikuroi</i> (strain CBS 195.34 / IMI 58289 / NRRL A-6831) (Bakanae and foot rot disease fungus) ( <i>Fusarium fujikuroi</i> )	FFUJ_02948	S0DZP7
<i>Gibberella fujikuroi</i> (strain CBS 195.34 / IMI 58289 / NRRL A-6831) (Bakanae and foot rot disease fungus) ( <i>Fusarium fujikuroi</i> )	FFUJ_12030	S0EMC6
<i>Aspergillus flavus</i> (strain ATCC 200026 / FGSC A1120 / NRRL 3357 / JCM 12722 / SRRC 167)	AFLA_109870	B8N941
<i>Togninia minima</i> (strain UCR-PA7) (Esca disease fungus) ( <i>Phaeoacremonium aleophilum</i> )	UCRPA7_1719	R8BTZ6
<i>Ajellomyces dermatitidis</i> (strain ATCC 18188 / CBS 674.68) ( <i>Blastomyces dermatitidis</i> )	BDDG_09783	F2TUC0
<i>Macrophomina phaseolina</i> (strain MS6) (Charcoal rot fungus)	MPH_10582	K2RHA5
<i>Neurospora crassa</i> (strain ATCC 24698 / 74-OR23-1A / CBS 708.71 / DSM 1257 / FGSC 987)	NCU08977	Q7S2Z2
<i>Neosartorya fischeri</i> (strain ATCC 1020 / DSM 3700 / FGSC A1164 / NRRL 181) ( <i>Aspergillus fischerianus</i> )	NFIA_008260	A1D156
<i>Fusarium pseudograminearum</i> (strain CS3096) (Wheat and barley crown-rot fungus)	FPSE_11742	K3U9J5
<i>Spathaspora passalidanum</i> (strain NRRL Y-27907 / 11-Y1)	SPAPADRAFT_54193	G3AJP0

Organism	Gene names	Accession No.
<i>Spathaspora passalidarum</i> (strain NRRL Y-27907 / 11-Y1)	SPAPADRAFT_67198	G3ANX7
<i>Trichophyton verrucosum</i> (strain HKI 0517)	TRV_07960	D4DL86
<i>Arthroderma gypseum</i> (strain ATCC MYA-4604 / CBS 118893) ( <i>Microsporium gypseum</i> )	MGYG_07264	E4V2J0
<i>Hypocrea jecorina</i> (strain QM6a) ( <i>Trichoderma reesei</i> )	TRIREDRAFT_43893	G0R7P8
<i>Trichophyton rubrum</i> MR1448	H110_00629	A0A022Z1G4
<i>Aspergillus ruber</i> CBS 135680	EURHEDRAFT_512125	A0A017SPR0
<i>Glarea lozoyensis</i> (strain ATCC 20868 / MF5171)	GLAREA_04397	S3D6C1
<i>Setosphaeria turcica</i> (strain 28A) (Northern leaf blight fungus) ( <i>Exserohilum turcicum</i> )	SETTUDRAFT_20639	R0K6H8
<i>Paracoccidioides brasiliensis</i> (strain Pb18)	PADG_06552	C1GH16
<i>Fusarium oxysporum</i> Fo47	FOZG_13577	W9JPG9
<i>Fusarium oxysporum</i> Fo47	FOZG_05344	W9KPH3
<i>Trichophyton rubrum</i> MR1459	H113_00628	A0A022ZY09
<i>Penicillium marneffei</i> (strain ATCC 18224 / CBS 334.59 / QM 7333)	PMAA_075740	B6QBY3
<i>Sphaenelia musiva</i> (strain SO2202) (Poplar stem canker fungus) ( <i>Septoria musiva</i> )	SEPMUDRAFT_154026	M3DAK6
<i>Gibberella moniliformis</i> (strain M3125 / FGSC 7600) (Maize ear and stalk rot fungus) ( <i>Fusarium verticillioides</i> )	FVEG_10526	W7N4P8
<i>Gibberella moniliformis</i> (strain M3125 / FGSC 7600) (Maize ear and stalk rot fungus) ( <i>Fusarium verticillioides</i> )	FVEG_08281	W7MVR9
<i>Pseudozyma antarctica</i> (strain T-34) (Yeast) ( <i>Candida antarctica</i> )	PANT_22d00298	M9MGF2
<i>Paracoccidioides brasiliensis</i> (strain Pb03)	PABG_07795	C0SJD4
<i>Rhizophagus irregularis</i> (strain DAOM 181602 / DAOM 197198 / MUCL 43194) (Arbuscular mycorrhizal fungus) ( <i>Glomus intraradices</i> )	GLOINDRAFT_82554	U9TF61
<i>Penicillium chrysogenum</i> (strain ATCC 28089 / DSM 1075 / Wisconsin 54-1255) ( <i>Penicillium notatum</i> )	Pc21g23700 PCH_Pc21g23700	B6HJ58
<i>Baudoinia compniacensis</i> (strain UAMH 10762) (Angels' share fungus)	BAUCODRAFT_274597	M2M6Z5
<i>Hypocrea atroviridis</i> (strain ATCC 20476 / IMI 206040) ( <i>Trichoderma atroviride</i> )	TRIATDRAFT_280929	G9NJ32
<i>Colletotrichum gloeosporioides</i> (strain Cg-14) (Anthracnose fungus) ( <i>Glomerella cingulata</i> )	CGLO_06642	T0LPH0
<i>Cordyceps militaris</i> (strain CM01) (Caterpillar fungus)	CCM_02665	G3JB34

Organism	Gene names	Accession No.
Pyronema omphalodes (strain CBS 100304) (Pyronema confluens)	PCON_13062	U4LKE9
Colletotrichum graminicola (strain M1.001 / M2 / FGSC 10212) (Maize anthracnose fungus) (Glomerella graminicola)	GLRG_08499	E3QR67
Glarea lozoyensis (strain ATCC 74030 / MF5533)	M7I_2117	H0EHX4
Fusarium oxysporum f. sp. cubense (strain race 4) (Panama disease fungus)	FOC4_g10002493	N1S969
Fusarium oxysporum f. sp. cubense (strain race 4) (Panama disease fungus)	FOC4_g10011461	N1RT80
Cochliobolus sativus (strain ND90Pr / ATCC 201652) (Common root rot and spot blotch fungus) (Bipolaris sorokiniana)	COCSADRAFT_295770	M2TBE4
Mixia osmundae (strain CBS 9802 / IAM 14324 / JCM 22182 / KY 12970)	Mo05571 E5Q_05571	G7E7S3
Mycosphaerella pini (strain NZE10 / CBS 128990) (Red band needle blight fungus) (Dothistroma septosporum)	DOTSEDRAFT_69651	N1PXR0
Grossmannia clavigera (strain kw1407 / UAMH 11150) (Blue stain fungus) (Graphiocladiella clavigera)	CMQ_1113	F0XC64
Fusarium oxysporum FOSC 3-a	FOYG_03004	W9IUE5
Fusarium oxysporum FOSC 3-a	FOYG_16040	W9HNP0
Fusarium oxysporum FOSC 3-a	FOYG_17058	W9HB31
Nectria haematococca (strain 77-13-4 / ATCC MYA-4622 / FGSC 9596 / MPVI) (Fusarium solani subsp. pisi)	NECHADRAFT_37686	C7YQL1
Nectria haematococca (strain 77-13-4 / ATCC MYA-4622 / FGSC 9596 / MPVI) (Fusarium solani subsp. pisi)	NECHADRAFT_77262	C7ZJ10
Tuber melanosporum (strain Mel28) (Perigord black truffle)	GSTUM_00010376001	D5GLS0
Ajellomyces dermatitidis (strain SLH14081) (Blastomyces dermatitidis)	BDBG_07633	C5JY19
Chaetomium globosum (strain ATCC 6205 / CBS 148.51 / DSM 1962 / NBRC 6347 / NRRL 1970) (Soil fungus)	CHGG_09885	Q2GQ69
Candida tenuis (strain ATCC 10573 / BCRC 21748 / CBS 615 / JCM 9827 / NBRC 10315 / NRRL Y- 1498 / VKM Y-70) (Yeast)	CANTEDRAFT_108652	G3B9Z1
Trichophyton rubrum CBS 100081	H102_00622	A0A022VKY4
Pyrenophora teres f. teres (strain 0-1) (Barley net blotch fungus) (Drechslera teres f. teres)	PTT_09421	E3RLZ3

Organism	Gene names	Accession No.
<i>Colletotrichum gloeosporioides</i> (strain Nara gc5) (Anthracnose fungus) ( <i>Glomerella cingulata</i> )	CGGC5_4608	L2GB29
<i>Gibberella zeae</i> (Wheat head blight fungus) ( <i>Fusarium graminearum</i> )	FG05_06918	A0A016PCS4
<i>Trichophyton soudanense</i> CBS 452.61	H105_00612	A0A022Y6A6
<i>Sclerotinia sclerotiorum</i> (strain ATCC 18683 / 1980 / Ss-1) (White mold) ( <i>Whetzelinia sclerotiorum</i> )	SS1G_07437	A7EQ37
<i>Fusarium oxysporum</i> f. sp. pisi HDV247	FOVG_14401	W9NWU8
<i>Fusarium oxysporum</i> f. sp. pisi HDV247	FOVG_02874	W9Q5V3
<i>Ustilago hordei</i> (strain Uh4875-4) (Barley covered smut fungus)	UHOR_03009	I2G1Z4
<i>Sporisorium reilianum</i> (strain SRZ2) (Maize head smut fungus)	sr12985	E6ZYF7
<i>Bipolaris zeicola</i> 26-R-13	COCCADRAFT_81154	W6YIP8
<i>Melanopsora larici-populina</i> (strain 98AG31 / pathotype 3-4-7) (Poplar leaf rust fungus)	MELLADRAFT_78490	F4RUZ8
<i>Fusarium oxysporum</i> f. sp. lycopersici (strain 4287 / CBS 123668 / FGSC 9935 / NRRL 34936) ( <i>Fusarium</i> vascular wilt of tomato)	FOXG_01901	J9MG95
<i>Fusarium oxysporum</i> f. sp. lycopersici (strain 4287 / CBS 123668 / FGSC 9935 / NRRL 34936) ( <i>Fusarium</i> vascular wilt of tomato)	FOXG_11941	J9N9S4
<i>Bipolaris victoriae</i> FI3	COCVIDRAFT_39053	W7EMJ8
<i>Debaryomyces hansenii</i> (strain ATCC 36239 / CBS 767 / JCM 1990 / NBRC 0083 / IGC 2968) (Yeast) ( <i>Torulasporea hansenii</i> )	DEHA2E04268g	Q6BQL4
<i>Clavispora lusitaniae</i> (strain ATCC 42720) (Yeast) ( <i>Candida lusitaniae</i> )	CLUG_01505	C4XZX3
<i>Candida albicans</i> (strain WO-1) (Yeast)	CAWG_02023	C4YME4
<i>Trichophyton rubrum</i> MR850	H100_00625	A0A022U0Q2
<i>Candida dubliniensis</i> (strain CD36 / ATCC MYA-646 / CBS 7987 / NCPF 3949 / NRRL Y-17841) (Yeast)	CD36_32890	B9WMC7
<i>Stromerella bombycolina</i>	AOX1	A0A024FB95
<i>Thielavia heterothallica</i> (strain ATCC 42464 / BCRC 31852 / DSM 1799) ( <i>Myceliophthora thermophila</i> )	MYCTH_103590	G2QJL7
<i>Claviceps purpurea</i> (strain 20.1) (Ergot fungus) ( <i>Sphacelia segetum</i> )	CPUR_07614	M1WFI4
<i>Aspergillus oryzae</i> (strain ATCC 42149 / RIB 40) (Yellow koji mold)	AO090023000571	Q2UH61
<i>Dictyostelium discoideum</i> (Slime mold)	DDB_0184181 DDB_G0292042	Q54DT6
<i>Triticum urartu</i> (Red wild einkorn) ( <i>Crithodium urartu</i> )	TRIUR3_22733	M7YME5

Organism	Gene names	Accession No.
<i>Solanum tuberosum</i> (Potato)	PGSC0003DMG400017211	M1BG07
<i>Oryza sativa</i> subsp. <i>japonica</i> (Rice)	OSJNBb0044B19.5 LOC_Os10g33540	Q8W5P8
<i>Oryza sativa</i> subsp. <i>japonica</i> (Rice)	OJ1234_B11.20 Os02g0621800	Q6K9N5
<i>Oryza sativa</i> subsp. <i>japonica</i> (Rice)	OSJNBa0001K12.5 LOC_Os10g33520	Q8W5P3
<i>Zea mays</i> (Maize)	ZEAMMB73_809149	C0P3J6
<i>Citrus clementina</i>	CICLE_v10011111mg	V4S9P4
<i>Citrus clementina</i>	CICLE_v10018992mg	V4U4C9
<i>Citrus clementina</i>	CICLE_v10004405mg	V4S9D3
<i>Citrus clementina</i>	CICLE_v10004403mg	V4RZZ6
<i>Morus notabilis</i>	L484_011703	W9RIK0
<i>Morus notabilis</i>	L484_005930	W9RET7
<i>Medicago truncatula</i> (Barrel medic) ( <i>Medicago tribuloides</i> )	MTR_1g075650	G7I4U3
<i>Arabidopsis thaliana</i> (Mouse-ear cress)		Q8LDP0
<i>Medicago truncatula</i> (Barrel medic) ( <i>Medicago tribuloides</i> )	MTR_4g081080	G7JF07
<i>Sinmondsia chinensis</i> (Jojoba) ( <i>Buxus chinensis</i> )		L7VfV2
<i>Prunus persica</i> (Peach) ( <i>Amygdalus persica</i> )	PRUPE_ppa018458mg	M5VXL1
<i>Aphanomyces astaci</i>	H257_07411	W4GI89
<i>Aphanomyces astaci</i>	H257_07412	W4GI44
<i>Aphanomyces astaci</i>	H257_07411	W4GKE3
<i>Aphanomyces astaci</i>	H257_07411	W4GK29
<i>Aphanomyces astaci</i>	H257_07411	W4GJ79
<i>Aphanomyces astaci</i>	H257_07411	W4GI38
<i>Phaeodactylum tricornutum</i> (strain CCAP 1055/1)	PHATRDRRAFT_48204	B7G6C1
<i>Hordeum vulgare</i> var. <i>distichum</i> (Two-rowed barley)		F2E4R4
<i>Hordeum vulgare</i> var. <i>distichum</i> (Two-rowed barley)		F2DZG1
<i>Hordeum vulgare</i> var. <i>distichum</i> (Two-rowed barley)		M0YPG7
<i>Hordeum vulgare</i> var. <i>distichum</i> (Two-rowed barley)		M0YPG6
<i>Hordeum vulgare</i> var. <i>distichum</i> (Two-rowed barley)		F2CUY4
<i>Ricinus communis</i> (Castor bean)	RCOM_0867830	B9S1S3
<i>Brassica rapa</i> subsp. <i>pekinensis</i> (Chinese cabbage) ( <i>Brassica pekinensis</i> )	BRA014947	M4DEM5
<i>Ricinus communis</i> (Castor bean)	RCOM_0258730	B9SV13

Organism	Gene names	Accession No.
<i>Brassica rapa</i> subsp. <i>pekinensis</i> (Chinese cabbage) ( <i>Brassica pekinensis</i> )	BRA001912	M4CCI2
<i>Brassica rapa</i> subsp. <i>pekinensis</i> (Chinese cabbage) ( <i>Brassica pekinensis</i> )	BRA012548	M4D7T8
<i>Brassica rapa</i> subsp. <i>pekinensis</i> (Chinese cabbage) ( <i>Brassica pekinensis</i> )	BRA024190	M4E5Y6
<i>Brassica rapa</i> subsp. <i>pekinensis</i> (Chinese cabbage) ( <i>Brassica pekinensis</i> )	BRA015283	M4DFL0
<i>Ricinus communis</i> (Castor bean)	RCOM_1168730	B9SS54
<i>Zea mays</i> (Maize)		C4J691
<i>Oryza glaberrima</i> (African rice)		I1P2B7
<i>Zea mays</i> (Maize)		B6SXM3
<i>Zea mays</i> (Maize)		C0HFU4
<i>Aegilops tauschii</i> (Tausch's goatgrass) ( <i>Aegilops squarrosa</i> )	F775_19577	R7W4J3
<i>Solanum habrochaites</i> (Wild tomato) ( <i>Lycopersicon hirsutum</i> )		R9R6T0
<i>Physcomitrella patens</i> subsp. <i>patens</i> (Moss)	PHYPADRAFT_124285	A9S535
<i>Physcomitrella patens</i> subsp. <i>patens</i> (Moss)	PHYPADRAFT_113581	A9RG13
<i>Physcomitrella patens</i> subsp. <i>patens</i> (Moss)	PHYPADRAFT_182504	A9S9A5
<i>Solanum pennellii</i> (Tomato) ( <i>Lycopersicon pennellii</i> )		R9R6Q1
<i>Vitis vinifera</i> (Grape)	VIT_02s0087g00630	F6HJ27
<i>Vitis vinifera</i> (Grape)	VIT_07s0005g03780	F6HZM3
<i>Vitis vinifera</i> (Grape)	VIT_05s0049g01400	F6H8T4
<i>Vitis vinifera</i> (Grape)	VITISV_019349	A5AH38
<i>Capsella rubella</i>	CARUB_v10013046mg	R0HIT3
<i>Capsella rubella</i>	CARUB_v10004212mg	R0GUX4
<i>Capsella rubella</i>	CARUB_v10004208mg	R0F3X6
<i>Capsella rubella</i>	CARUB_v10012453mg	R0ILD0
<i>Capsella rubella</i>	CARUB_v10004208mg	R0GUX1
<i>Eutrema salsugineum</i> (Saltwater cress) ( <i>Sisymbrium salsugineum</i> )	EUTSA_v10024496mg	V4MD54
<i>Eutrema salsugineum</i> (Saltwater cress) ( <i>Sisymbrium salsugineum</i> )	EUTSA_v10020141mg	V4NM59
<i>Eutrema salsugineum</i> (Saltwater cress) ( <i>Sisymbrium salsugineum</i> )	EUTSA_v10024496mg	V4LUR9
<i>Eutrema salsugineum</i> (Saltwater cress) ( <i>Sisymbrium salsugineum</i> )	EUTSA_v10024528mg	V4P767
<i>Eutrema salsugineum</i> (Saltwater cress) ( <i>Sisymbrium salsugineum</i> )	EUTSA_v10006882mg	V4L2P6
<i>Selaginella moellendorffii</i> (Spikemoss)	SELMODRAFT_87684	D8R6Z6
<i>Selaginella moellendorffii</i> (Spikemoss)	SELMODRAFT_87621	D8R6Z5

Organism	Gene names	Accession No.
Selaginella moellendorffii (Spikemoss)	SELMODRAFT_74601	D8QN81
Selaginella moellendorffii (Spikemoss)	SELMODRAFT_73531	D8QN82
Sorghum bicolor (Sorghum) (Sorghum vulgare)	Sb04g026390 SORBIDRAFT_04g026390	C5XXS4
Sorghum bicolor (Sorghum) (Sorghum vulgare)	Sb04g026370 SORBIDRAFT_04g026370	C5XXS1
Sorghum bicolor (Sorghum) (Sorghum vulgare)	Sb01g019470 SORBIDRAFT_01g019470	C5WYH6
Sorghum bicolor (Sorghum) (Sorghum vulgare)	Sb01g019480 SORBIDRAFT_01g019480	C5WYH7
Sorghum bicolor (Sorghum) (Sorghum vulgare)	Sb01g019460 SORBIDRAFT_01g019460	C5WYH5
Solanum pimpinellifolium (Currant tomato) (Lycopersicon pimpinellifolium)		R9R6J2
Phaseolus vulgaris (Kidney bean) (French bean)	PHAVU_007G124200g	V7BGM7
Phaseolus vulgaris (Kidney bean) (French bean)	PHAVU_011G136600g	V7AI35
Phaseolus vulgaris (Kidney bean) (French bean)	PHAVU_001G162800g	V7D063
Solanum tuberosum (Potato)	PGSC0003DMG400024294	M1C923
Solanum tuberosum (Potato)	PGSC0003DMG400018458	M1BKV4
Solanum tuberosum (Potato)	PGSC0003DMG400018458	M1BKV3
Glycine max (Soybean) (Glycine hispida)		K7LK61
Glycine max (Soybean) (Glycine hispida)		K7KXQ9
Populus trichocarpa (Western balsam poplar) (Populus balsamifera subsp. trichocarpa)	POPTR_0008s16920g	B9HKS3
Picea sitchensis (Sitka spruce) (Pinus sitchensis)		B8LQ84
Populus trichocarpa (Western balsam poplar) (Populus balsamifera subsp. trichocarpa)	POPTR_0004s24310g	U5GKQ5
Populus trichocarpa (Western balsam poplar) (Populus balsamifera subsp. trichocarpa)	POPTR_0010s07980g	B9HSG9
Glycine max (Soybean) (Glycine hispida)		I1N9S7
Glycine max (Soybean) (Glycine hispida)		I1LSK5
Setaria italica (Foxtail millet) (Panicum italicum)	Si034362m.g	K4A658
Solanum lycopersicum (Tomato) (Lycopersicon esculentum)	Solyc09g072610.2	K4CUT7
Setaria italica (Foxtail millet) (Panicum italicum)	Si016380m.g	K3YQ38
Solanum lycopersicum (Tomato) (Lycopersicon esculentum)		R9R6I9
Solanum lycopersicum (Tomato) (Lycopersicon esculentum)	Solyc09g090350.2	K4CW61
Solanum lycopersicum (Tomato) (Lycopersicon esculentum)	Solyc08g005630.2	K4CI54
Solanum lycopersicum (Tomato) (Lycopersicon esculentum)	Solyc08g075240.2	K4CMP1



Organism	Gene names	Accession No.
Setaria italica (Foxtail millet) ( <i>Panicum italicum</i> )	Si034359m.g	K4A655
Setaria italica (Foxtail millet) ( <i>Panicum italicum</i> )	Si034354m.g	K4A650
Mimulus guttatus (Spotted monkey flower) (Yellow monkey flower)	MIMGU_mgv1a001896mg	A0A022PU07
Mimulus guttatus (Spotted monkey flower) (Yellow monkey flower)	MIMGU_mgv1a022390mg	A0A022RAV4
Mimulus guttatus (Spotted monkey flower) (Yellow monkey flower)	MIMGU_mgv1a001868mg	A0A022S2E6
Mimulus guttatus (Spotted monkey flower) (Yellow monkey flower)	MIMGU_mgv1a001883mg	A0A022S275
Mimulus guttatus (Spotted monkey flower) (Yellow monkey flower)	MIMGU_mgv1a001761mg	A0A022QNF0
Musa acuminata subsp. malaccensis (Wild banana) ( <i>Musa malaccensis</i> )		M0SNA8
Musa acuminata subsp. malaccensis (Wild banana) ( <i>Musa malaccensis</i> )		M0RUT7
Musa acuminata subsp. malaccensis (Wild banana) ( <i>Musa malaccensis</i> )		M0RUK3
Saprolegnia diclina VS20	SDRG_10901	T0RG89
Brachypodium distachyon (Purple false brome) ( <i>Trachynia distachya</i> )	BRADI3G49085	I1IBP7
Brachypodium distachyon (Purple false brome) ( <i>Trachynia distachya</i> )	BRADI3G28677	I1I4N2
Brachypodium distachyon (Purple false brome) ( <i>Trachynia distachya</i> )	BRADI3G28657	I1I4N0
Oryza sativa subsp. indica (Rice)	OsI_34012	B8BHG0
Oryza sativa subsp. indica (Rice)	OsI_08118	B8AFT8
Oryza sativa subsp. indica (Rice)	OsI_34008	A2ZSH1
Oryza sativa subsp. indica (Rice)	OsI_34014	B8BHG1
Oryza sativa subsp. japonica (Rice)	LOC_Os10g33460	Q7XDG3
Oryza sativa subsp. japonica (Rice)	Os10g0474800	Q0IX12
Oryza sativa subsp. japonica (Rice)	Os10g0474966	C7J7R1
Oryza sativa subsp. japonica (Rice)	OSJNBa0001K12.13	Q8W5N7
Oryza sativa subsp. japonica (Rice)	OsJ_31873	B9G683
Oryza sativa subsp. japonica (Rice)	OsJ_31875	B9G684
Oryza sativa subsp. japonica (Rice)	OSJNBa0001K12.3	Q8W5P5
Arabidopsis lyrata subsp. lyrata (Lyre-leaved rock- cress)	ARALYDRAFT_470376	D7KDA3
Arabidopsis lyrata subsp. lyrata (Lyre-leaved rock- cress)	ARALYDRAFT_479855	D7L3B6
Arabidopsis lyrata subsp. lyrata (Lyre-leaved rock- cress)	ARALYDRAFT_491906	D7MDA9

Organism	Gene names	Accession No.
Arabidopsis lyrata subsp. lyrata (Lyre-leaved rock-cress)	ARALYDRAFT_914728	D7MGS9

[0089] In some embodiments, an alcohol dehydrogenase (ADH, Table 4) is used to catalyze the conversion of a fatty alcohol to a fatty aldehyde. A number of ADHs identified from alkanotrophic organisms, *Pseudomonas fluorescens* NRRL B-1244 (Hou *et al.* 1983),  
5 *Pseudomonas butanovora* ATCC 43655 (Vangnai and Arp 2001), and *Acinetobacter sp.* strain M-1 (Tani *et al.* 2000), have shown to be active on short to medium-chain alkyl alcohols (C<sub>2</sub> to C<sub>14</sub>). Additionally, commercially available ADHs from Sigma, Horse liver ADH and Baker's yeast ADH have detectable activity for substrates with length C<sub>10</sub> and greater. The reported activities for the longer fatty alcohols may be impacted by the  
10 difficulties in solubilizing the substrates. For the yeast ADH from Sigma, little to no activity is observed for C<sub>12</sub> to C<sub>14</sub> aldehydes by (Tani *et al.* 2000), however, activity for C<sub>12</sub> and C<sub>16</sub> hydroxy- $\omega$ -fatty acids has been observed (Lu *et al.* 2010). Recently, two ADHs were characterized from *Geobacillus thermodenitrificans* NG80-2, an organism that degrades C<sub>15</sub> to C<sub>36</sub> alkanes using the LadA hydroxylase. Activity was detected from methanol to 1-  
15 triacontanol (C<sub>30</sub>) for both ADHs, with 1-octanol being the preferred substrate for ADH2 and ethanol for ADH1 (Liu *et al.* 2009).

[0090] The use of ADHs in whole-cell bioconversions has been mostly focused on the production of chiral alcohols from ketones (Ernst *et al.* 2005) (Schroer *et al.* 2007). Using the ADH from *Lactobacillus brevis* and coupled cofactor regeneration with isopropanol,  
20 Schroer *et al.* reported the production of 797 g of (R)-methyl-3 hydroxybutanoate from methyl acetoacetate, with a space time yield of 29 g/L/h (Schroer *et al.* 2007). Examples of aliphatic alcohol oxidation in whole-cell transformations have been reported with commercially obtained *S. cerevisiae* for the conversion of hexanol to hexanal (Presecki *et al.* 2012) and 2-heptanol to 2-heptanone (Cappaert and Larroche 2004).

25 Table 4. Exemplary alcohol dehydrogenase enzymes.

Organism	Gene Name	Accession No.
Bactrocera oleae (Olive fruit fly) ( <i>Dacus oleae</i> )	ADH	Q9NAR7
Cupriavidus necator (Alcaligenes eutrophus) ( <i>Ralstonia eutropha</i> )	adh	P14940
Drosophila adiantola (Fruit fly) ( <i>Idionyia adiantola</i> )	Adh	Q00669

Organism	Gene Name	Accession No.
<i>Drosophila affinisdisjuncta</i> (Fruit fly) ( <i>Idiomyia affinisdisjuncta</i> )	Adh	P21518
<i>Drosophila ambigua</i> (Fruit fly)	Adh	P25139
<i>Drosophila borealis</i> (Fruit fly)	Adh	P48584
<i>Drosophila differens</i> (Fruit fly)	Adh	P22245
<i>Drosophila equinoxialis</i> (Fruit fly)	Adh	Q9NG42
<i>Drosophila flavomontana</i> (Fruit fly)	Adh	P48585
<i>Drosophila guanche</i> (Fruit fly)	Adh	Q09009
<i>Drosophila hawaiiensis</i> (Fruit fly)	Adh	P51549
<i>Drosophila heteroneura</i> (Fruit fly)	Adh	P21898
<i>Drosophila inumigrans</i> (Fruit fly)	Adh	Q07588
<i>Drosophila insularis</i> (Fruit fly)	Adh	Q9NG40
<i>Drosophila lebanonensis</i> (Fruit fly) ( <i>Scaptodrosophila lebanonensis</i> )	Adh	P10807
<i>Drosophila mauritiana</i> (Fruit fly)	Adh	P07162
<i>Drosophila madeirensis</i> (Fruit fly)	Adh	Q09010
<i>Drosophila mimica</i> (Fruit fly) ( <i>Idiomyia mimica</i> )	Adh	Q00671
<i>Drosophila nigra</i> (Fruit fly) ( <i>Idiomyia nigra</i> )	Adh	Q00672
<i>Drosophila oreana</i> (Fruit fly)	Adh	P07159
<i>Drosophila pseudoobscura bogotana</i> (Fruit fly)	Adh	P84328
<i>Drosophila picticornis</i> (Fruit fly) ( <i>Idiomyia picticornis</i> )	Adh	P23361
<i>Drosophila planitibia</i> (Fruit fly)	Adh	P23277
<i>Drosophila paulistorum</i> (Fruit fly)	Adh	Q9U8S9
<i>Drosophila silvestris</i> (Fruit fly)	Adh	P23278
<i>Drosophila subobscura</i> (Fruit fly)	Adh	Q03384
<i>Drosophila teissieri</i> (Fruit fly)	Adh	P28484
<i>Drosophila tsacasi</i> (Fruit fly)	Adh	P51550
<i>Fragaria ananassa</i> (Strawberry)	ADH	P17648
<i>Malus domestica</i> (Apple) ( <i>Pyrus malus</i> )	ADH	P48977
<i>Scaptomyza albovittata</i> (Fruit fly)	Adh	P25988
<i>Scaptomyza crassifemur</i> (Fruit fly) ( <i>Drosophila crassifemur</i> )	Adh	Q00670
<i>Sulfolobus</i> sp. (strain RC3)	adh	P50381
<i>Zaprionus tuberculatus</i> (Vinegar fly)	Adh	P51552
<i>Geobacillus stearothermophilus</i> ( <i>Bacillus stearothermophilus</i> )	adh	P42327
<i>Drosophila mayaguana</i> (Fruit fly)	Adh, Adh2	P25721
<i>Drosophila melanogaster</i> (Fruit fly)	Adh, CG3481	P00334
<i>Drosophila pseudoobscura pseudoobscura</i> (Fruit fly)	Adh, GA17214	Q6LCE4
<i>Drosophila simulans</i> (Fruit fly)	Adh, GD23968	Q24641
<i>Drosophila yakuba</i> (Fruit fly)	Adh, GE19037	P26719

Organism	Gene Name	Accession No.
<i>Drosophila ananassae</i> (Fruit fly)	Adh, GF14888	Q50L96
<i>Drosophila erecta</i> (Fruit fly)	Adh, GG25120	P28483
<i>Drosophila grimshawi</i> (Fruit fly) ( <i>Idiomyia grimshawi</i> )	Adh, GH13025	P51551
<i>Drosophila willistoni</i> (Fruit fly)	Adh, GK18290	Q05114
<i>Drosophila persimilis</i> (Fruit fly)	Adh, GL25993	P37473
<i>Drosophila sechellia</i> (Fruit fly)	Adh, GM15656	Q9GN94
<i>Cupriavidus necator</i> (strain ATCC 17699 / H16 / DSM 428 / Stanier 337) ( <i>Ralstonia eutropha</i> )	adh, H16_A0757	Q0KDL6
<i>Mycobacterium tuberculosis</i> (strain CDC 1551 / Oshkosh)	adh, MT1581	P9WQC2
<i>Staphylococcus aureus</i> (strain MW2)	adh, MW0568	Q8NXU1
<i>Mycobacterium tuberculosis</i> (strain ATCC 25618 / H37Rv)	adh, Rv1530	P9WQC3
<i>Staphylococcus aureus</i> (strain N315)	adh, SA0562	Q7A742
<i>Staphylococcus aureus</i> (strain bovine RF122 / ET3-1)	adh, SAB0557	Q2YSX0
<i>Sulfolobus acidocaldarius</i> (strain ATCC 33909 / DSM 639 / JCM 8929 / NBRC 15157 / NCIMB 11770)	adh, Saci_2057	Q4J781
<i>Staphylococcus aureus</i> (strain COL)	adh, SACOL0660	Q5HI63
<i>Staphylococcus aureus</i> (strain NCTC 8325)	adh, SAOUHSC_00608	Q2G0G1
<i>Staphylococcus aureus</i> (strain MRSA252)	adh, SAR0613	Q6GJ63
<i>Staphylococcus aureus</i> (strain MSSA476)	adh, SAS0573	Q6GBM4
<i>Staphylococcus aureus</i> (strain USA300)	adh, SAUSA300_0594	Q2FJ31
<i>Staphylococcus aureus</i> (strain Mu50 / ATCC 700699)	adh, SAV0605	Q99W07
<i>Staphylococcus epidermidis</i> (strain ATCC 12228)	adh, SE_0375	Q8CQ56
<i>Staphylococcus epidermidis</i> (strain ATCC 35984 / RP62A)	adh, SERP0257	Q5HRD6
<i>Sulfolobus solfataricus</i> (strain ATCC 35092 / DSM 1617 / JCM 11322 / P2)	adh, SSO2536	P39462
<i>Sulfolobus tokodaii</i> (strain DSM 16993 / JCM 10545 / NBRC 100140 / 7)	adh, STK_25770	Q96XE0
<i>Anas platyrhynchos</i> (Domestic duck) ( <i>Anas boschas</i> )	ADH1	P30350
<i>Apteryx australis</i> (Brown kiwi)	ADH1	P49645
<i>Ceratitis capitata</i> (Mediterranean fruit fly) ( <i>Tephritis capitata</i> )	ADH1	P48814
<i>Ceratitis cosyra</i> (Mango fruit fly) ( <i>Trypeta cosyra</i> )	ADH1	Q70UN9
<i>Gallus gallus</i> (Chicken)	ADH1	P23991
<i>Columba livia</i> (Domestic pigeon)	ADH1	P86883
<i>Coturnix coturnix japonica</i> (Japanese quail) ( <i>Coturnix japonica</i> )	ADH1	P19631

Organism	Gene Name	Accession No.
<i>Drosophila hydei</i> (Fruit fly)	Adh1	P23236
<i>Drosophila montana</i> (Fruit fly)	Adh1	P48586
<i>Drosophila mettleri</i> (Fruit fly)	Adh1	P22246
<i>Drosophila mulleri</i> (Fruit fly)	Adh1	P07161
<i>Drosophila navojoa</i> (Fruit fly)	Adh1	P12854
<i>Geomys attwateri</i> (Attwater's pocket gopher) ( <i>Geomys bursarius attwateri</i> )	ADH1	Q9Z2M2
<i>Geomys bursarius</i> (Plains pocket gopher)	ADH1	Q64413
<i>Geomys knoxjonesi</i> (Knox Jones's pocket gopher)	ADH1	Q64415
<i>Hordeum vulgare</i> (Barley)	ADH1	P05336
<i>Kluyveromyces marxianus</i> (Yeast) ( <i>Candida kefyr</i> )	ADH1	Q07288
<i>Zea mays</i> (Maize)	ADH1	P00333
<i>Mesocricetus auratus</i> (Golden hamster)	ADH1	P86885
<i>Pennisetum americanum</i> (Pearl millet) ( <i>Pennisetum glaucum</i> )	ADH1	P14219
<i>Petunia hybrida</i> (Petunia)	ADH1	P25141
<i>Oryctolagus cuniculus</i> (Rabbit)	ADH1	Q03505
<i>Solanum tuberosum</i> (Potato)	ADH1	P14673
<i>Struthio camelus</i> (Ostrich)	ADH1	P80338
<i>Trifolium repens</i> (Creeping white clover)	ADH1	P13603
<i>Zea luxurians</i> (Guatemalan teosinte) ( <i>Euchlaena luxurians</i> )	ADH1	Q07264
<i>Saccharomyces cerevisiae</i> (strain ATCC 204508 / S288c) (Baker's yeast)	ADH1, ADC1, YOL086C, O0947	P00330
<i>Arabidopsis thaliana</i> (Mouse-ear cress)	ADH1, ADH, At1g77120, F22K20.19	P06525
<i>Schizosaccharomyces pombe</i> (strain 972 / ATCC 24843) (Fission yeast)	adh1, adh, SPCC13B11.01	P00332
<i>Drosophila lacicola</i> (Fruit fly)	Adh1, Adh-1	Q27404
<i>Mus musculus</i> (Mouse)	Adh1, Adh-1	P00329
<i>Peromyscus maniculatus</i> (North American deer mouse)	ADH1, ADH-1	P41680
<i>Rattus norvegicus</i> (Rat)	Adh1, Adh-1	P06757
<i>Drosophila virilis</i> (Fruit fly)	Adh1, Adh-1, GJ18208	B4M8Y0
<i>Scheffersomyces stipitis</i> (strain ATCC 58785 / CBS 6054 / NBRC 10063 / NRRL Y-11545) (Yeast) ( <i>Pichia stipitis</i> )	ADH1, ADH2, PICST_68558	O00097
<i>Aspergillus flavus</i> (strain ATCC 200026 / FGSC A1120 / NRRL 3357 / JCM 12722 / SRRC 167)	adh1, AFLA_048690	P41747
<i>Neurospora crassa</i> (strain ATCC 24698 / 74-OR23-1A / CBS 708.71 / DSM 1257 / FGSC 987)	adh-1, B17C10.210, NCU01754	Q9P6C8
<i>Candida albicans</i> (Yeast)	ADH1, CAD	P43067
<i>Oryza sativa</i> subsp. <i>japonica</i> (Rice)	ADH1, DUPR11.3,	Q2R8Z5

Organism	Gene Name	Accession No.
	Os11g0210300, LOC_Os11g10480, OsJ_032001	
<i>Drosophila mojavensis</i> (Fruit fly)	Adh1, GI17644	P09370
<i>Kluyveromyces lactis</i> (strain ATCC 8585 / CBS 2359 / DSM 70799 / NBRC 1267 / NRRL Y-1140 / WM37) (Yeast) ( <i>Candida sphaerica</i> )	ADH1, KLLA0F21010g	P20369
<i>Oryza sativa</i> subsp. <i>indica</i> (Rice)	ADH1, OsI_034290	Q75ZX4
<i>Pongo abelii</i> (Sumatran orangutan) ( <i>Pongo pygmaeus abelii</i> )	ADH1A	Q5RBP7
<i>Homo sapiens</i> (Human)	ADH1A, ADH1	P07327
<i>Macaca mulatta</i> (Rhesus macaque)	ADH1A, ADH1	P28469
<i>Pan troglodytes</i> (Chimpanzee)	ADH1B	Q5R1W2
<i>Papio hamadryas</i> (Hamadryas baboon)	ADH1B	P14139
<i>Homo sapiens</i> (Human)	ADH1B, ADH2	P00325
<i>Homo sapiens</i> (Human)	ADH1C, ADH3	P00326
<i>Papio hamadryas</i> (Hamadryas baboon)	ADH1C, ADH3	Q97959
<i>Ceratitis capitata</i> (Mediterranean fruit fly) ( <i>Tephritis capitata</i> )	ADH2	P48815
<i>Ceratitis cosyra</i> (Mango fruit fly) ( <i>Trypeta cosyra</i> )	ADH2	Q70UP5
<i>Ceratitis rosa</i> (Natal fruit fly) ( <i>Pterandrus rosa</i> )	ADH2	Q70UP6
<i>Drosophila arizonae</i> (Fruit fly)	Adh2	P27581
<i>Drosophila buzzatii</i> (Fruit fly)	Adh2	P25720
<i>Drosophila hydei</i> (Fruit fly)	Adh2	P23237
<i>Drosophila montana</i> (Fruit fly)	Adh2	P48587
<i>Drosophila mulleri</i> (Fruit fly)	Adh2	P07160
<i>Drosophila wheeleri</i> (Fruit fly)	Adh2	P24267
<i>Entamoeba histolytica</i>	ADH2	Q24803
<i>Hordeum vulgare</i> (Barley)	ADH2	P10847
<i>Kluyveromyces marxianus</i> (Yeast) ( <i>Candida kefyri</i> )	ADH2	Q9P4C2
<i>Zea mays</i> (Maize)	ADH2	P04707
<i>Oryza sativa</i> subsp. <i>indica</i> (Rice)	ADH2	Q4R1E8
<i>Solanum lycopersicum</i> (Tomato) ( <i>Lycopersicon esculentum</i> )	ADH2	P28032
<i>Solanum tuberosum</i> (Potato)	ADH2	P14674
<i>Scheffersomyces stipitis</i> (strain ATCC 58785 / CBS 6054 / NBRC 10063 / NRRL Y-11545) (Yeast) ( <i>Pichia stipitis</i> )	ADH2, ADH1, PICST_27980	O13309
<i>Arabidopsis thaliana</i> (Mouse-ear cress)	ADH2, ADHIII, FDH1, At5g43940, MRH10.4	Q96533
<i>Saccharomyces cerevisiae</i> (strain ATCC 204508 / S288c) (Baker's yeast)	ADH2, ADR2, YMR303C, YM9952.05C	P00331
<i>Candida albicans</i> (strain SC5314 / ATCC MYA-2876) (Yeast)	ADH2, Ca41C10.04, CaO19.12579,	Q94038

Organism	Gene Name	Accession No.
	CaO19.5113	
<i>Oryza sativa</i> subsp. japonica (Rice)	ADH2, DUPR11.1, Os11g0210500, LOC_Os11g10510	Q0ITW7
<i>Drosophila mojavensis</i> (Fruit fly)	Adh2, GI17643	P09369
<i>Kluyveromyces lactis</i> (strain ATCC 8585 / CBS 2359 / DSM 70799 / NBRC 1267 / NRRL Y-1140 / WM37) (Yeast) ( <i>Candida sphaerica</i> )	ADH2, KLLA0F18260g	P49383
<i>Oryctolagus cuniculus</i> (Rabbit)	ADH2-1	O46649
<i>Oryctolagus cuniculus</i> (Rabbit)	ADH2-2	O46650
<i>Hordeum vulgare</i> (Barley)	ADH3	P10848
<i>Solanum tuberosum</i> (Potato)	ADH3	P14675
<i>Kluyveromyces lactis</i> (strain ATCC 8585 / CBS 2359 / DSM 70799 / NBRC 1267 / NRRL Y-1140 / WM37) (Yeast) ( <i>Candida sphaerica</i> )	ADH3, KLLA0B09064g	P49384
<i>Saccharomyces cerevisiae</i> (strain ATCC 204508 / S288c) (Baker's yeast)	ADH3, YMR083W, YM9582.08	P07246
<i>Homo sapiens</i> (Human)	ADH4	P08319
<i>Mus musculus</i> (Mouse)	Adh4	Q9QYY9
<i>Rattus norvegicus</i> (Rat)	Adh4	Q64563
<i>Struthio camelus</i> (Ostrich)	ADH4	P80468
<i>Kluyveromyces lactis</i> (strain ATCC 8585 / CBS 2359 / DSM 70799 / NBRC 1267 / NRRL Y-1140 / WM37) (Yeast) ( <i>Candida sphaerica</i> )	ADH4, KLLA0F13530g	P49385
<i>Schizosaccharomyces pombe</i> (strain 972 / ATCC 24843) (Fission yeast)	adh4, SPAC5H10.06c	Q09669
<i>Saccharomyces cerevisiae</i> (strain YJM789) (Baker's yeast)	ADH4, ZRG5, SCY_1818	A6ZTT5
<i>Saccharomyces cerevisiae</i> (strain ATCC 204508 / S288c) (Baker's yeast)	ADH4, ZRG5, YGL256W, NRC465	P10127
<i>Saccharomyces pastorianus</i> (Lager yeast) ( <i>Saccharomyces cerevisiae</i> x <i>Saccharomyces eubayanus</i> )	ADH5	Q6XQ67
<i>Bos taurus</i> (Bovine)	ADH5	Q3ZC42
<i>Equus caballus</i> (Horse)	ADH5	P19854
<i>Mus musculus</i> (Mouse)	Adh5, Adh-2, Adh2	P28474
<i>Rattus norvegicus</i> (Rat)	Adh5, Adh-2, Adh2	P12711
<i>Oryctolagus cuniculus</i> (Rabbit)	ADH5, ADH3	O19053
<i>Homo sapiens</i> (Human)	ADH5, ADHX, FDH	P11766
<i>Dictyostelium discoideum</i> (Slime mold)	adh5, DDB_G0281865	Q54TC2
<i>Saccharomyces cerevisiae</i> (strain ATCC 204508 / S288c) (Baker's yeast)	ADH5, YBR145W, YBR1122	P38113
<i>Homo sapiens</i> (Human)	ADH6	P28332

Organism	Gene Name	Accession No.
<i>Peromyscus maniculatus</i> (North American deer mouse)	ADH6	P41681
<i>Pongo abelii</i> (Sumatran orangutan) ( <i>Pongo pygmaeus abelii</i> )	ADH6	Q5R7Z8
<i>Rattus norvegicus</i> (Rat)	Adh6	Q5XI95
<i>Homo sapiens</i> (Human)	ADH7	P40394
<i>Rattus norvegicus</i> (Rat)	Adh7	P41682
<i>Mus musculus</i> (Mouse)	Adh7, Adh-3, Adh3	Q64437
<i>Mycobacterium tuberculosis</i> (strain CDC 1551 / Oshkosh)	adhA, MT1911	P9WQC0
<i>Rhizobium meliloti</i> (strain 1021) ( <i>Ensifer meliloti</i> ) ( <i>Sinorhizobium meliloti</i> )	adhA, RA0704, SMa1296	O31186
<i>Mycobacterium tuberculosis</i> (strain ATCC 25618 / H37Rv)	adhA, Rv1862	P9WQC1
<i>Zymomonas mobilis</i> subsp. <i>mobilis</i> (strain ATCC 31821 / ZM4 / CP4)	adhA, ZMO1236	P20368
<i>Mycobacterium bovis</i> (strain ATCC BAA-935 / AF2122/97)	adhB, Mb0784c	Q7U1B9
<i>Mycobacterium tuberculosis</i> (strain CDC 1551 / Oshkosh)	adhB, MT0786	P9WQC6
<i>Mycobacterium tuberculosis</i> (strain ATCC 25618 / H37Rv)	adhB, Rv0761c, MTCY369.06c	P9WQC7
<i>Zymomonas mobilis</i> subsp. <i>mobilis</i> (strain ATCC 31821 / ZM4 / CP4)	adhB, ZMO1596	P0DJA2
<i>Zymomonas mobilis</i> subsp. <i>mobilis</i> (strain ATCC 10988 / DSM 424 / LMG 404 / NCIMB 8938 / NRRL B-806 / ZM1)	adhB, Zmob_1541	F8DVL8
<i>Mycobacterium tuberculosis</i> (strain CDC 1551 / Oshkosh)	adhD, MT3171	P9WQB8
<i>Mycobacterium tuberculosis</i> (strain ATCC 25618 / H37Rv)	adhD, Rv3086	P9WQB9
<i>Clostridium acetobutylicum</i> (strain ATCC 824 / DSM 792 / JCM 1419 / LMG 5710 / VKM B-1787)	adhE, aad, CA_P0162	P33744
<i>Escherichia coli</i> (strain K12)	adhE, ana, b1241, JW1228	P0A9Q7
<i>Escherichia coli</i> O157:H7	adhE, Z2016, ECs1741	P0A9Q8
<i>Rhodobacter sphaeroides</i> (strain ATCC 17023 / 2.4.1 / NCIB 8253 / DSM 158)	adhI, RHOS4_11650, RSP_2576	P72324
<i>Oryza sativa</i> subsp. <i>indica</i> (Rice)	ADHIII, OsI_009236	A2XAZ3
<i>Escherichia coli</i> (strain K12)	adhP, yddN, b1478, JW1474	P39451
<i>Geobacillus stearothermophilus</i> ( <i>Bacillus stearothermophilus</i> )	adhT	P12311



Organism	Gene Name	Accession No.
<i>Emericella nidulans</i> (strain FGSC A4 / ATCC 38163 / CBS 112.46 / NRRL 194 / M139) ( <i>Aspergillus nidulans</i> )	alcA, AN8979	P08843
<i>Emericella nidulans</i> (strain FGSC A4 / ATCC 38163 / CBS 112.46 / NRRL 194 / M139) ( <i>Aspergillus nidulans</i> )	alc, AN3741	P54202
<i>Emericella nidulans</i> (strain FGSC A4 / ATCC 38163 / CBS 112.46 / NRRL 194 / M139) ( <i>Aspergillus nidulans</i> )	alcC, adh3, AN2286	P07754
<i>Arabidopsis thaliana</i> (Mouse-ear cress)	At1g22430, F12K8.22	Q9SK86
<i>Arabidopsis thaliana</i> (Mouse-ear cress)	At1g22440, F12K8.21	Q9SK87
<i>Arabidopsis thaliana</i> (Mouse-ear cress)	At1g32780, F6N18.16	A1L4Y2
<i>Arabidopsis thaliana</i> (Mouse-ear cress)	At1g64710, F13O11.3	Q8VZ49
<i>Arabidopsis thaliana</i> (Mouse-ear cress)	At4g22110, FIN20.210	Q0V7W6
<i>Arabidopsis thaliana</i> (Mouse-ear cress)	At5g24760, T4C12_30	Q8LEB2
<i>Arabidopsis thaliana</i> (Mouse-ear cress)	At5g42250, K5J14.5	Q9FH04
<i>Zea mays</i> (Maize)	FDH	P93629
<i>Drosophila melanogaster</i> (Fruit fly)	Fdh, gfd, ODH, CG6598	P46415
<i>Bacillus subtilis</i> (strain 168)	gbsB, BSU31050	P71017
<i>Caenorhabditis elegans</i>	H24K24.3	Q17335
<i>Oryza sativa</i> subsp. japonica (Rice)	Os02g0815500, LOC_Os02g57040, OsJ_008550, P0643F09.4	Q0DWH1
<i>Mycobacterium tuberculosis</i> (strain ATCC 25618 / H37Rv)	Rv1895	O07737
<i>Caenorhabditis elegans</i>	sodh-1, K12G11.3	Q17334
<i>Caenorhabditis elegans</i>	sodh-2, K12G11.4	O45687
<i>Pseudomonas</i> sp.	terPD	P33010
<i>Escherichia coli</i> (strain K12)	viaY, b3589, JW5648	P37686
<i>Moraxella</i> sp. (strain TAE123)		P81786
<i>Alligator mississippiensis</i> (American alligator)		P80222
<i>Catharanthus roseus</i> (Madagascar periwinkle) ( <i>Vinca rosea</i> )		P85440
<i>Gadus morhua</i> subsp. callarias (Baltic cod) ( <i>Gadus callarias</i> )		P26325
<i>Naja naja</i> (Indian cobra)		P80512
<i>Pisum sativum</i> (Garden pea)		P12886
<i>Pelophylax perezi</i> (Perez's frog) ( <i>Rana perezi</i> )		P22797
<i>Saara hardwickii</i> (Indian spiny-tailed lizard) ( <i>Uromastix hardwickii</i> )		P25405
<i>Saara hardwickii</i> (Indian spiny-tailed lizard) ( <i>Uromastix hardwickii</i> )		P25406

Organism	Gene Name	Accession No.
Equus caballus (Horse)		P00327
Equus caballus (Horse)		P00328
Geobacillus stearothermophilus (Bacillus stearothermophilus)		P42328
Gadus morhua (Atlantic cod)		P81600
Gadus morhua (Atlantic cod)		P81601
Myxine glutinosa (Atlantic hagfish)		P80360
Octopus vulgaris (Common octopus)		P81431
Pisum sativum (Garden pea)		P80572
Saara hardwickii (Indian spiny-tailed lizard) (Uromastyx hardwickii)		P80467
Scyliorhinus canicula (Small-spotted catshark) (Squalus canicula)		P86884
Sparus aurata (Gilthead sea bream)		P79896

[0091] In some embodiments, an  $\alpha$ -dioxygenase is used to catalyze the conversion of a fatty acid to a fatty aldehyde (Hamberg *et al.* 2005). Alpha-dioxygenases catalyze the conversion of a  $C_n$  fatty acid to a  $C_{n-1}$  aldehyde and may serve as an alternative to both ADH and AOX for fatty aldehyde production if a fatty acid is used as a biotransformation substrate. Due to the chain shortening of the dioxygenase reaction, this route requires a different synthesis pathway compared to the ADH and AOX routes. Biotransformations of *E. coli* cells expressing a rice  $\alpha$ -dioxygenase exhibited conversion of C10, C12, C14 and C16 fatty acids to the corresponding  $C_{n-1}$  aldehydes. With the addition of the detergent Triton X 100, 3.7 mM of pentadecanal (0.8 g/L) was obtained after 3 hours from hexadecanoic acid with 74% conversion (Kaehne *et al.* 2011). Exemplary  $\alpha$ -dioxygenases are shown in Table 5.

Table 5. Exemplary alpha-dioxygenases.

Entry	Organism	Gene names
Q9SGH6	Arabidopsis thaliana (Mouse-ear cress)	DOX1 DIOX1 PADOX-1 PIOX At3g01420 T13O15.6
Q9C9U3	Arabidopsis thaliana (Mouse-ear cress)	DOX2 DIOX2 At1g73680 F25P22.10
P14550	Homo sapiens (Human)	AKR1A1 ALDR1 ALR
Q69EZ9	Solanum lycopersicum (Tomato) (Lycopersicon esculentum)	LOC543896
Q5WM33	Solanum lycopersicum (Tomato) (Lycopersicon esculentum)	alpha-DOX2
Q69F00	Solanum lycopersicum (Tomato) (Lycopersicon esculentum)	
D7LAG3	Arabidopsis lyrata subsp. lyrata (Lyre-leaved rock-cress)	ALPHA-DOX1 ARALYDRAFT 317048

Entry	Organism	Gene names
D8LJL3	Ectocarpus siliculosus (Brown alga)	DOX Esi 0026 0091
E3U9P5	Nicotiana attenuata (Coyote tobacco)	adox2

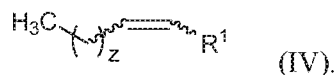
### Synthesis of Polyenes via Metathesis Reactions

[0092] In some embodiments, the metathesis reaction partner is a protected alcohol according to Formula IIa:



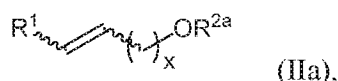
wherein R<sup>2a</sup> is an alcohol protecting group,

and the metathesis product is a compound according to Formula IV:



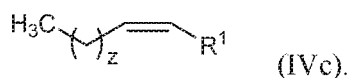
10 [0093] In some embodiments, R<sup>1</sup> is C<sub>2-18</sub> alkenyl. Such embodiments can provide polyene pheromones as described in more detail below.

[0094] In some embodiments, the metathesis reaction partner is a protected alcohol according to Formula IIa:

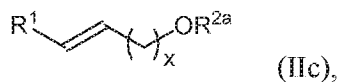


wherein R<sup>2a</sup> is an alcohol protecting group,

15 and the metathesis product is a compound according to Formula IVc:

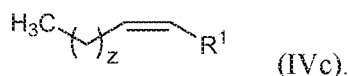


[0095] In some embodiments, the metathesis reaction partner is a protected alcohol according to Formula IIc:



20 wherein R<sup>2a</sup> is an alcohol protecting group,

and the metathesis product is a compound according to Formula IVc:

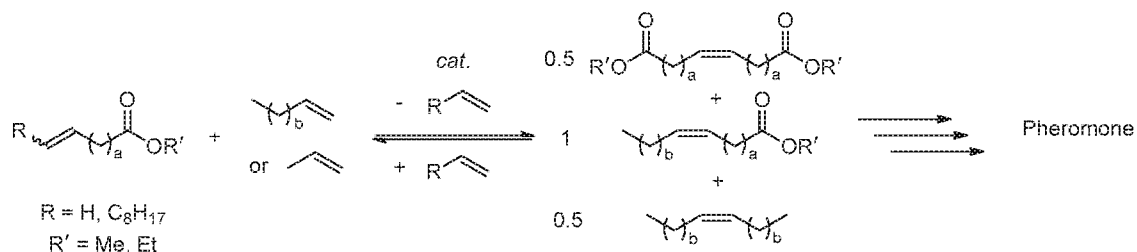


**Metathesis of Fatty Acid Esters**

[0096] Fatty acid alkyl esters (FAAE) can be reduced to either aldehydes or alcohols by the use of well-defined homogenous and heterogeneous methodologies. Therefore, in some cases it can be useful to produce fatty olefin derivatives via Z-selective cross-metathesis of a

5 FAAE with an olefin as shown in Scheme 4.

Scheme 4



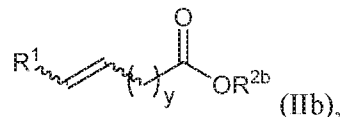
[0097] Products obtained from metathesis of protected fatty acid alkyl esters can be converted to a number of pheromones, as set forth in Table 6.

10 Table 6. Pheromones accessible from fatty acid alkyl ester metathesis products.

Olefin	Metathesis Reaction Partner	Metathesis Product	Exemplary Pheromone derived from Metathesis Product	Pheromone CAS #
propylene	oleate	(Z)-9-undecenoate	(Z)-9-undecenyl acetate	85576-13-2
1-butene	oleate	(Z)-9-dodecenoate	(Z)-9-dodecenal	56219-03-5
1-butene	oleate	(Z)-9-dodecenoate	(Z)-9-dodecenyl acetate	16974-11-1
1-pentene	oleate	(Z)-9-tridecenoate	(Z)-9-tridecenyl acetate	35835-78-0
1-hexene	oleate	(Z)-tetradec-9-enoate	(Z)-9-tetradecenal	53939-27-8
1-hexene	oleate	(Z)-tetradec-9-enoate	(Z)-9-tetradecenyl acetate	16725-53-4
1-hexene	oleate	(Z)-tetradec-9-enoate	(Z)-9-tetradecenyl formate	56776-10-4
1-hexene	oleate	(Z)-tetradec-9-enoate	(Z)-9-tetradecenyl nitrate	143816-21-1
1-heptene	oleate	(Z)-9-pentadecenoate	(Z)-9-pentadecenyl acetate	64437-41-8
1-octene	oleate	(Z)-9-hexadecenoate	(Z)-9-hexadecenal	56219-04-6
1-octene	oleate	(Z)-9-hexadecenoate	(Z)-9-hexadecenyl acetate	34010-20-3
propylene	9-decenoate	(Z)-9-undecenoate	(Z)-9-undecenyl acetate	85576-13-2
1-butene	9-decenoate	(Z)-9-dodecenoate	(Z)-9-dodecenal	56219-03-5
1-butene	9-decenoate	(Z)-9-dodecenoate	(Z)-9-dodecenyl acetate	16974-11-1
1-pentene	9-decenoate	(Z)-9-tridecenoate	(Z)-9-tridecenyl acetate	35835-78-0
1-hexene	9-decenoate	(Z)-tetradec-9-enoate	(Z)-9-tetradecenal	53939-27-8

Olefin	Metathesis Reaction Partner	Metathesis Product	Exemplary Pheromone derived from Metathesis Product	Pheromone CAS #
1-hexene	9-decenoate	(Z)-tetradec-9-enoate	(Z)-9-tetradecenyl acetate	16725-53-4
1-hexene	9-decenoate	(Z)-tetradec-9-enoate	(Z)-9-tetradecenyl formate	56776-10-4
1-hexene	9-decenoate	(Z)-tetradec-9-enoate	(Z)-9-tetradecenyl nitrate	143816-21-1
1-heptene	9-decenoate	(Z)-9-pentadecenoate	(Z)-9-pentadecenyl acetate	64437-41-8
1-octene	9-decenoate	(Z)-9-hexadecenoate	(Z)-9-hexadecenal	56219-04-6
1-octene	9-decenoate	(Z)-9-hexadecenoate	(Z)-9-hexadecenyl acetate	34010-20-3
propylene	10-undecenoate	(Z)-10-dodecenoate	(Z)-10-dodecenyl acetate	35148-20-0
1-butene	10-undecenoate	(Z)-10-tridecenoate	(Z)-10-tridecenyl acetate	64437-24-7
1-pentene	10-undecenoate	(Z)-10-tetradecenoate	(Z)-10-tetradecenyl acetate	35153-16-3
1-hexene	10-undecenoate	(Z)-10-pentadecenoate	(Z)-10-pentadecenal	60671-80-9
1-hexene	10-undecenoate	(Z)-10-pentadecenoate	(Z)-10-pentadecenyl acetate	64437-43-0
1-heptene	10-undecenoate	(Z)-10-hexadecenoate	(Z)-10-hexadecenyl acetate	56218-71-4

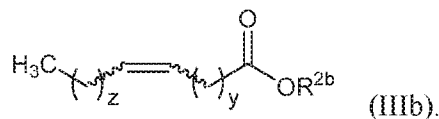
[0098] Accordingly, some embodiments of the invention provide methods wherein the metathesis reaction partner is an ester according to Formula IIb:



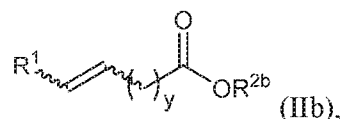
5 wherein  $\text{R}^{2b}$  is  $\text{C}_{1-8}$  alkyl and subscript  $y$  is an integer ranging from 0 to 17;

and

wherein the metathesis product is a compound according to Formula IIIb:



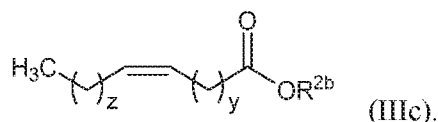
10 [0099] In some embodiments, the metathesis reaction partner is an ester according to Formula IIb:



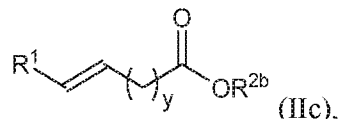
wherein  $\text{R}^{2b}$  is  $\text{C}_{1-8}$  alkyl and subscript  $y$  is an integer ranging from 0 to 17;

and

the metathesis product is a compound according to Formula IIIc:

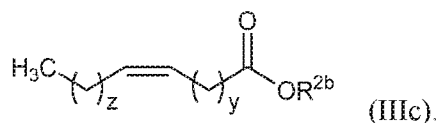


[0100] In some embodiments, the metathesis reaction partner is an ester according to Formula IIc:



5                    wherein R<sup>2b</sup> is C<sub>1-8</sub> alkyl and subscript y is an integer ranging from 0 to 17;  
and

the metathesis product is a compound according to Formula IIIc:



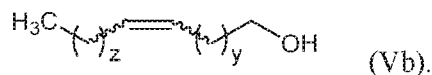
[0101] Metathesis products according to Formula IIIc can be prepared using a number of  
10 Z-selective catalysts as described below.

[0102] In some embodiments, the methods can be used to prepare products according to Formula IIIb or IIIc wherein y is 0 and z is 4; or y is 1 and z is 3; or y is 3 and z is 1; or y is 4 and z is 0; or y is 0 and z is 5; or y is 1 and z is 4; or y is 2 and z is 3; or y is 3 and z is 2; or y is 4 and z is 1; or y is 5 and z is 0; or y is 0 and z is 6; or y is 1 and z is 5; or y is 2 and z is 4;  
15 or y is 4 and z is 2; or y is 5 and z is 1; or y is 6 and z is 0; or y is 0 and z is 7; or y is 1 and z is 6; or y is 2 and z is 5; or y is 3 and z is 4; or y is 4 and z is 3; or y is 5 and z is 2; or y is 6 and z is 1; or y is 7 and z is 0; or y is 0 and z is 8; or y is 1 and z is 7; or y is 2 and z is 6; or y is 3 and z is 5; or y is 5 and z is 3; or y is 6 and z is 2; or y is 7 and z is 1; or y is 8 and z is 0; or y is 0 and z is 9; or y is 1 and z is 8; or y is 2 and z is 7; or y is 3 and z is 6; or y is 4 and z is 5; or y is 5 and z is 4; or y is 6 and z is 3; or y is 7 and z is 2; or y is 8 and z is 1; or y is 9 and z is 0; or y is 0 and z is 10; or y is 1 and z is 9; or y is 2 and z is 8; or y is 3 and z is 7; or y is 4 and z is 6; or y is 6 and z is 4; or y is 7 and z is 3; or y is 8 and z is 2; or y is 9 and z is 1; or y is 10 and z is 0; or y is 0 and z is 11; or y is 1 and z is 10; or y is 2 and z is 9; or y is 3 and z is 8; or y is 4 and z is 7; or y is 5 and z is 6; or y is 6 and z is 5; or y is 7 and z is 4; or y is 8 and z is 3; or y is 9 and z is 2; or y is 10 and z is 1; or y is 11 and z is 0; or y is 0 and z is 12; or y is 1 and z is 11; or y is 2 and z is 10; or y is 3 and z is 9; or y is 4 and z is 8; or y is 5 and z is 7; or y is 7 and z is 5; or y is 8 and z is 4; or y is 9 and z is 3; or y is 10 and z is 2; or

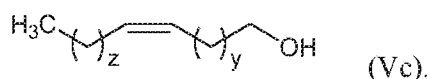
y is 11 and z is 1; or y is 12 and z is 0; or y is 0 and z is 13; or y is 1 and z is 12; or y is 2 and z is 11; or y is 3 and z is 10; or y is 4 and z is 9; or y is 5 and z is 8; or y is 6 and z is 7; or y is 7 and z is 6; or y is 8 and z is 5; or y is 9 and z is 4; or y is 10 and z is 3; or y is 11 and z is 2; or y is 12 and z is 1; or y is 13 and z is 0; or y is 0 and z is 14; or y is 1 and z is 13; or y is 2 and z is 12; or y is 3 and z is 11; or y is 4 and z is 10; or y is 5 and z is 9; or y is 6 and z is 8; or y is 7 and z is 7; or y is 8 and z is 6; or y is 9 and z is 5; or y is 10 and z is 4; or y is 11 and z is 3; or y is 12 and z is 2; or y is 13 and z is 1; or y is 14 and z is 0; or y is 0 and z is 15; or y is 1 and z is 14; or y is 2 and z is 13; or y is 3 and z is 12; or y is 4 and z is 11; or y is 5 and z is 10; or y is 6 and z is 9; or y is 7 and z is 8; or y is 8 and z is 7; or y is 9 and z is 6; or y is 10 and z is 5; or y is 11 and z is 4; or y is 12 and z is 3; or y is 13 and z is 2; or y is 14 and z is 1; or y is 15 and z is 0; or y is 0 and z is 16; or y is 1 and z is 15; or y is 2 and z is 14; or y is 3 and z is 13; or y is 4 and z is 12; or y is 5 and z is 11; or y is 6 and z is 10; or y is 7 and z is 9; or y is 8 and z is 8; or y is 9 and z is 7; or y is 10 and z is 6; or y is 11 and z is 5; or y is 12 and z is 4; or y is 13 and z is 3; or y is 14 and z is 2; or y is 15 and z is 1; or y is 16 and z is 0; or y is 1 and z is 16; or y is 2 and z is 15; or y is 3 and z is 14; or y is 4 and z is 13; or y is 5 and z is 12; or y is 6 and z is 11; or y is 7 and z is 10; or y is 8 and z is 9; or y is 9 and z is 8; or y is 10 and z is 7; or y is 11 and z is 6; or y is 12 and z is 5; or y is 13 and z is 4; or y is 14 and z is 3; or y is 15 and z is 2; or y is 16 and z is 1; or y is 17 and z is 0; or y is 0 and z is 17; or y is 1 and z is 17; or y is 2 and z is 16; or y is 3 and z is 15; or y is 4 and z is 14; or y is 5 and z is 13; or y is 6 and z is 12; or y is 7 and z is 11; or y is 8 and z is 10; or y is 9 and z is 9; or y is 10 and z is 8; or y is 11 and z is 7; or y is 12 and z is 6; or y is 13 and z is 5; or y is 14 and z is 4; or y is 15 and z is 3; or y is 16 and z is 2; or y is 17 and z is 1. In some embodiments, both y and z are 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, or 17.

### Conversion of Fatty Acid Ester Metathesis Products to Fatty Olefin Derivatives

[0103] In some embodiments, converting the metathesis product to the fatty olefin derivative includes reducing the metathesis product of Formula IIIb to form an alkenol according to Formula Vb:



[0104] In some embodiments, converting the metathesis product to the fatty olefin derivative includes reducing the metathesis product of Formula IIIc to form an alkenol according to Formula Vc:



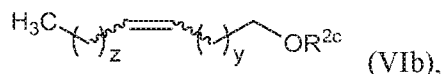
[0105] Any suitable conditions for converting the product of Formula IIIb to the alkenol of Formula Vb can be used in conjunction with the method of the invention. Homogenous or heterogenous conditions can be used. Examples of homogenous conditions include, but are not limited to: hydrogenolysis using ligated precious metal catalysts (Tan, *et al. Org. Lett.* 2015, 17 (3), 454; Spasyuk, D. *et al. J. Am. Chem. Soc.* 2015, 137, 3743; WO 2014/139030), metal hydride-catalyzed reduction using silane reagents (Mimoun, H. *J. Org. Chem.* 1999, 64, 2582.; U.S. Pat. No. 6,533,960); and reduction using aluminum reagents such as lithium aluminum hydride, sodium bis(2-methoxyethoxy)aluminumhydride (also known by the tradename RED-AL), or diisobutyl aluminum hydride (CN 103319704; Chandrasekhar, *et al. Tetrahedron Lett.* 1998, 39, 909). Unsaturated fatty alcohols can also be prepared via hydrogenolysis with heterogeneous catalysts, such as ZnO or CuO/ZnO supported on chromite, alumina, or other material. Typically, 1-2 molar equivalents of the reducing agent with respect to the fatty acid ester metathesis product will be used. In some embodiments, around 1.0, 1.1, 1.2, 1.3, 1.4, or 1.5 molar equivalents of the reducing agent with respect to the fatty acid ester is used to form the corresponding alkenol.

[0106] Any suitable solvent can be used for reducing the fatty acid ester metathesis product. Suitable solvents include, but are not limited to, toluene, methylene chloride, ethyl acetate, acetonitrile, tetrahydrofuran, benzene, chloroform, diethyl ether, dimethyl formamide, dimethyl sulfoxide, petroleum ether, and mixtures thereof. The reduction reaction is typically conducted at temperatures ranging from around -78°C to about 25°C for a period of time sufficient to form the alkenol. The reaction can be conducted for a period of time ranging from a few minutes to several hours or longer, depending on the particular fatty acid ester and reducing agent used in the reaction. For example, the reduction of a methyl (Z)-tetradec-9-enoate with an aluminum reagent (*e.g.*, sodium bis(2-methoxyethoxy)-aluminumhydride) can be conducted for 1-2 hours at a temperature ranging from around 0°C to around 20°C.

[0107] In some embodiments, the alkenol is the fatty olefin derivative. In some embodiments, the alkenol is a pheromone.

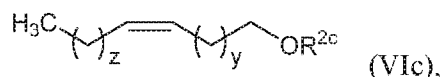


[0108] In some embodiments, converting the metathesis product to the fatty olefin derivative further includes acylating the alkenol of Formula Vb, thereby forming a fatty olefin derivative according to Formula VIb:



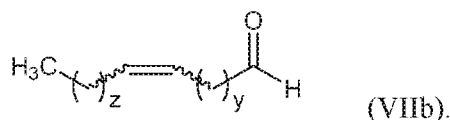
5 wherein  $\text{R}^{2c}$  is  $\text{C}_{1-6}$  acyl. The acylation step can be conducted as described above.

[0109] In some embodiments, converting the metathesis product to the fatty olefin derivative further includes acylating the alkenol of Formula Vc, thereby forming a fatty olefin derivative according to Formula VIc:

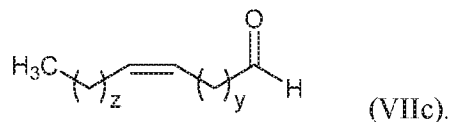


10 wherein  $\text{R}^{2c}$  is  $\text{C}_{1-6}$  acyl. The acylation step can be conducted as described above.

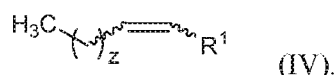
[0110] In some embodiments, converting the metathesis product to the fatty olefin derivative further includes oxidizing the alkenol of Formula Vb, thereby forming a fatty olefin derivative according to Formula VIIb:



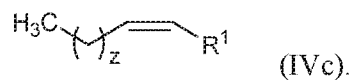
15 [0111] In some embodiments, converting the metathesis product to the fatty olefin derivative further includes oxidizing the alkenol of Formula Vc, thereby forming a fatty olefin derivative according to Formula VIIc:



20 [0112] In some embodiments, the metathesis reaction partner is an ester according to Formula IIb or Formula IIc as described above, and the metathesis product is a compound according to Formula IV:



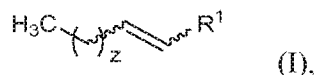
25 [0113] In some embodiments, the metathesis reaction partner is an ester according to Formula IIb or Formula IIc as described above, and the metathesis product is a compound according to Formula IVc:



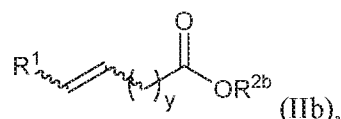
[0114] In some embodiments,  $\text{R}^1$  in Formula IV or Formula IVc is  $\text{C}_{2-18}$  alkenyl.

[0115] In another embodiment, the invention provides a method for synthesizing a fatty olefin derivative, the method comprising:

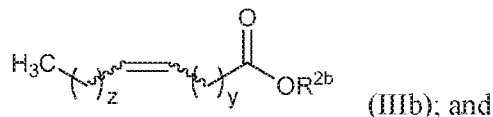
- 5 a) contacting an olefin according to Formula I



with a metathesis reaction partner according to Formula IIb



10 in the presence of a metathesis catalyst under conditions sufficient to form a metathesis product according to Formula IIIb:



b) converting the metathesis product to the fatty olefin derivative;

wherein:

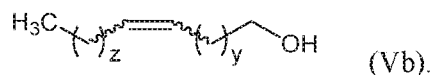
15 each  $\text{R}^1$  is independently selected from the group consisting of H,  $\text{C}_{1-18}$  alkyl, and  $\text{C}_{2-18}$  alkenyl;

$\text{R}^{2b}$  is  $\text{C}_{1-8}$  alkyl;

subscript y is an integer ranging from 0 to 17; and

subscript z is an integer ranging from 0 to 17.

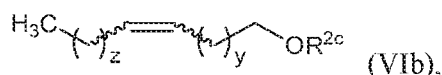
20 [0116] In some embodiments where the metathesis reaction partner according to Formula IIb is employed, converting the metathesis product to the fatty olefin derivative comprises reducing the metathesis product to form an alkenol according to Formula Vb:



[0117] In some embodiments where the metathesis reaction partner according to Formula IIb is employed, the alkenol is the fatty olefin derivative.

25 [0118] In some embodiments where the metathesis reaction partner according to Formula IIb is employed, converting the metathesis product to the fatty olefin derivative further

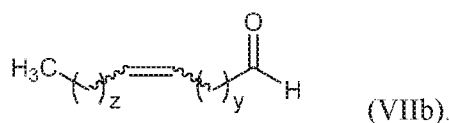
comprises acylating the alkenol, thereby forming a fatty olefin derivative according to Formula VIb:



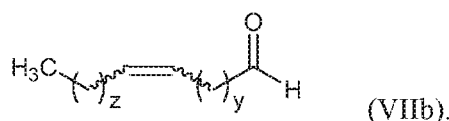
wherein  $\text{R}^{2c}$  is  $\text{C}_{1-6}$  acyl.

5 [0119] In some embodiments where the metathesis reaction partner according to Formula IIb is employed,  $\text{R}^1$  is H,  $\text{R}^{2b}$  is methyl, subscript  $y$  is 7, and subscript  $z$  is 3. In some such embodiments,  $\text{R}^1$  is H,  $\text{R}^{2b}$  is methyl, subscript  $y$  is 7, subscript  $z$  is 3, and  $\text{R}^{2c}$  is acetyl.

[0120] In some embodiments where the metathesis reaction partner according to Formula IIb is employed, converting the metathesis product to the fatty olefin derivative further  
10 comprises oxidizing the alkenol, thereby forming a fatty olefin derivative according to Formula VIIb:

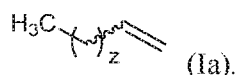


[0121] In some embodiments where the metathesis reaction partner according to Formula IIb is employed, converting the metathesis product to the fatty olefin derivative further  
15 comprises reducing the metathesis product, thereby forming a fatty olefin derivative according to Formula VIIIb:



[0122] In some embodiments,  $\text{R}^1$  is H,  $\text{R}^{2b}$  is methyl, subscript  $y$  is 7, and subscript  $z$  is 3 in the fatty olefin derivative according to Formula VIIIb.

20 [0123] In some embodiments where the metathesis reaction partner according to Formula IIb is employed, the olefin has a structure according to Formula Ia:



[0124] In some embodiments, subscript  $z$  is 3 in the olefin according to Formula Ia.

[0125] In some embodiments where the metathesis reaction partner according to Formula IIb is employed, the metathesis product comprises a Z olefin. In some embodiments, at least  
25 about 90% of the olefin is a Z olefin. In some embodiments, the metathesis catalyst is a Z-

selective molybdenum catalyst or a Z-selective tungsten catalyst as described below. In some embodiments, the metathesis catalyst has a structure according to Formula 2 as described below. In some embodiments, the metathesis catalyst has a structure according to Formula 2a as described below.

5 [0126] In another embodiment, the invention provides a method for synthesizing a fatty olefin derivative as described above wherein the olefin according to Formula I is a linear C<sub>3</sub>-C<sub>12</sub> alpha olefin, the metathesis reaction partner according to Formula IIb is a Δ<sup>9</sup>-unsaturated fatty acid alkyl ester, the metathesis catalyst is a Z-selective metathesis catalyst, and the metathesis product according to Formula IIIb is a C<sub>11</sub>-C<sub>20</sub> (Z)-9-unsaturated fatty acid  
10 alkyl ester. In some such embodiments, converting the metathesis product to the fatty olefin derivative comprises contacting the C<sub>11</sub>-C<sub>20</sub> (Z)-9-unsaturated fatty acid alkyl ester with a reducing agent under conditions sufficient to form a C<sub>11</sub>-C<sub>20</sub> (Z)-9-fatty alcohol. In some such embodiments, the reducing agent is sodium bis(2-methoxyethoxy)aluminum hydride.

[0127] In some embodiments, converting the metathesis product to the fatty olefin  
15 derivative further comprises contacting the C<sub>11</sub>-C<sub>20</sub> (Z)-9-fatty alcohol with an acylating agent in the presence of a base under conditions sufficient to form an acetate ester of the C<sub>11</sub>-C<sub>20</sub> (Z)-9-fatty alcohol. In some such embodiments, the acylating agent is acetic anhydride.

[0128] In some embodiments, converting the metathesis product to the fatty olefin  
20 derivative further comprises oxidizing the C<sub>11</sub>-C<sub>20</sub> (Z)-9-fatty alcohol to form a C<sub>11</sub>-C<sub>20</sub> (Z)-9-alkenal.

[0129] In some embodiments, converting the metathesis product to the fatty olefin  
derivative comprises contacting the C<sub>11</sub>-C<sub>20</sub> (Z)-9-fatty acid alkyl ester with a reducing agent  
under conditions sufficient to form a C<sub>11</sub>-C<sub>20</sub> (Z)-9-alkenal. In some such embodiments, the  
25 reducing agent is amine-modified sodium bis(2-methoxyethoxy)aluminumhydride. The amine-modified sodium bis(2-methoxyethoxy)aluminumhydride can be generated *in situ* via reaction of the sodium bis(2-methoxyethoxy)aluminumhydride with either a primary amine or secondary amine (as described, for example, by Shin, *et al. Bull. Korean Chem. Soc.* 2014, 35, 2169, which is incorporated herein by reference). In some such embodiments, the  
30 metathesis catalyst has a structure according to Formula 2a as described below.

[0130] In another embodiment, the invention provides a method for synthesizing a fatty olefin derivative as described above wherein: the fatty acid derivative is (Z)-tetradec-9-en-1-

yl acetate; the olefin according to Formula I is hex-1-ene, the metathesis reaction partner according to Formula IIb is a  $\Delta^9$ -unsaturated fatty acid alkyl ester, the metathesis catalyst is a Z-selective metathesis catalyst, and the metathesis product according to Formula IIIb is an alkyl ester of (Z)-9-tetradec-9-enoate; and wherein converting the metathesis product to the fatty olefin derivative comprises: contacting the alkyl ester of (Z)-9-tetradec-9-enoate with a  
5 reducing agent under conditions sufficient to form (Z)-tetradec-9-en-1-ol, and acylating the (Z)-tetradec-9-en-1-ol to form the (Z)-tetradec-9-en-1-yl acetate.

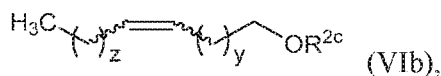
[0131] In some such embodiments, the metathesis reaction partner according to Formula IIb is methyl 9-decenoate and the metathesis product is methyl (Z)-tetradec-9-enoate. In some  
10 such embodiments, the reducing agent is sodium bis(2-methoxyethoxy)aluminumhydride. In some such embodiments, acylating the (Z)-tetradec-9-en-1-ol comprises contacting the (Z)-tetradec-9-en-1-ol with an acylating agent in the presence of a base under conditions sufficient to form (Z)-tetradec-9-en-1-yl acetate. In some such embodiments, the acylating agent is acetic anhydride. In some such embodiments, the metathesis catalyst has a structure  
15 according to Formula 2a as described below.

[0132] In another embodiment, the invention provides a method for synthesizing a fatty olefin derivative as described above, wherein the fatty acid derivative is (Z)-tetradec-9-enal, the olefin according to Formula I is hex-1-ene, the metathesis reaction partner according to Formula IIb is a  $\Delta^9$ -unsaturated fatty acid alkyl ester, the metathesis catalyst is a Z-selective  
20 metathesis catalyst, and the metathesis product according to Formula IIIb is an alkyl ester of (Z)-9-tetradec-9-enoate; and wherein converting the metathesis product to the fatty olefin derivative comprises contacting the alkyl ester of (Z)-9-tetradec-9-enoate with a reducing agent under conditions sufficient to form the (Z)-tetradec-9-enal. In some such embodiments, the reducing agent is amine-modified sodium bis(2-methoxyethoxy) aluminumhydride. The  
25 amine-modified sodium bis(2-methoxyethoxy) aluminumhydride can be generated as described above. In some such embodiments, the  $\Delta^9$ -unsaturated fatty acid alkyl ester according to Formula IIg is methyl 9-decenoate and the metathesis product is methyl (Z)-tetradec-9-enoate. In some such embodiments, the metathesis catalyst has a structure according to Formula 2a as described below.

[0133] In another embodiment, the invention provides a method for synthesizing a fatty olefin derivative as described above wherein the fatty acid derivative is (Z)-tetradec-9-enal, the olefin according to Formula I is hex-1-ene, the metathesis reaction partner according to

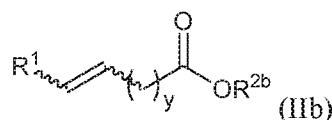
Formula IIb is a  $\Delta^9$ -unsaturated fatty acid alkyl ester, the metathesis catalyst is a Z-selective metathesis catalyst, and the metathesis product according to Formula IIb is an alkyl ester of (Z)-tetradec-9-enoate; and wherein converting the metathesis product to the fatty olefin derivative comprises contacting the alkyl ester of (Z)-tetradec-9-enoate with a reducing agent under conditions sufficient to form (Z)-tetradec-9-en-1-ol, and oxidizing the (Z)-tetradec-9-en-1-ol to form the (Z)-tetradec-9-enal. In some such embodiments, the reducing agent is sodium bis(2-methoxyethoxy)aluminumhydride. In some such embodiments, the  $\Delta^9$ -unsaturated fatty acid alkyl ester according to Formula IIg is methyl 9-decenoate and the metathesis product is methyl (Z)-tetradec-9-enoate. In some such embodiments, the metathesis catalyst has a structure according to Formula 2a as described below.

[0134] In another embodiment, the invention provides a method for synthesizing a fatty olefin derivative according to Formula VIb:

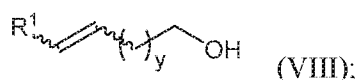


the method comprising:

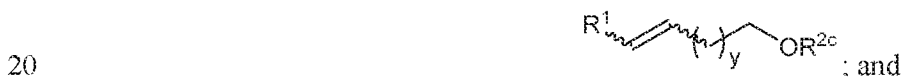
15 i) reducing an alkyl ester according to Formula IIb



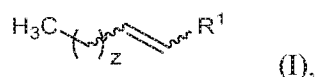
to form an alkenol according to Formula VIII



ii) acylating the alkenol to form an acylated alkenol according to Formula IX



20 iii) contacting the acylated alkenol with an olefin according to Formula I



in the presence of a metathesis catalyst under conditions sufficient to form the fatty olefin derivative; wherein:

25  $\text{R}^1$  is selected from the group consisting of H,  $\text{C}_{1-18}$  alkyl, and  $\text{C}_{2-18}$  alkenyl;

$\text{R}^{2b}$  is  $\text{C}_{1-8}$  alkyl,

$\text{R}^{2c}$  is  $\text{C}_{1-6}$  acyl,

subscript y is an integer ranging from 0 to 17;

subscript  $z$  is an integer ranging from 0 to 17; and

the metathesis catalyst is a tungsten catalyst or a molybdenum catalyst.

[0135] In some embodiments,  $R^1$  is H,  $R^{2b}$  is methyl,  $R^{2c}$  is acetyl, subscript  $y$  is 7, and subscript  $z$  is 3 in the method for synthesizing a fatty olefin derivative according to Formula 5  
5 VIb. In some embodiments, the metathesis product comprises an *E* olefin. In some embodiments, the metathesis product comprises a *Z*-olefin. In some embodiments, the metathesis catalyst is a *Z*-selective molybdenum catalyst or a *Z*-selective tungsten catalyst. In some embodiments, the metathesis catalyst has a structure according to Formula 2 as described below. In some embodiments, the metathesis catalyst has a structure according to  
10 Formula 2a as described below.

#### Metathesis catalysts

[0136] The catalysts employed in the present invention generally employ metals which can mediate a particular desired chemical reaction. In general, any transition metal (*e.g.*, having  $d$  electrons) can be used to form the catalyst, *e.g.*, a metal selected from one of Groups 3-12 of  
15 the periodic table or from the lanthanide series. In some embodiments, the metal is selected from Groups 3-8, or, in some cases, from Groups 4-7. In some embodiments, the metal is selected from Group 6. The term “Group 6” refers to the transition metal group comprising chromium, molybdenum, and tungsten. Additionally, the present invention may also include the formation of heterogeneous catalysts containing forms of these elements (*e.g.*, by  
20 immobilizing a metal complex on an insoluble substrate, for example, silica).

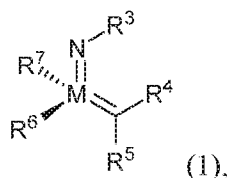
[0137] The methods of the invention can be assessed in terms of the selectivity of the metathesis reaction—that is, the extent to which the reaction produces a particular olefin isomer, whether a *Z* olefin (*i.e.*, a *cis* olefin) or an *E* olefin (*i.e.*, a *trans* olefin).

[0138] In general, *Z*-selective catalysts provide metathesis products wherein greater than  
25 15% (w/w) of the olefin is a *Z* olefin. For example, the metathesis product can contain the *Z* olefin in an amount ranging from about 20% to about 100%. The metathesis product can contain the *Z* olefin in an amount ranging from about 25% to about 95%, or from about 30% to about 90%, or from about 35% to about 85%, or from about 40% to about 80%, or from about 45% to about 75%, or from about 50% to about 70%, or from about 55% to about 65%.  
30 The metathesis product can contain the *Z* olefin in an amount ranging from about 15% to about 20%, or from about 20% to about 25%, or from about 25% to about 30%, or from about 30% to about 35%, or from about 35% to about 40%, or from about 40% to about 45%,

or from about 45% to about 50%, or from about 50% to about 60%, or from about 60% to about 65%, or from about 65% to about 70%, or from about 70% to about 75%, or from about 75% to about 80%, or from about 80% to about 85%, or from about 85% to about 90%, or from about 90% to about 95%, or from about 95% to about 99%. The metathesis product  
 5 can contain the *Z* olefin in an amount of about 55%, 60%, 65%, 70%, 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% (w/w).

[0139] In general, *E*-selective catalysts provide metathesis products at least about 85% (w/w) of the olefin is an *E* olefin. For example, the metathesis product can contain the *E* olefin in an amount ranging from about 86% to about 100%. The metathesis product can  
 10 contain the *E* olefin in an amount ranging from about 86% to about 99%, or from about 88% to about 98%, or from about 90% to about 96%, or from about 92% to about 94%. The metathesis product can contain the *E* olefin in an amount ranging from about 86% to about 89%, or from about 89% to about 92%, or from about 92% to about 95%, or from about 95% to about 98%. The metathesis product can contain the *E* olefin in an amount of about 86%,  
 15 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% (w/w).

[0140] In some embodiments, the metathesis catalyst has a structure according to Formula 1:



wherein:

20 M is Mo or W;

$R^3$  is selected from optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aliphatic, and optionally substituted heteroaliphatic;

each of  $R^4$  and  $R^5$  is independently selected from hydrogen, optionally substituted aliphatic, optionally substituted heteroaliphatic, optionally substituted aryl, and  
 25 optionally substituted heteroaryl;

$R^6$  is selected from -O-alkyl, -O-heteroalkyl, -O-aryl, -O-heteroaryl, -N( $R^n$ )-alkyl, -N( $R^n$ )-heteroalkyl, -N( $R^n$ )-aryl, and -N( $R^n$ )-heteroaryl,

wherein each  $R^n$  is independently selected from hydrogen, an amino protecting group, and optionally substituted alkyl,

30 and wherein  $R^6$  is optionally substituted; and



$R^7$  is selected from aryl, heteroaryl, alkyl, heteroalkyl, cycloalkyl, heterocycloalkyl, -O-alkyl, -O-heteroalkyl, -O-aryl, and -O-heteroaryl, each of which is optionally substituted, or

$R^7$  is halogen.

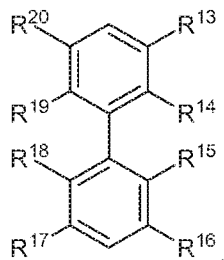
5 [0141] In some embodiments, the metathesis catalyst has a structure according to Formula 1 and the metathesis product comprises a Z olefin.

[0142] In some embodiments,  $R^6$  is an optionally substituted asymmetric -O-aryl group and  $R^7$  is an optionally substituted heteroaryl group.

10 [0143] In some cases, the metal complex includes one or more oxygen-containing ligands lacking a plane of symmetry or nitrogen-containing ligands lacking a plane of symmetry (*i.e.*, asymmetric ligands). In some embodiments, such ligands can coordinate the metal atom via an oxygen atom (*e.g.*, via a hydroxyl group), or other atom of the ligand. The oxygen-containing ligand can coordinate the metal atom via one site of the ligand, *i.e.*, the ligand may be a monodentate ligand.

15 [0144] In some embodiments, a ligand can comprise two sites capable of binding the metal center, wherein a first site is bonded to a protecting group, or other group, that may reduce the ability of the first site to coordinate the metal, and the second site coordinates the metal center. For example, the ligand can be a [1,1'-binaphthalene]-2,2'-diol (BINOL) derivative having two hydroxyl groups, wherein one hydroxyl group is bonded to a protecting group  
20 (*e.g.*, a silyl protecting group) and another hydroxyl group coordinates the metal center.

[0145] In some embodiments, an asymmetric oxygen-containing ligand is of the following structure:



wherein:

25  $R^{13}$  is an optionally substituted group selected from aryl, heteroaryl, alkyl, or heteroalkyl;

$R^{14}$  is hydrogen, -OH, halogen, -OPG, or an optionally substituted group selected from aliphatic, heteroaliphatic, aryl, aryloxy, heteroaryl, heteroaryloxy, acyl, and acyloxy;

5 or, together  $R^{13}$  and  $R^{14}$  are joined to form an optionally substituted partially unsaturated or aryl ring;

$R^{15}$  is -OH, -OPG, or an optionally substituted amino group;

$R^{16}$  is hydrogen, halogen, an optionally substituted group selected from aliphatic, heteroaliphatic, aryl, heteroaryl, or acyl;

10 each of  $R^{17}$ ,  $R^{18}$ ,  $R^{19}$ , and  $R^{20}$  is independently aryl, heteroaryl, aliphatic, heteroaliphatic, or acyl, optionally substituted;

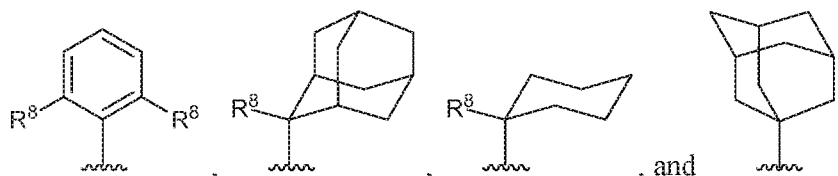
or, together  $R^{17}$  and  $R^{18}$  are joined to form an optionally substituted partially unsaturated or aryl ring;

or, together  $R^{19}$  and  $R^{20}$  are joined to form an optionally substituted partially unsaturated or aryl ring; and

15 each PG is independently a hydroxyl protecting group.

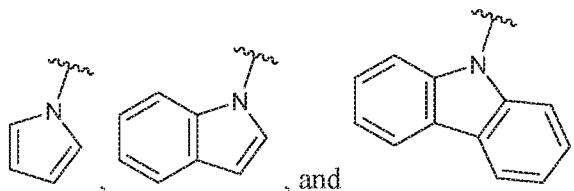
[0146] In some embodiments,  $R^3$  is an optionally substituted group selected from aryl and aliphatic.

[0147] In some embodiments,  $R^3$  is selected from

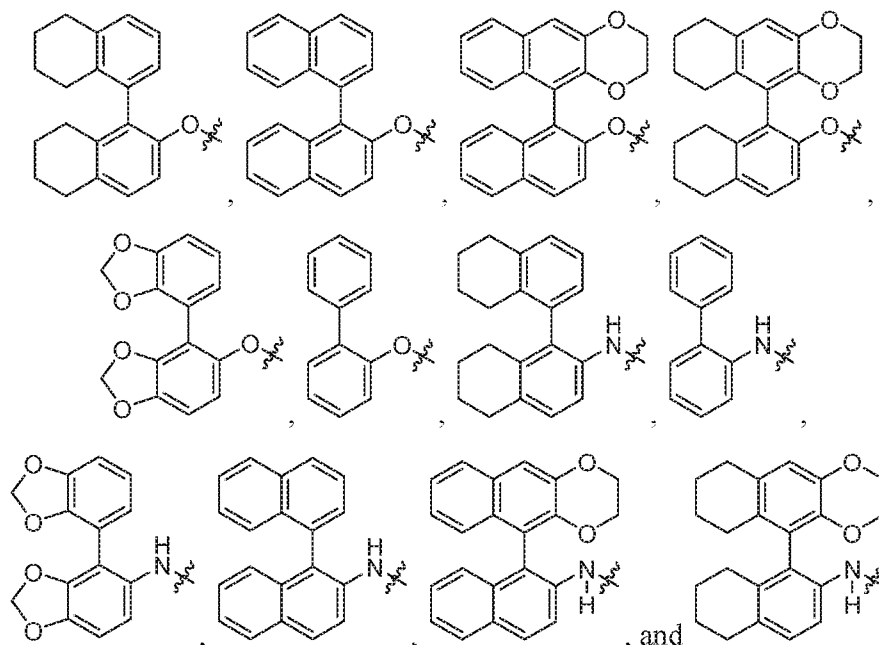


20 wherein each  $R^8$  is independently hydrogen or a monovalent substituent.

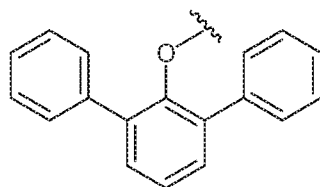
[0148] In some embodiments,  $R^7$  is an optionally substituted group selected from



[0149] In some embodiments,  $R^6$  is an optionally substituted group selected from



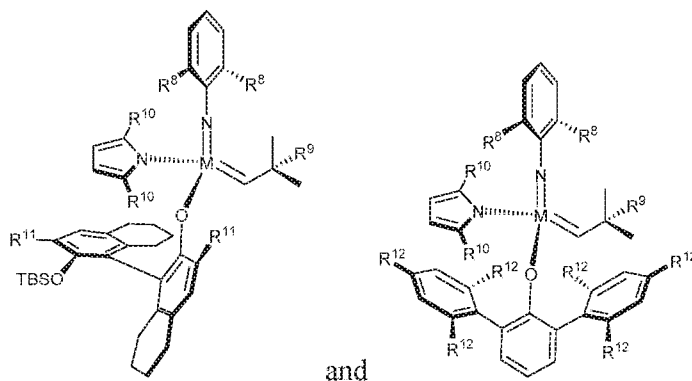
[0150] In some embodiments, R<sup>6</sup> is



5

which is optionally substituted.

[0151] In some embodiments, the metathesis catalyst is selected from



and

wherein M is Mo or W;

10

each R<sup>8</sup> is independently selected from halo and alkyl;

R<sup>9</sup> is selected from the group of consisting of alkyl, aryl, alkenyl, and heteroaryl;

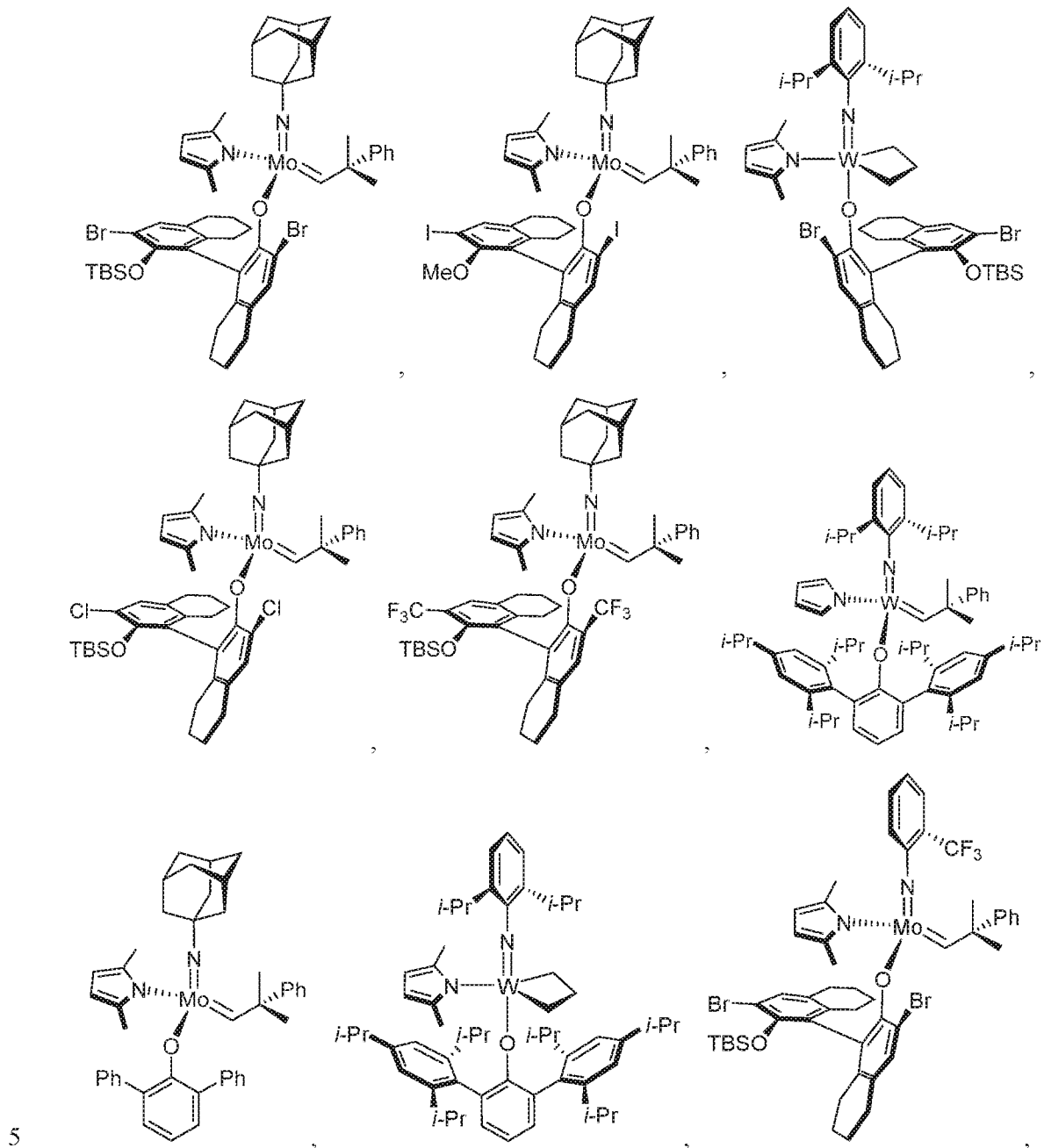
each R<sup>10</sup> is independently selected from hydrogen, halo, alkyl, aryl, and

heteroaryl;

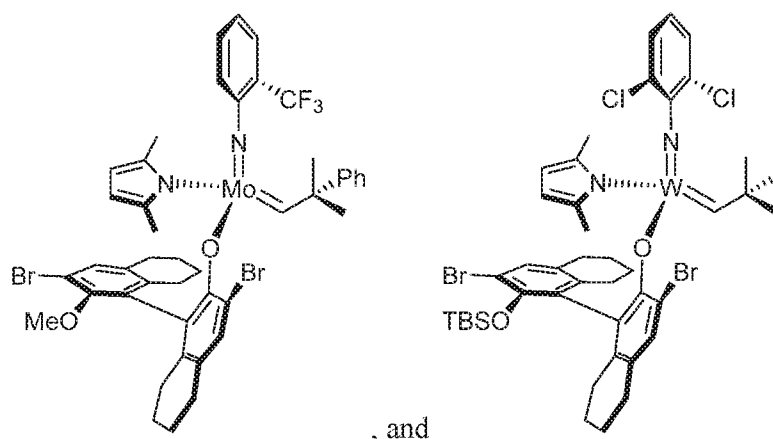
each R<sup>11</sup> is independently selected from halo, alkyl, aryl, and heteroaryl; and

each R<sup>12</sup> is independently an optionally substituted alkyl.

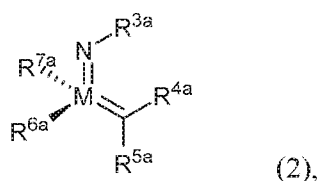
[0152] In some embodiments, the metathesis catalyst is selected from:



5



[0153] In some embodiments, the metathesis catalyst has a structure according to Formula 2:



5           wherein:

M is Mo or W;

R<sup>3a</sup> is selected from optionally substituted aryl, optionally substituted heteroaryl, optionally substituted alkyl, optionally substituted heteroalkyl, optionally substituted cycloalkyl, and optionally substituted heterocycloalkyl, and

10           R<sup>4a</sup> and R<sup>5a</sup> are independently selected from hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted aryl, and optionally substituted heteroaryl;

15           R<sup>7a</sup> is selected from optionally substituted alkyl, optionally substituted alkoxy, optionally substituted heteroalkyl, optionally substituted aryl, optionally substituted aryloxy, optionally substituted heteroaryl, optionally substituted silylalkyl, and optionally substituted silyloxy; and

R<sup>6a</sup> is R<sup>8a</sup>-X-, wherein

X is O or S and R<sup>8a</sup> is optionally substituted aryl; or

20           X is O and R<sup>8a</sup> is SiR<sup>9a</sup>R<sup>10a</sup>R<sup>11a</sup> or CR<sup>12a</sup>R<sup>13a</sup>R<sup>14a</sup>, wherein R<sup>9a</sup>, R<sup>10a</sup>, R<sup>11a</sup>, R<sup>12a</sup>, R<sup>13a</sup>, and R<sup>14a</sup> are independently selected from optionally substituted alkyl and optionally substituted phenyl; or

R<sup>6a</sup> and R<sup>7a</sup> are linked together and are bonded to M via oxygen.

[0154] In some embodiments, the metathesis catalyst has a structure according to Formula 2 and the metathesis product comprises a Z olefin.

[0155] In some embodiments, the catalyst is a compound of Formula 2 wherein:

$R^{7a}$  is selected from the group consisting of alkyl, alkoxy, heteroalkyl, aryl, aryloxy, and heteroaryl, each of which is optionally substituted; and

X is O or S and  $R^{8a}$  is optionally substituted aryl; or  
X is O and  $R^{8a}$  is  $CR^{12a}R^{13a}R^{14a}$ .

[0156] In some embodiments, the catalyst is a compound of Formula 2 wherein:

$R^{3a}$  is selected from the group consisting of 2,6-dimethylphenyl; 2,6-diisopropylphenyl; 2,6-dichlorophenyl; and adamant-1-yl;

$R^{4a}$  is selected from the group consisting of  $-C(CH_3)_2C_6H_5$  and  $-C(CH_3)_3$ ;

$R^{5a}$  is H;

$R^{7a}$  is selected from the group consisting of pyrrol-1-yl; 2,5-dimethyl-pyrrol-1-yl; triphenylsilyloxy; triisopropylsilyloxy; 2-phenyl-1,1,1,3,3,3-hexafluoro-prop-2-yloxy; 2-methyl-1,1,1,3,3,3-hexafluoro-prop-2-yloxy; 9-phenyl-fluorene-9-yloxy; 2,6-diphenylphenoxy; and *t*-butyloxy; and

$R^{6a}$  is  $R^{8a}-X-$ , wherein

X = O and

$R^{8a}$  is phenyl which bears two substituents in the ortho positions with respect to O, or which bears at least three substituents, from which two substituents are in the ortho positions with respect to O and one substituent is in the para position with respect to O; or

$R^{8a}$  is selected from the group consisting of optionally substituted 8-(naphthalene-1-yl)-naphthalene-1-yl; optionally substituted 8-phenylnaphthalene-1-yl; optionally substituted quinoline-8-yl; triphenylsilyl; triisopropylsilyl; triphenylmethyl; tri(4-methylphenyl)methyl; 9-phenyl-fluorene-9-yl; 2-phenyl-1,1,1,3,3,3-hexafluoro-prop-2-yl; 2-methyl-1,1,1,3,3,3-hexafluoro-prop-2-yl; and *t*-butyl.

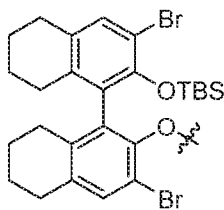
[0157] In some embodiments, the catalyst is a compound of Formula 2 wherein:

$R^{7a}$  is selected from the group consisting of pyrrol-1-yl; 2,5-dimethyl-pyrrol-1-yl; and

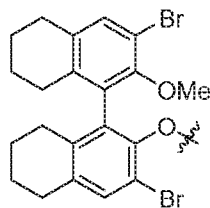
$R^{8a}$  is phenyl which bears two substituents in the ortho positions with respect to O, or which bears at least three substituents, from which two substituents are in the ortho positions with respect to O and one substituent is in the para position with respect to O; or

$R^{8a}$  is selected from the group consisting of optionally substituted 8-(naphthalene-1-yl)-naphthalene-1-yl and optionally substituted 8-phenylnaphthalene-1-yl.

[0158] In some embodiments, the catalyst is a compound of Formula 2 wherein  $R^4$  is selected from 4-bromo-2,6-diphenylphenoxy; 4-fluoro-2,6-diphenylphenoxy; 4-methyl-2,6-diphenylphenoxy; 4-methoxy-2,6-diphenylphenoxy; 4-dimethylamino-2,6-diphenylphenoxy; 2,4,6-triphenylphenoxy; 4-fluoro-2,6-dimesitylphenoxy; 4-bromo-2,6-di-*tert*-butylphenoxy; 4-methoxy-2,6-di-*tert*-butylphenoxy; 4-methyl-2,6-di-*tert*-butylphenoxy; 2,4,6-tri-*tert*-butylphenoxy; 4-bromo-2,3,5,6-tetraphenylphenoxy; 4-bromo-2,6-di(4-bromophenyl)-3,5-diphenylphenoxy; 2,6-diphenylphenoxy; 2,3,5,6-tetraphenylphenoxy; 2,6-di(*tert*-butyl)phenoxy; 2,6-di(2,4,6-triisopropylphenyl)phenoxy; triphenylsilyloxy; triisopropylsilyloxy; triphenylmethyloxy; tri(4-methylphenyl)methyloxy; 2-phenyl-1,1,1,3,3,3-hexafluoro-prop-2-yloxy; 2-methyl-1,1,1,3,3,3-hexafluoro-prop-2-yloxy; 9-phenyl-fluorene-9-yloxy; *t*-butyloxy;

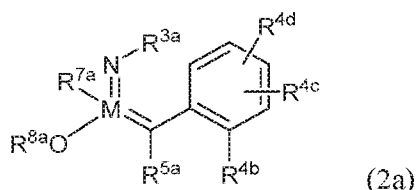


15 wherein TBS is *t*-butyldimethylsilyl; or



wherein Me = methyl.

[0159] In some embodiments, the metathesis catalyst has a structure according to Formula 2a:



20

wherein:

$R^{3a}$  is aryl, heteroaryl, alkyl, or cycloalkyl, each of which is optionally substituted;

$R^{7a}$  is pyrrolyl, imidazolyl, indolyl, pyrazolyl, azaindolyl, or indazolyl, each of which is optionally substituted;

$R^{8a}$  is optionally substituted aryl;

$R^{5a}$  is a hydrogen atom, alkyl, or alkoxy;

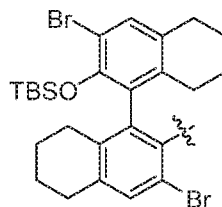
5  $R^{4b}$  is a hydrogen atom,  $-O-(C_{1-6} \text{ alkyl})$ ,  $-CH_2-O-(C_{1-6} \text{ alkyl})$ , heteroalkoxy, or  $-N(C_{1-6} \text{ alkyl})_2$ ; and

$R^{4c}$  and  $R^{4d}$  are independently a hydrogen atom,  $C_{1-6}$  alkyl,  $C_{1-6}$  alkoxy, a halogen atom,  $-NO_2$ , an amide, or a sulfonamide.

10 [0160] In some embodiments, the metathesis catalyst has a structure according to Formula 2a and the metathesis product comprises a Z olefin.

[0161] In some embodiments,  $R^{3a}$  in the metathesis catalyst according to Formula 2a is phenyl, 2,6-dichlorophenyl, 2,6-dimethylphenyl, 2,6-diisopropylphenyl, 2-trifluoromethylphenyl, pentafluorophenyl, tert-butyl, or 1-adamantyl.

[0162] In some embodiments,  $R^{8a}$  is

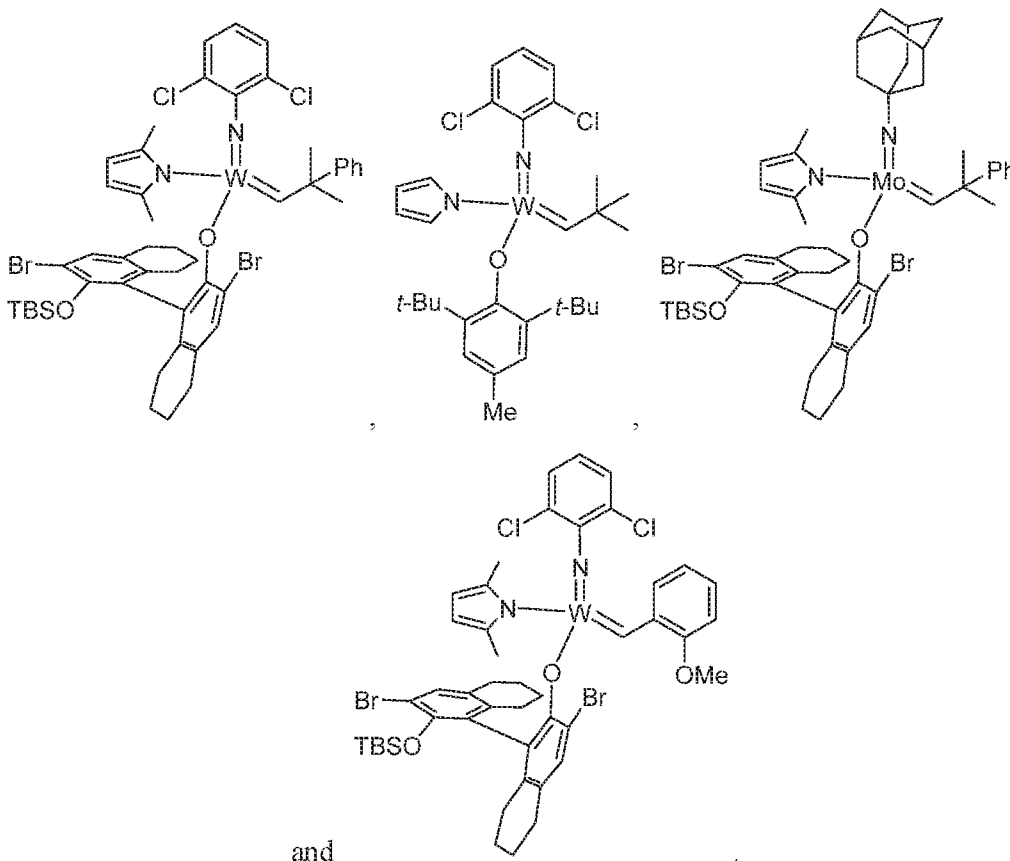


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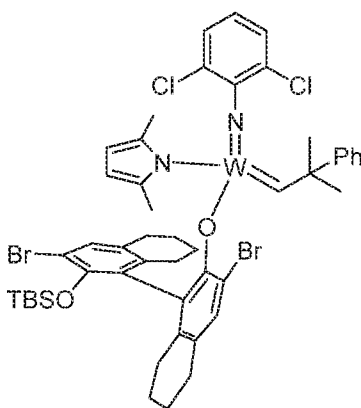
[0163] In some embodiments,  $R^{4b}$  is methoxy,  $R^{4c}$  is hydrogen, and  $R^{4d}$  is hydrogen.



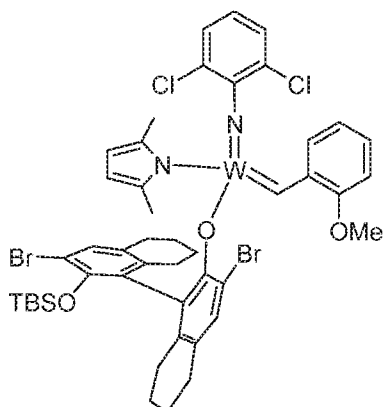
[0164] In some embodiments, the metathesis catalyst is selected from the group consisting of:



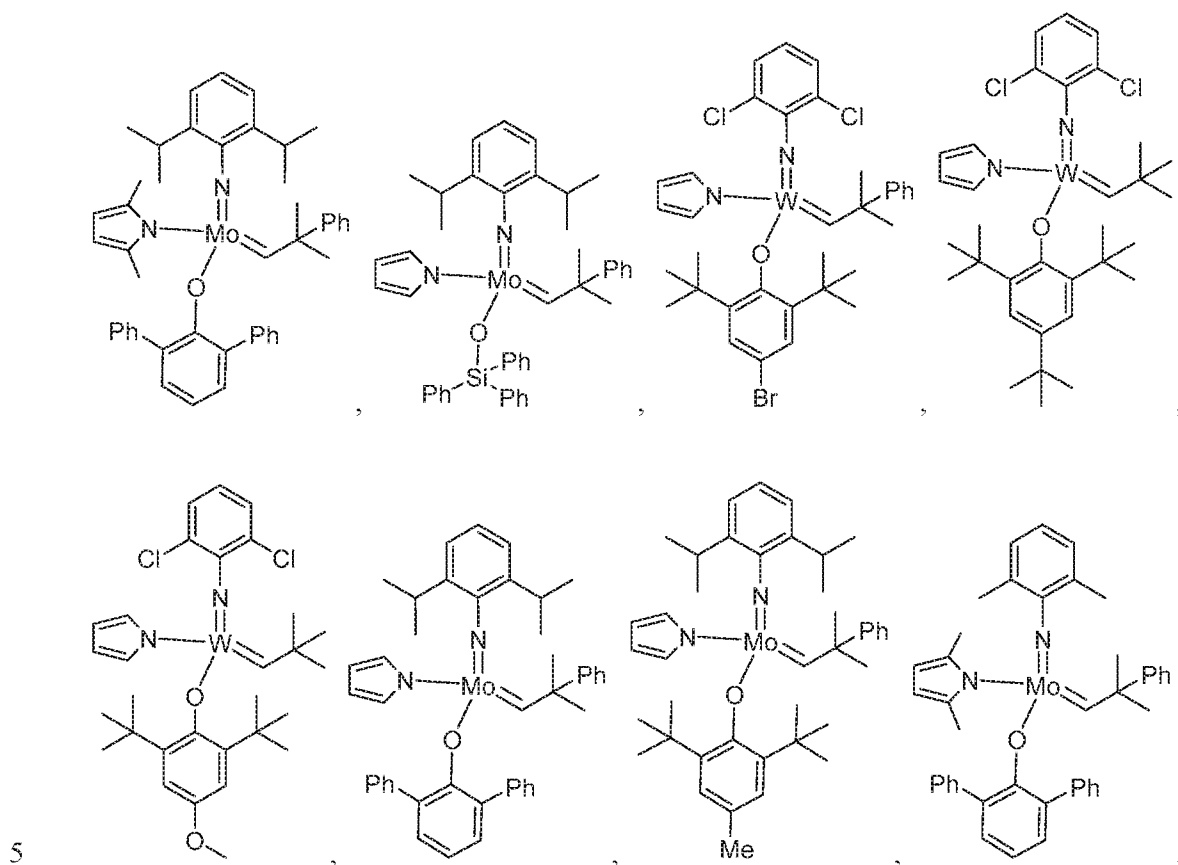
5 [0165] In some embodiments, the metathesis catalyst is

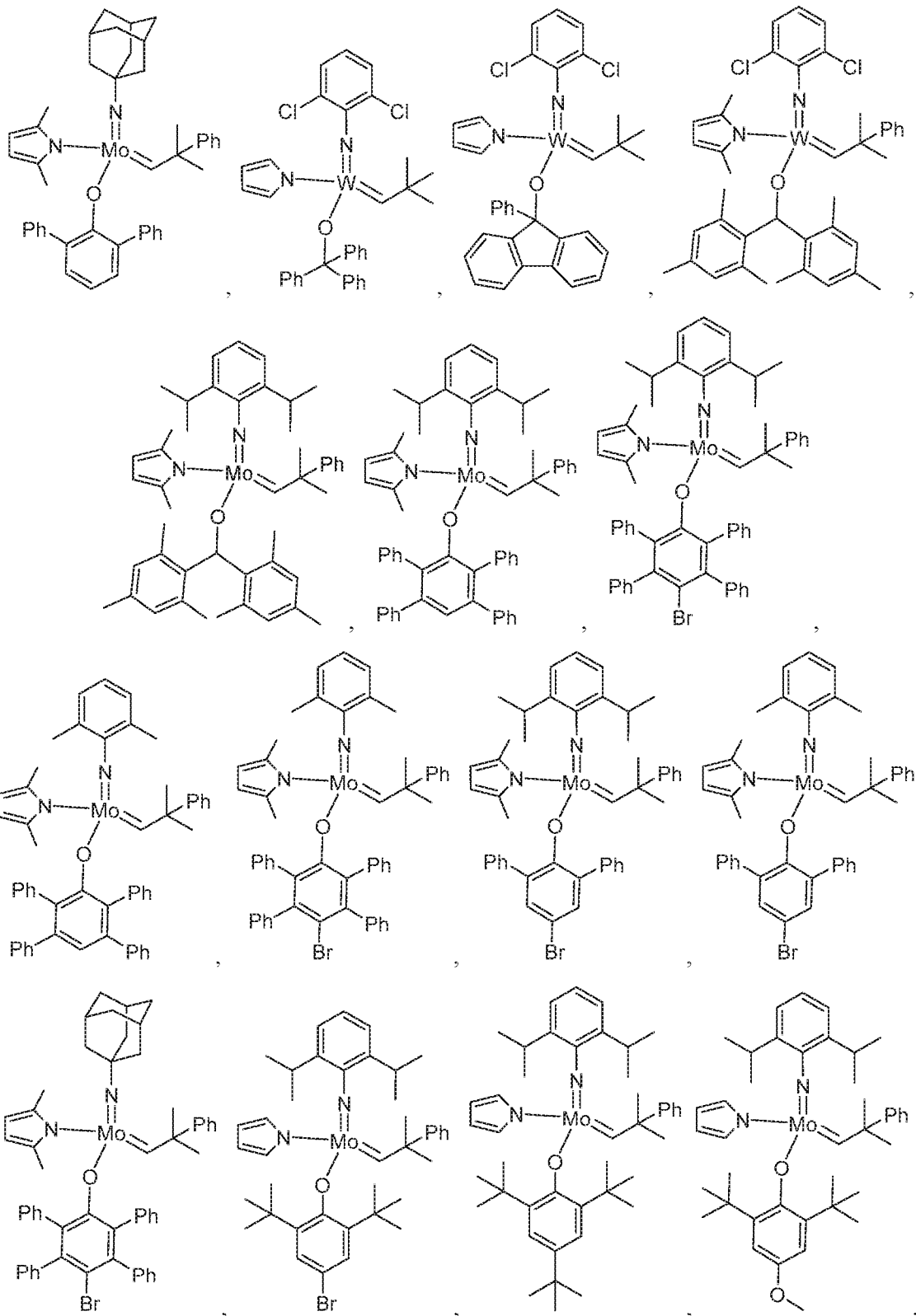


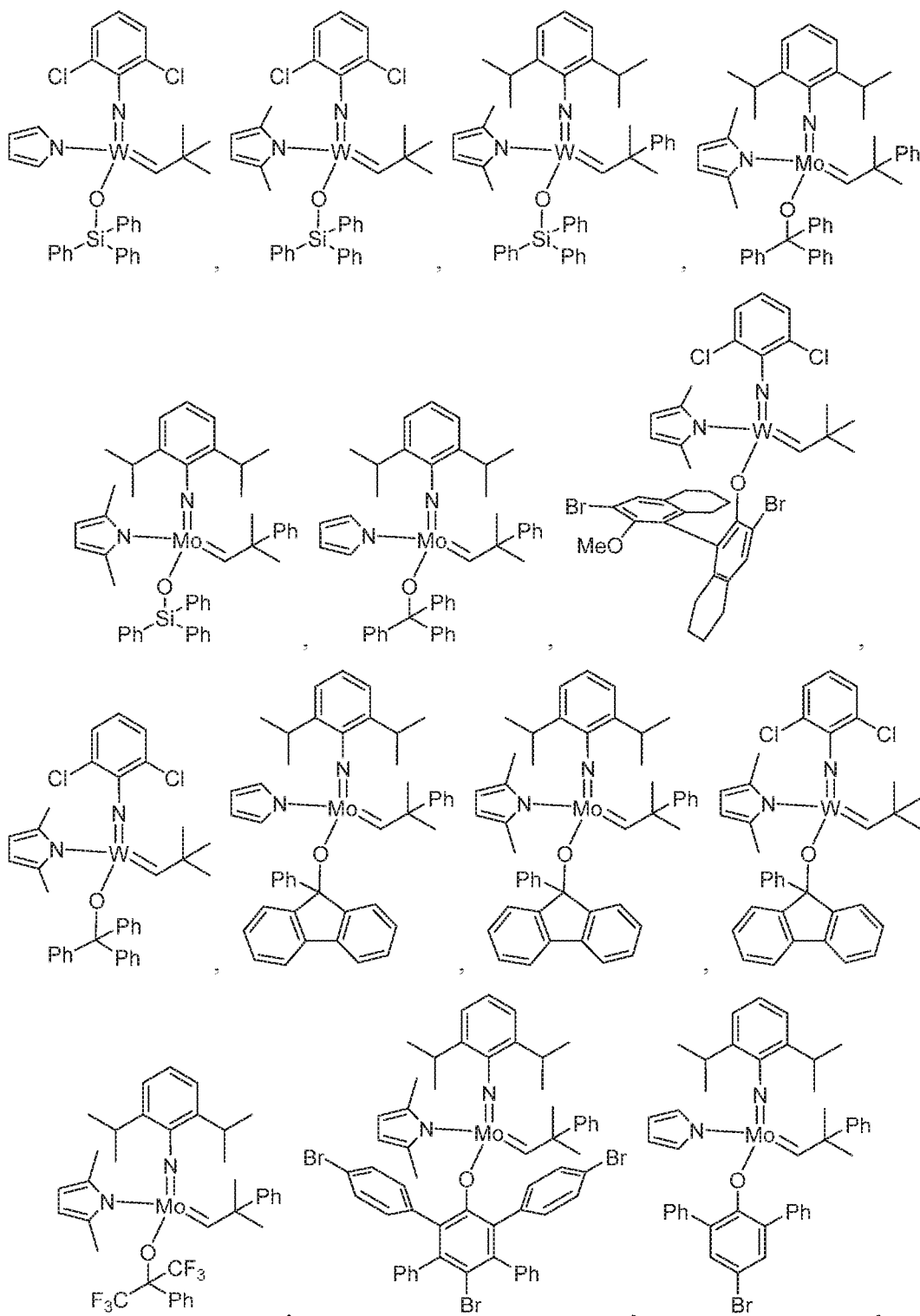
[0166] In some embodiments, the metathesis catalyst is

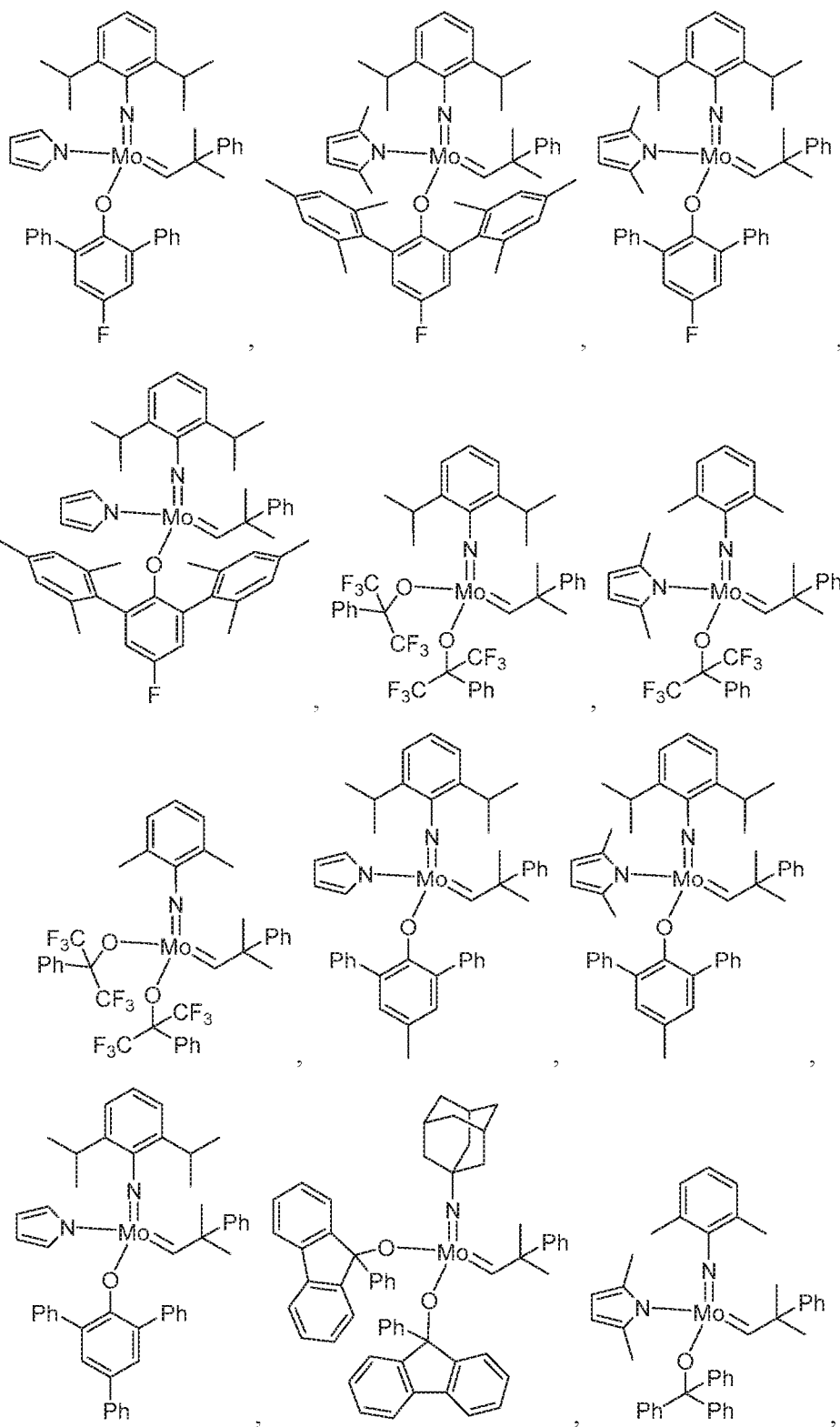


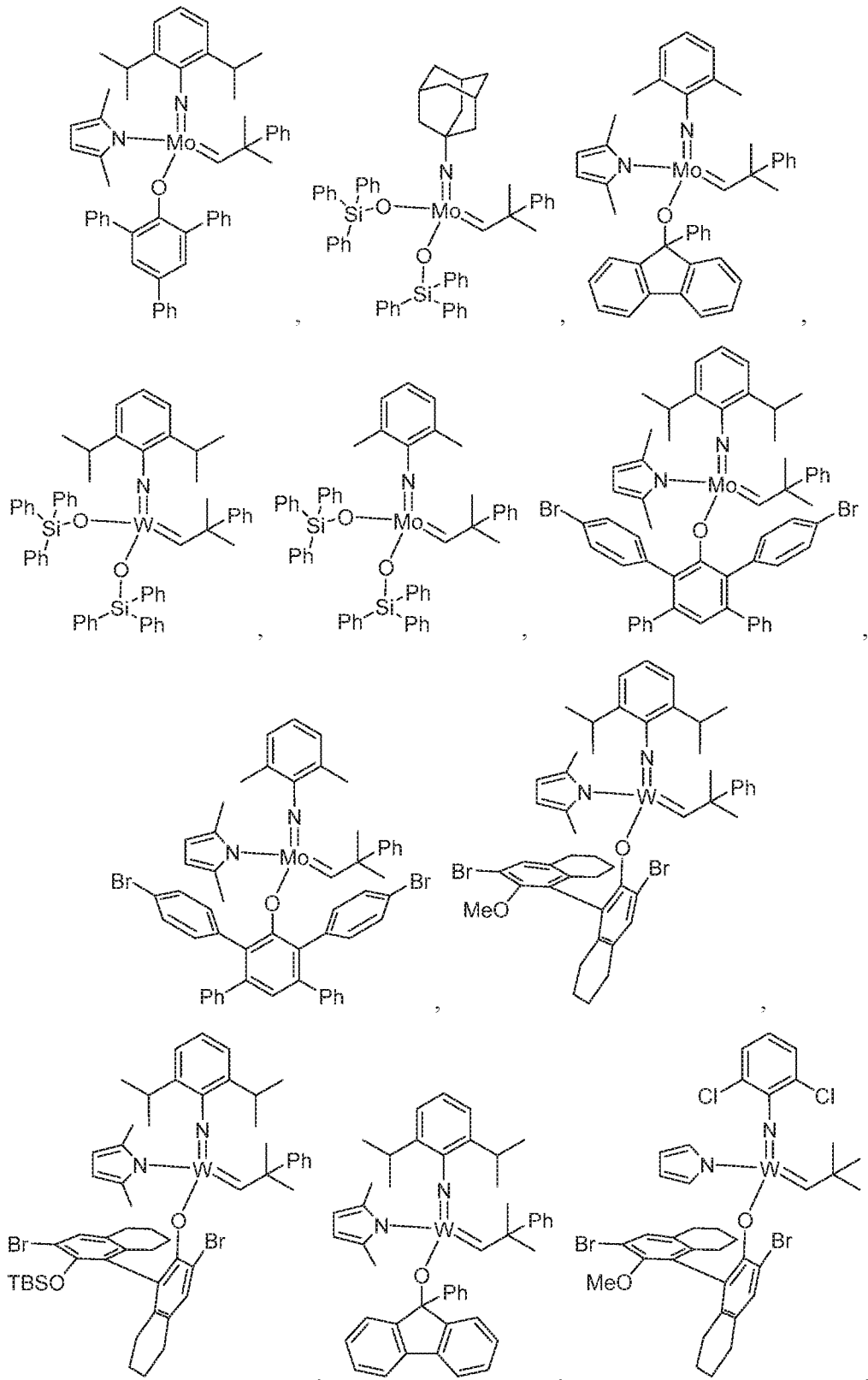
[0167] In some embodiments, the metathesis catalyst is selected from:

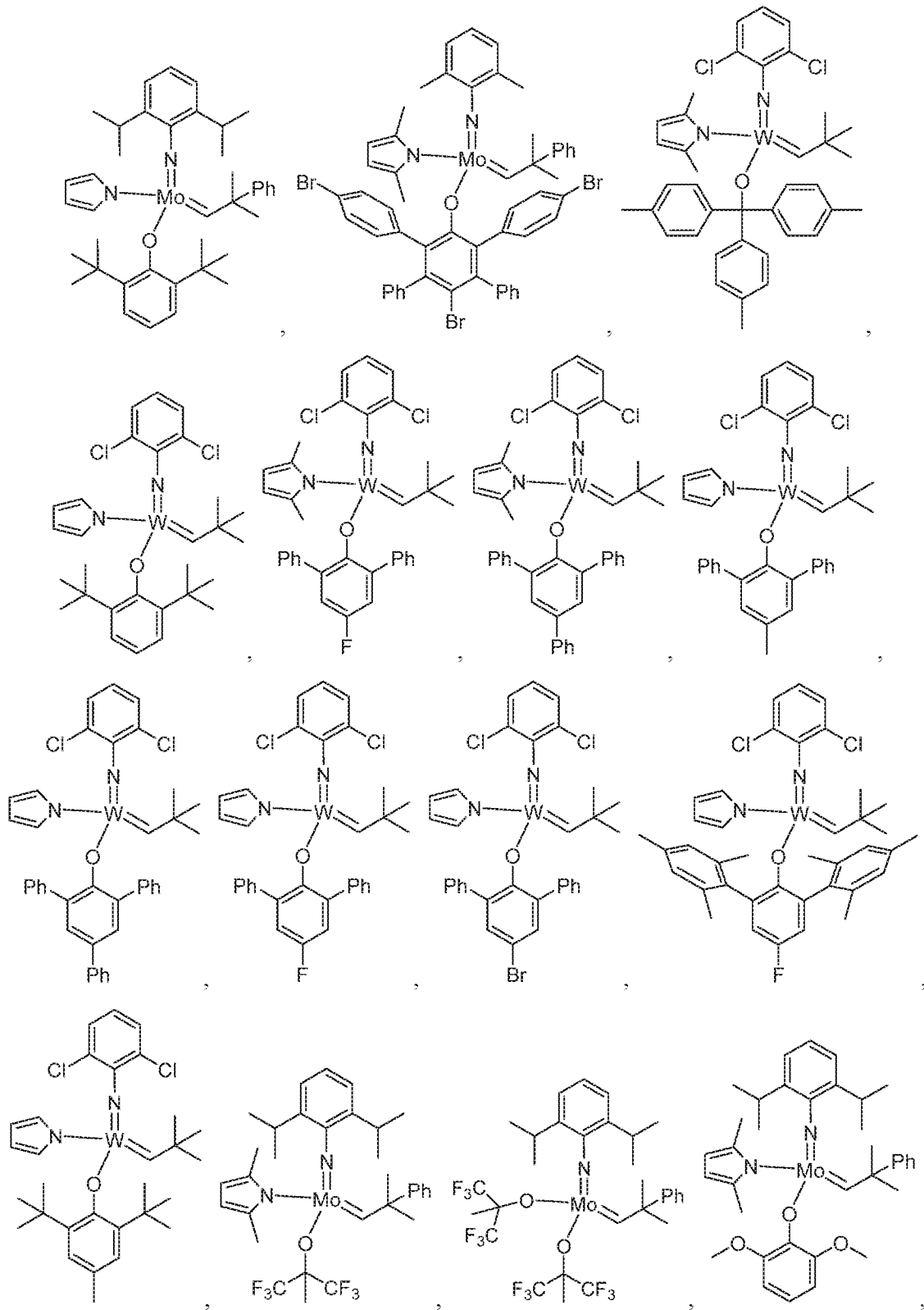


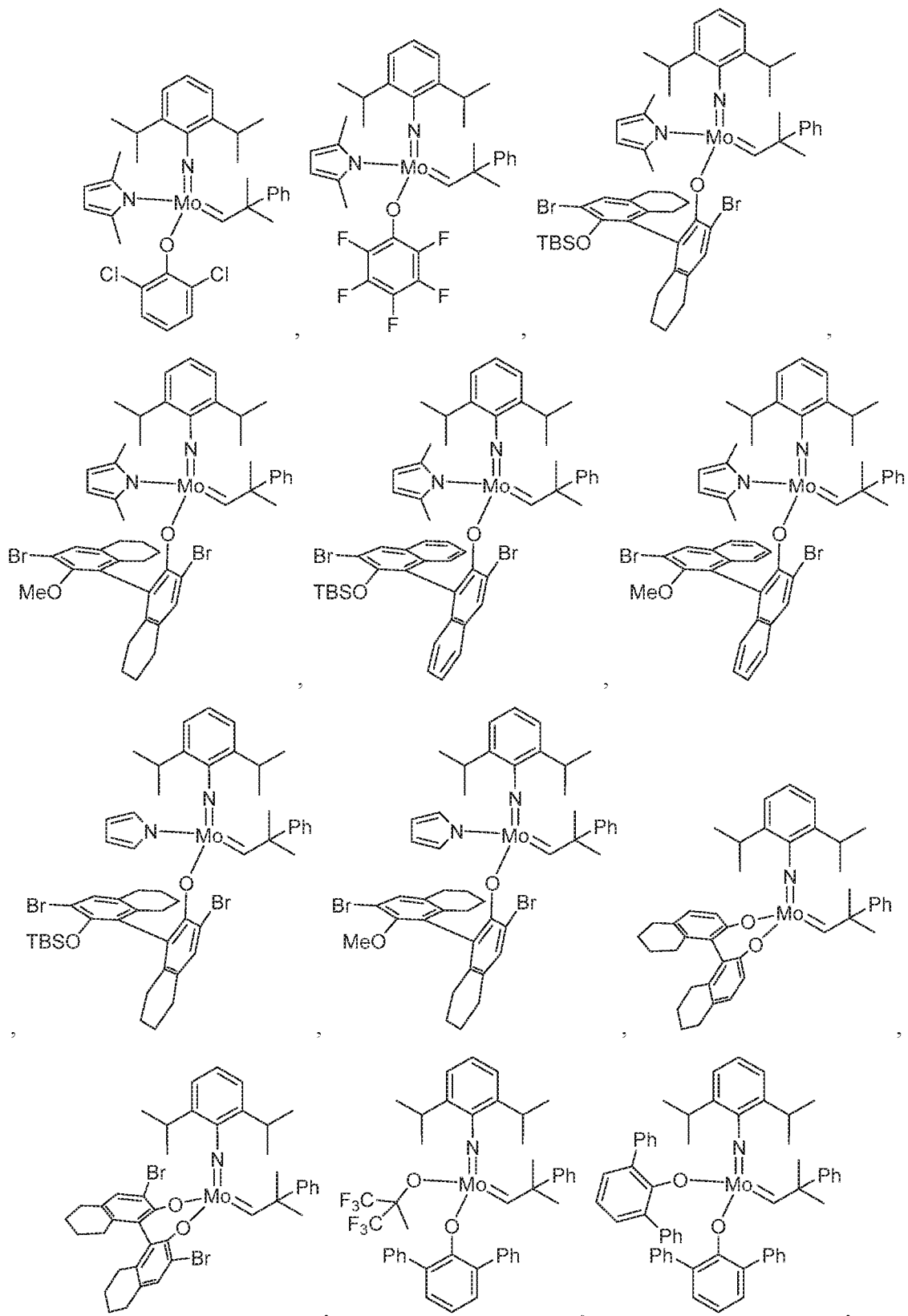




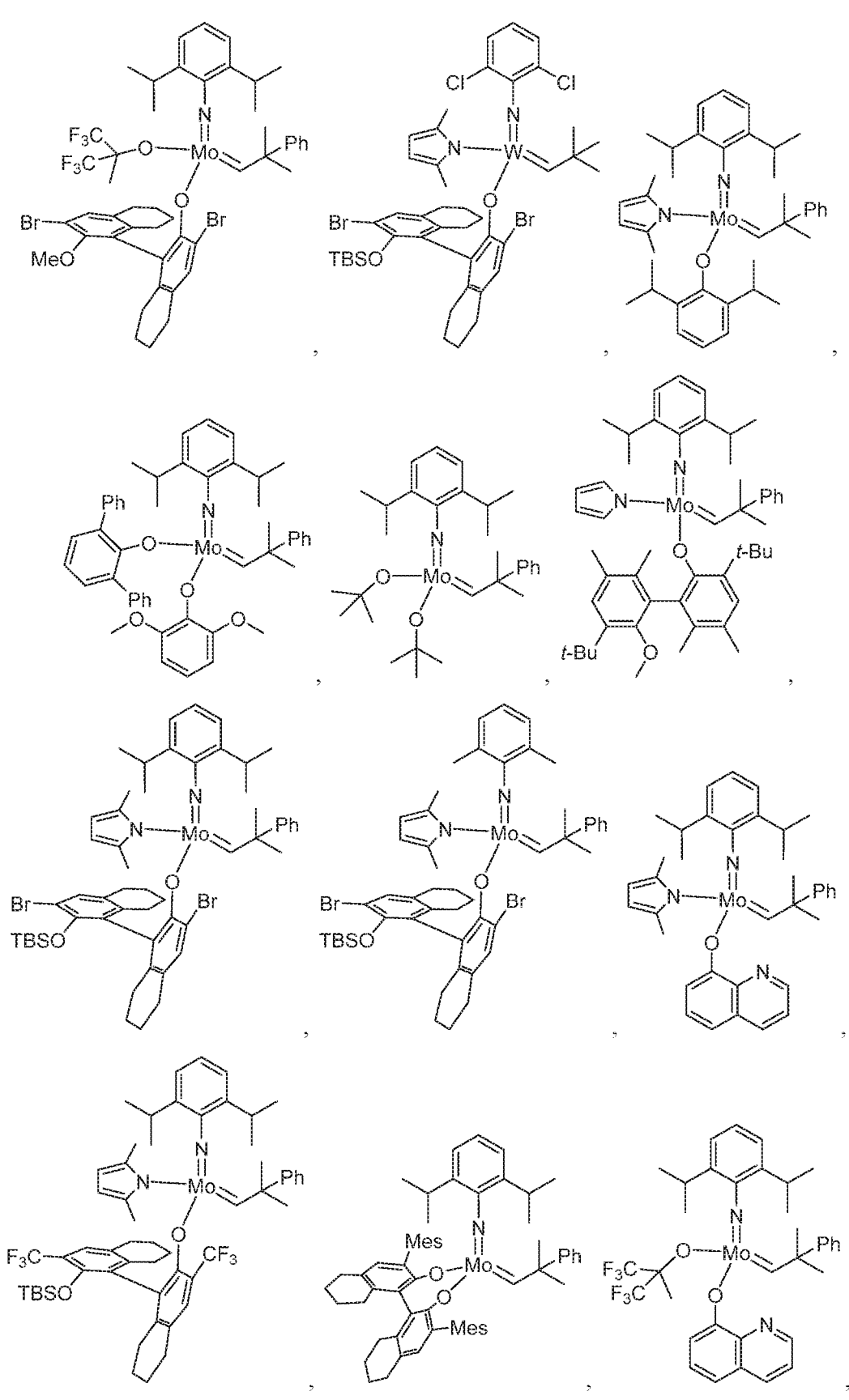


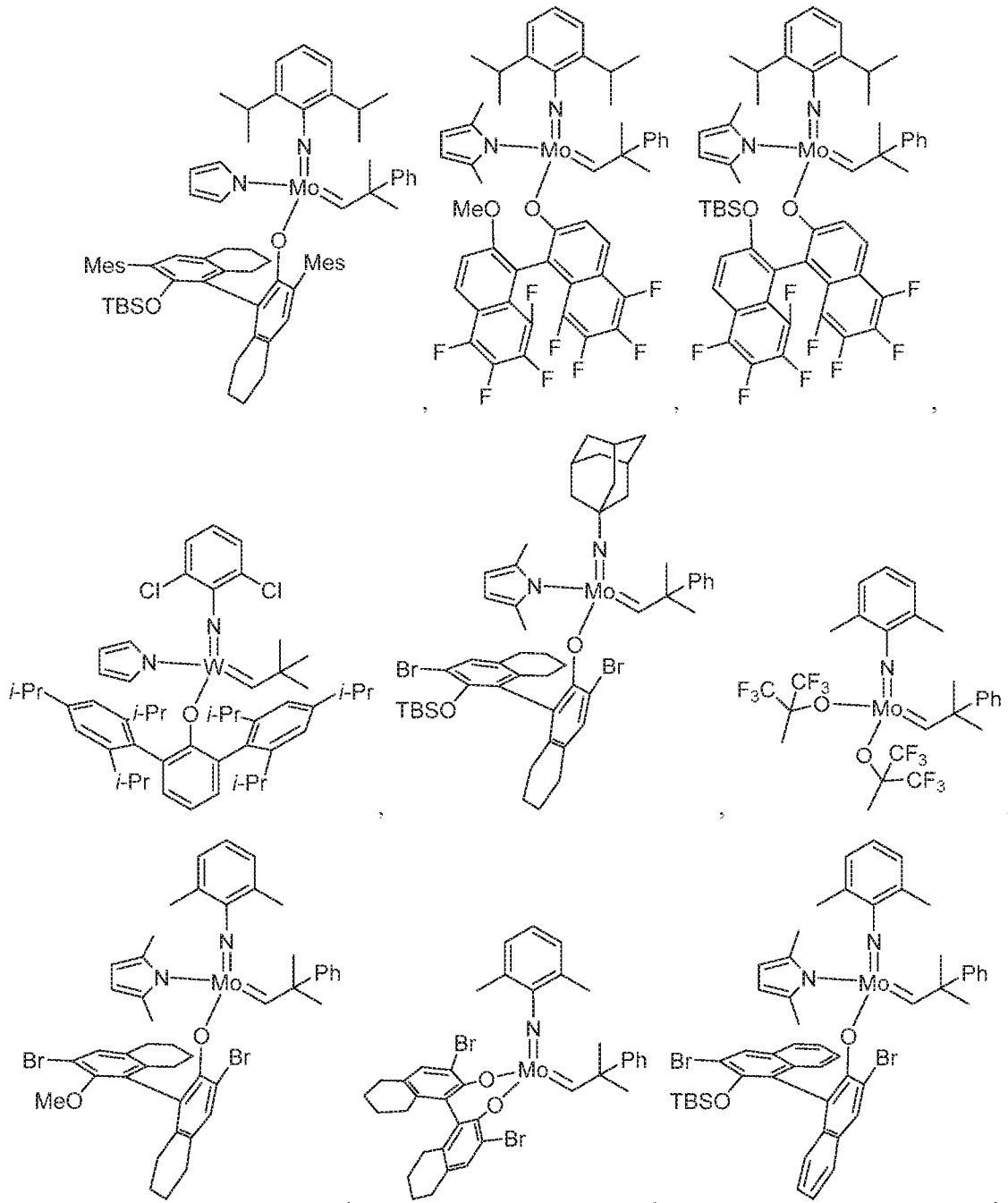


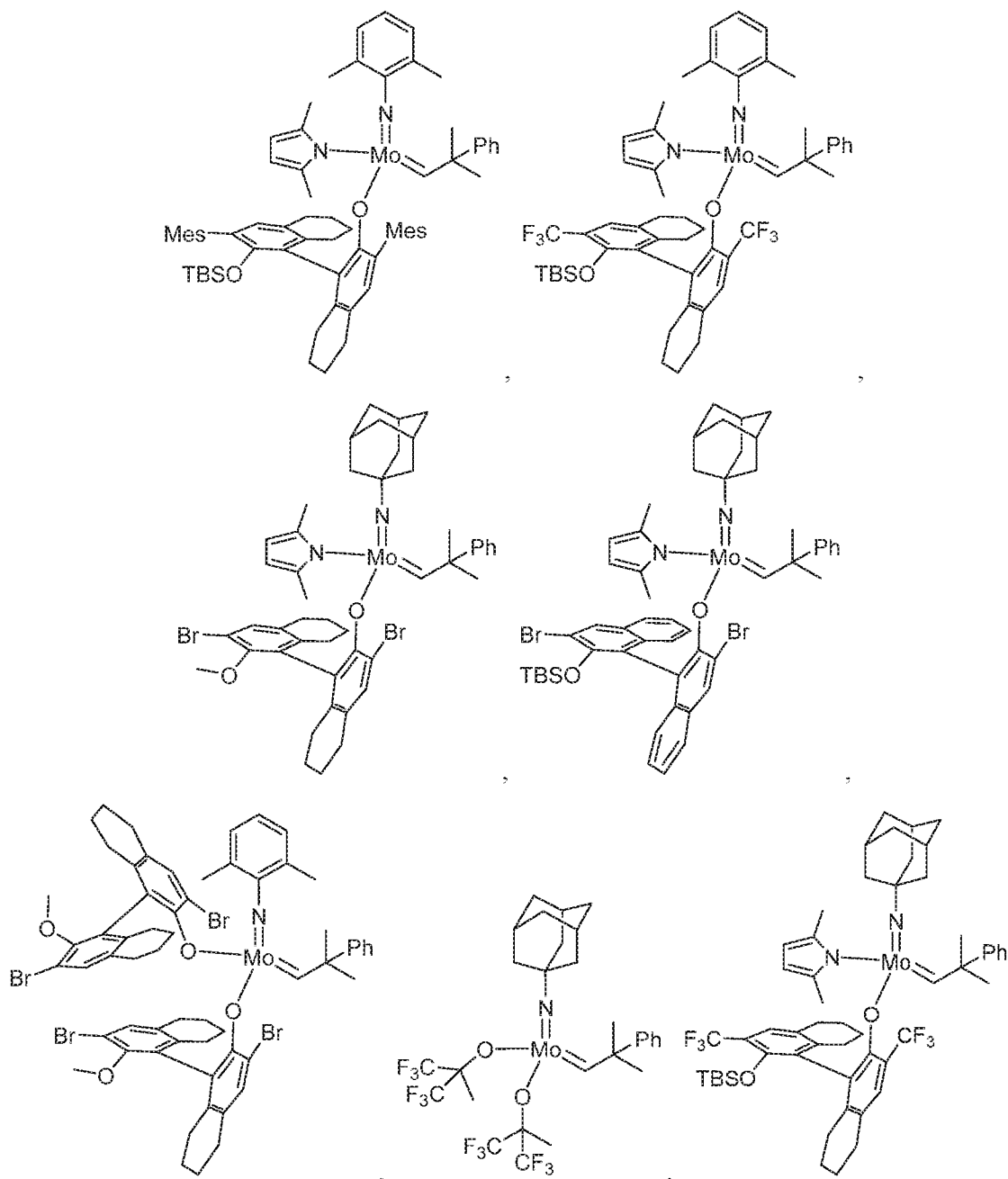


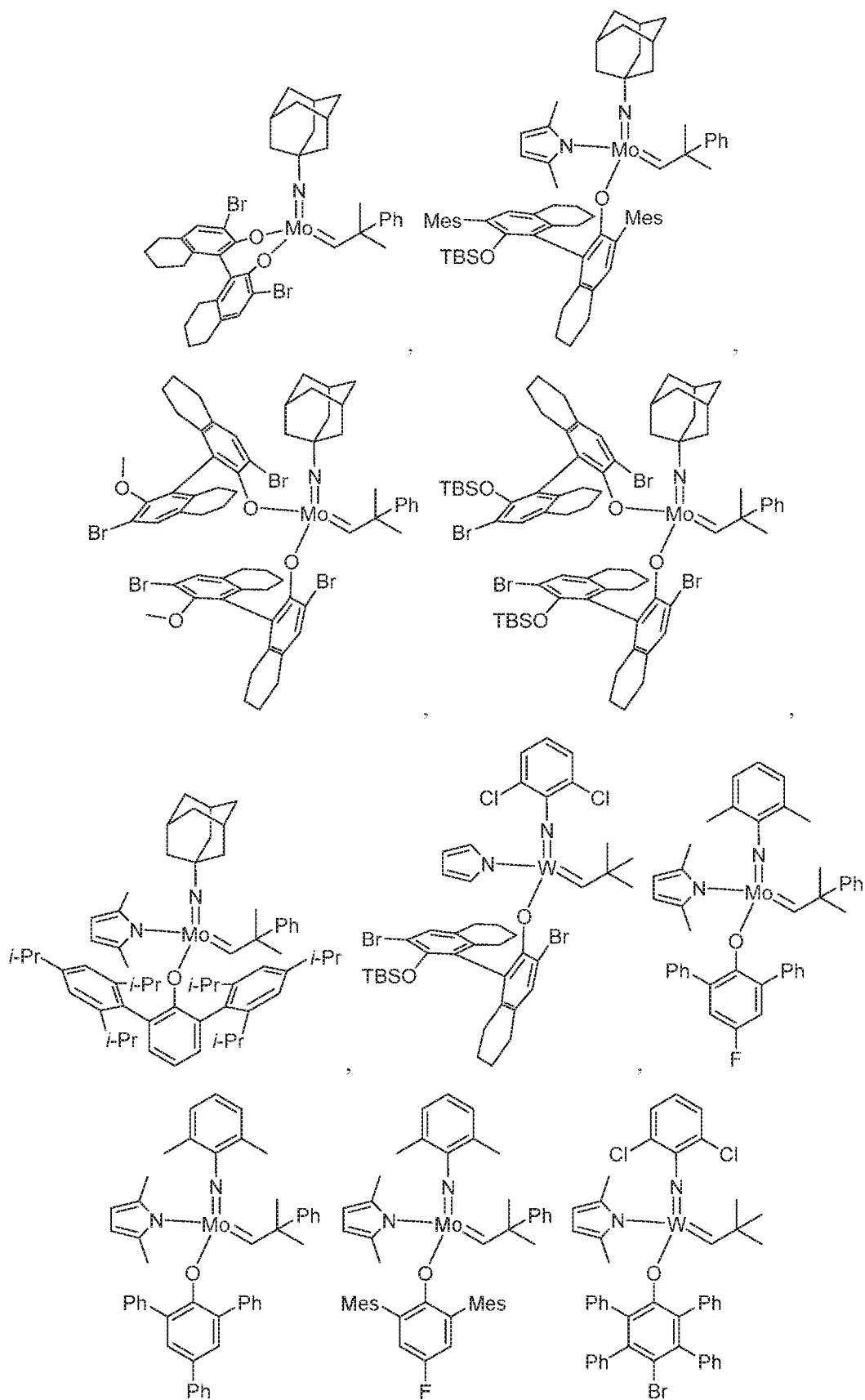


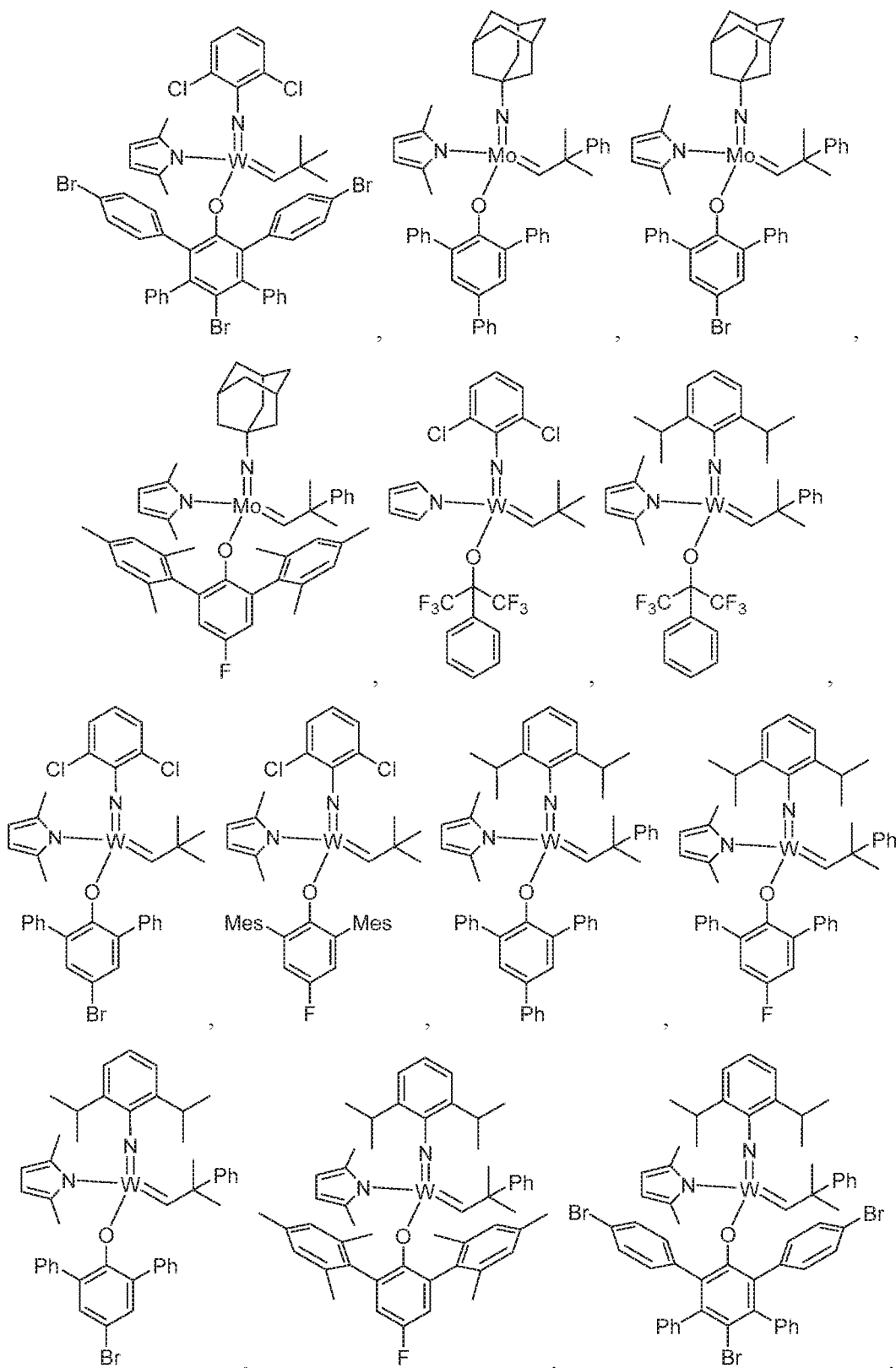


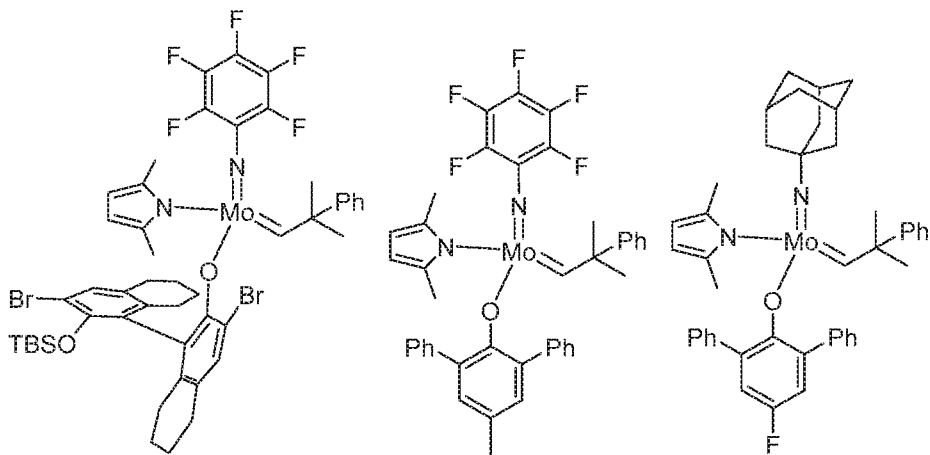
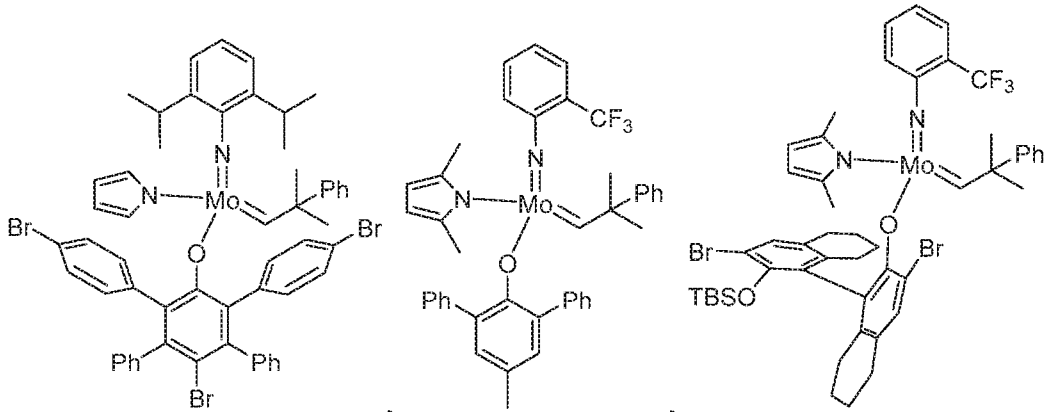
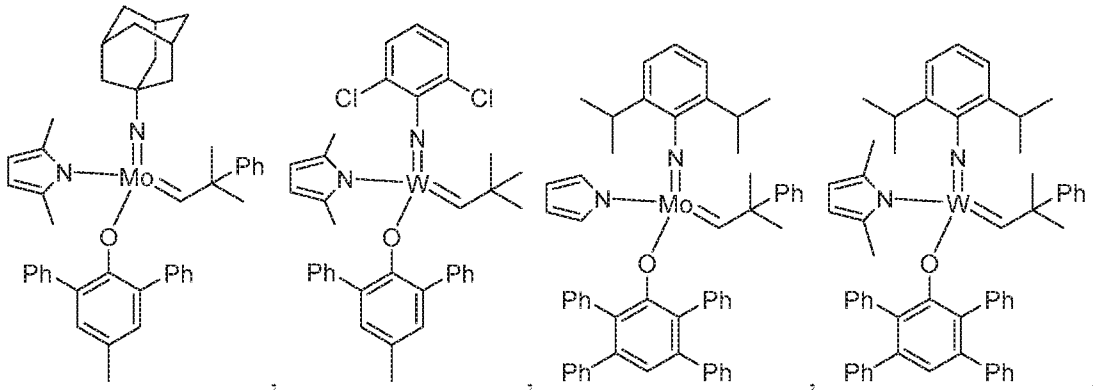
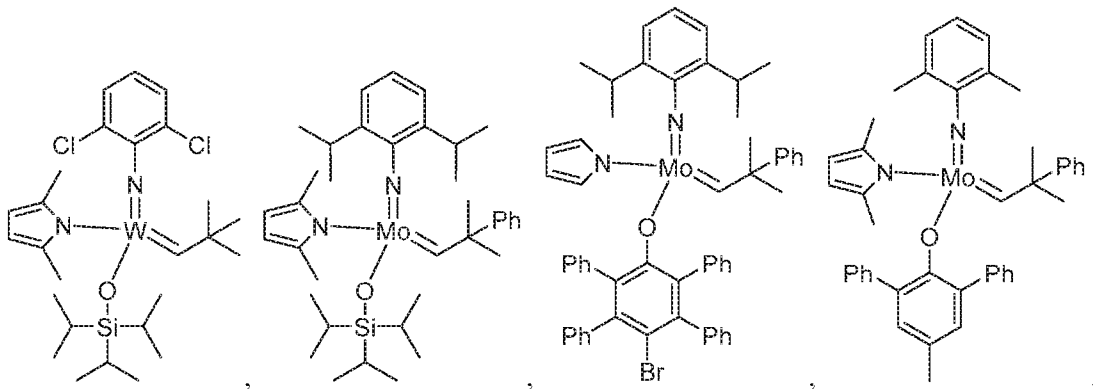


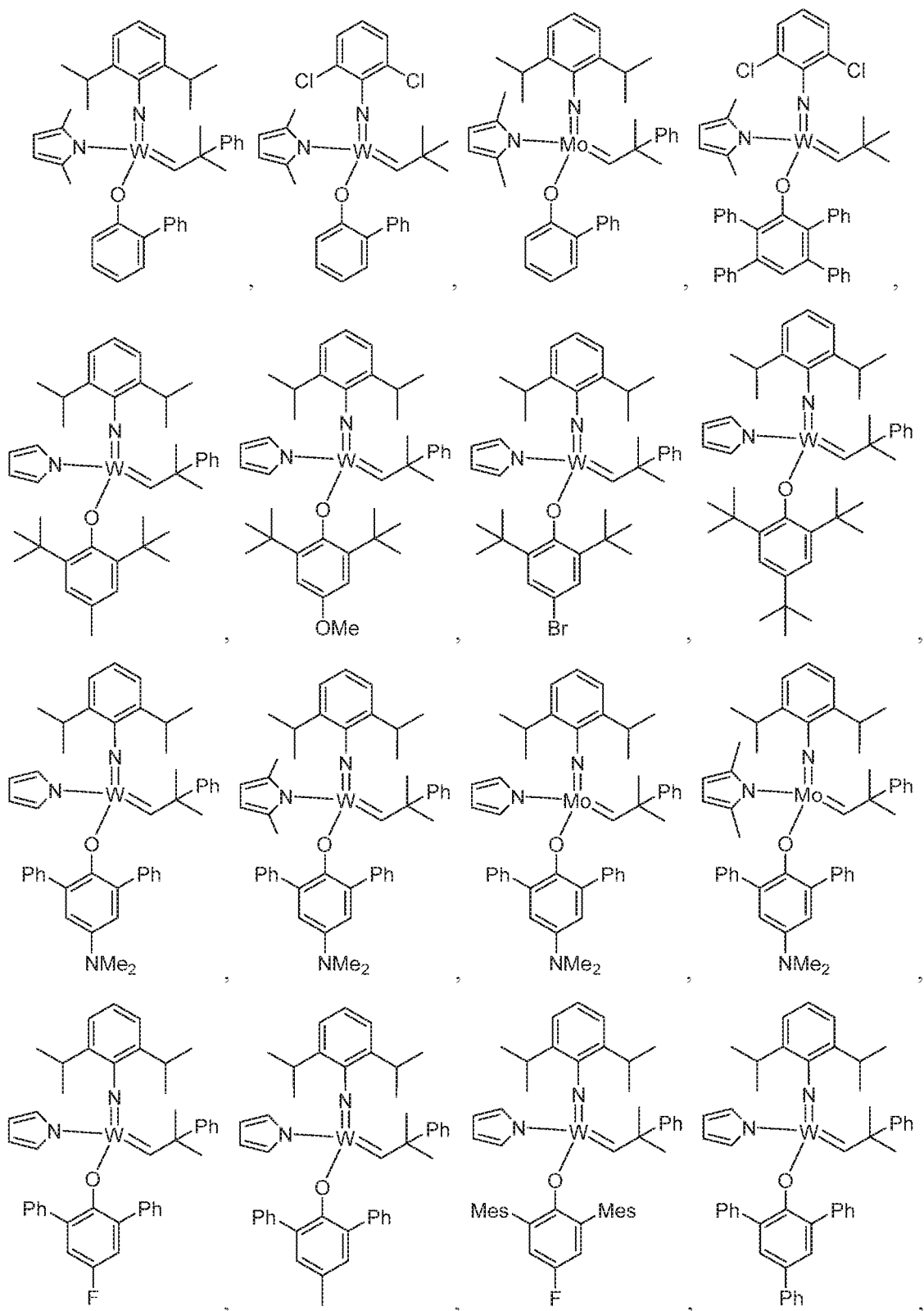


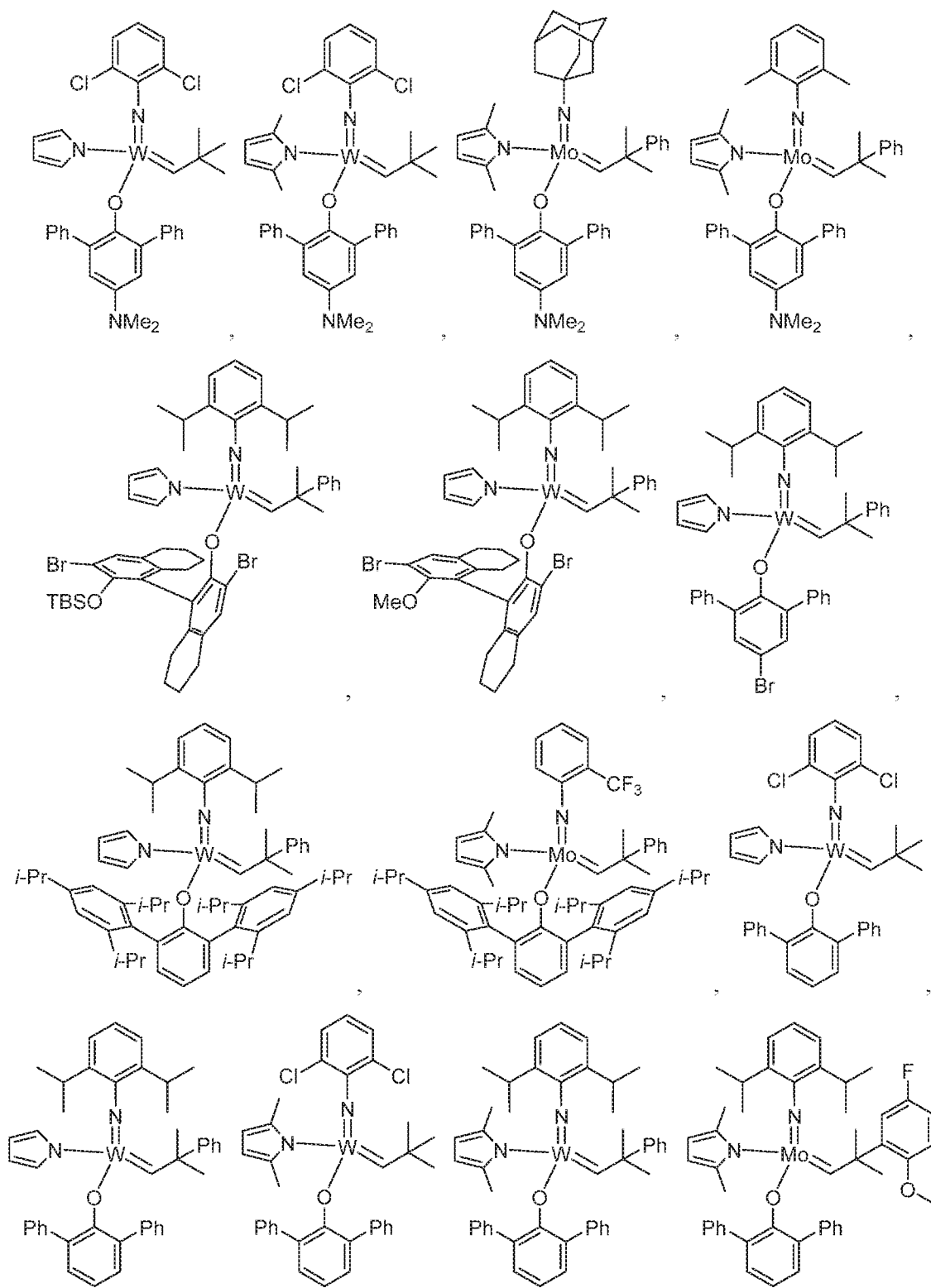




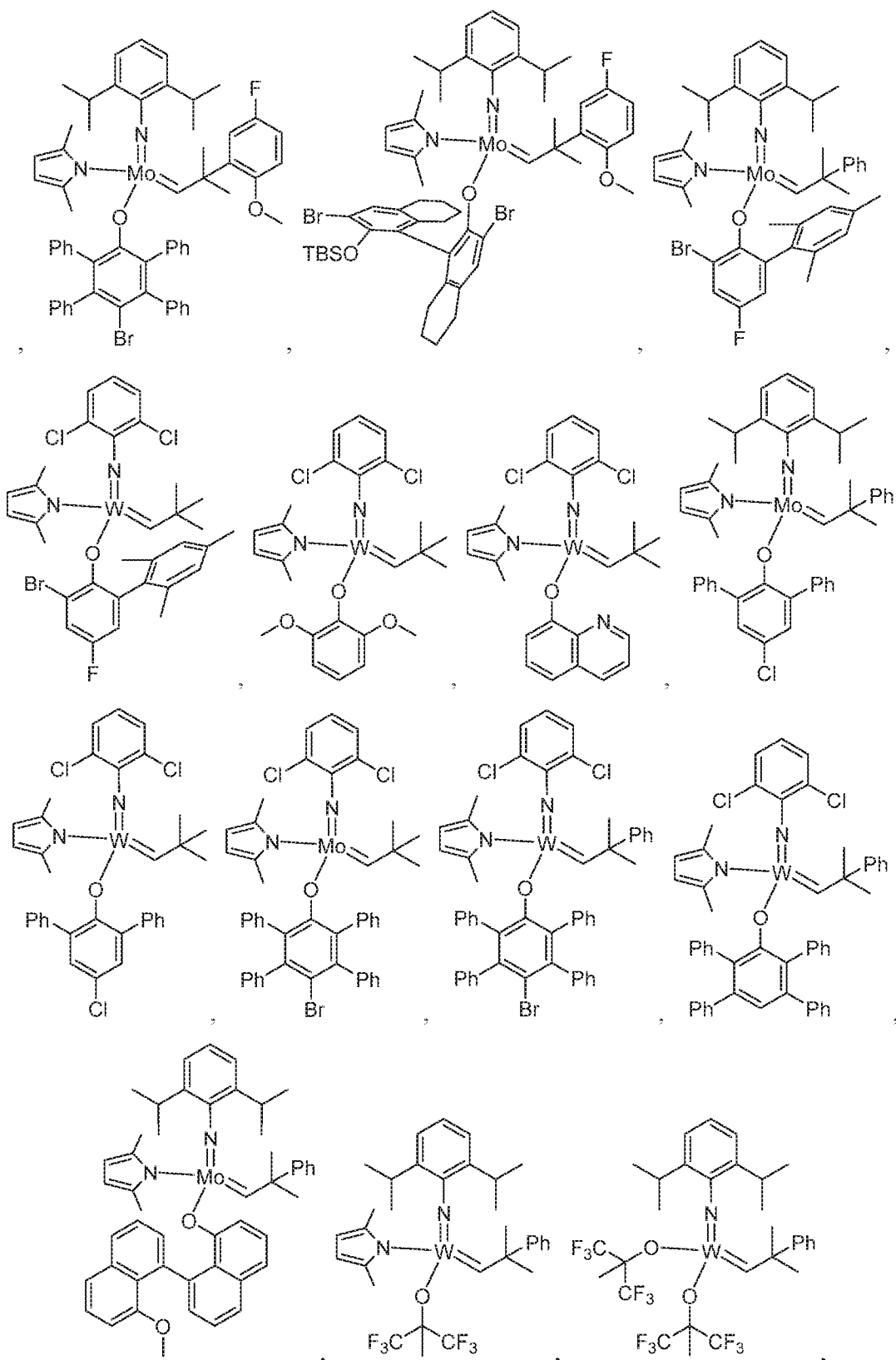


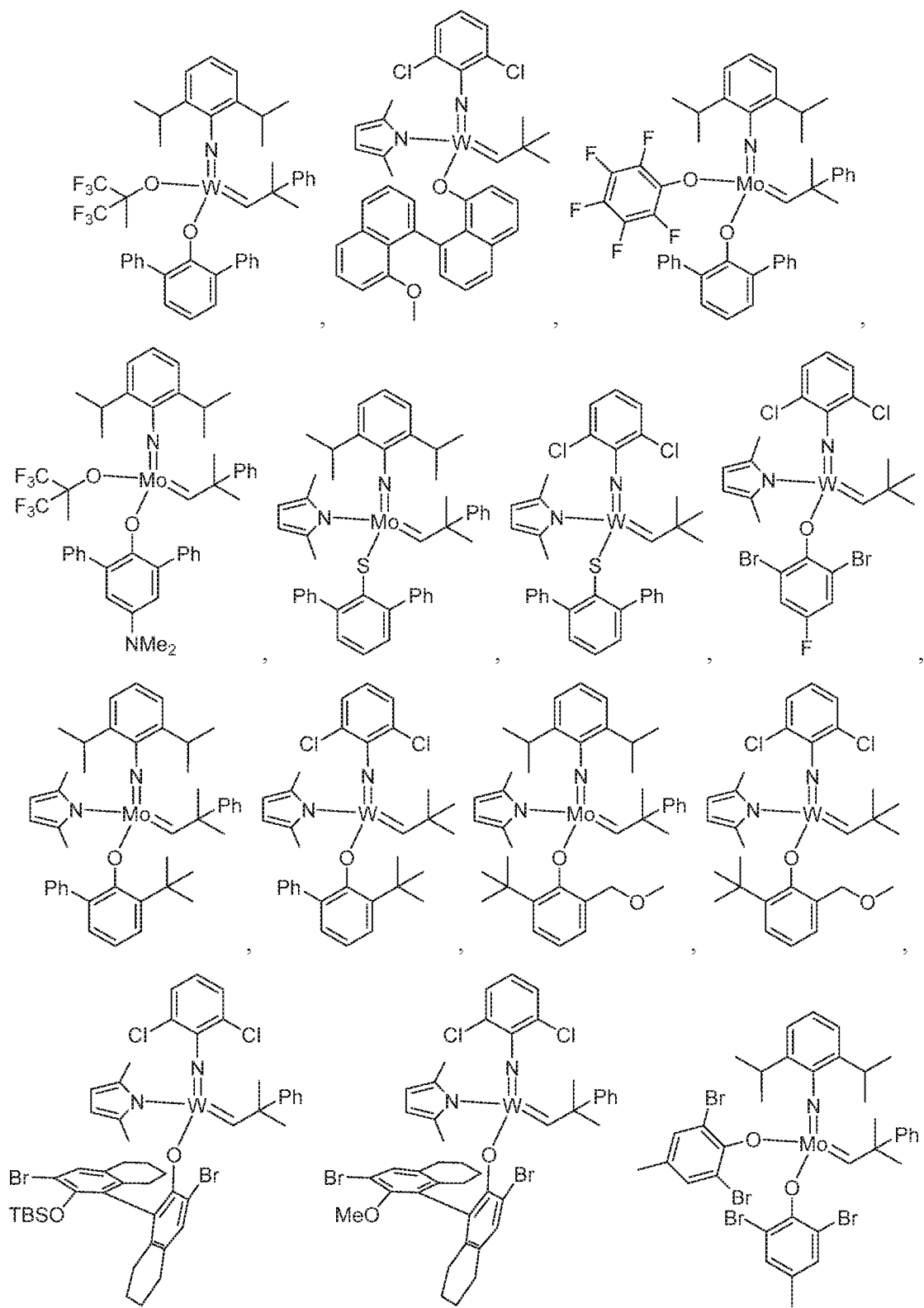


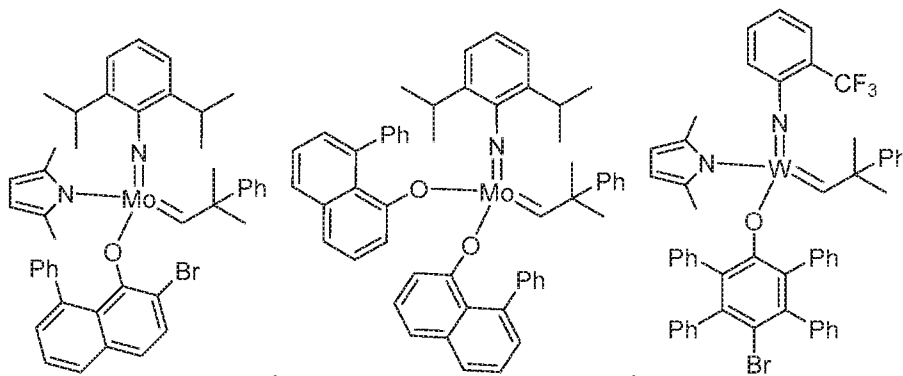
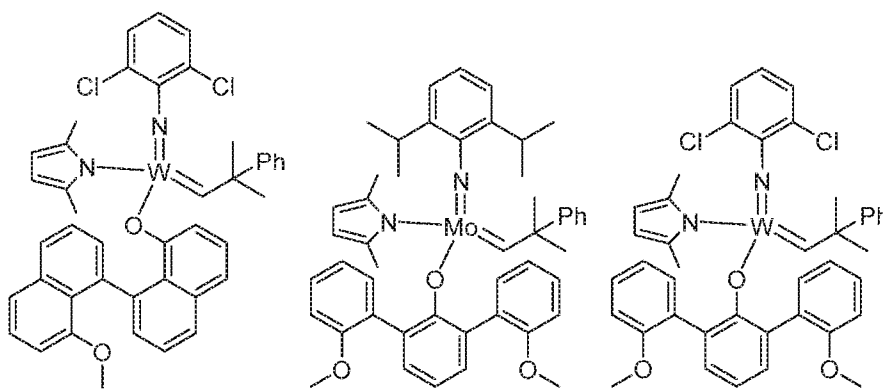
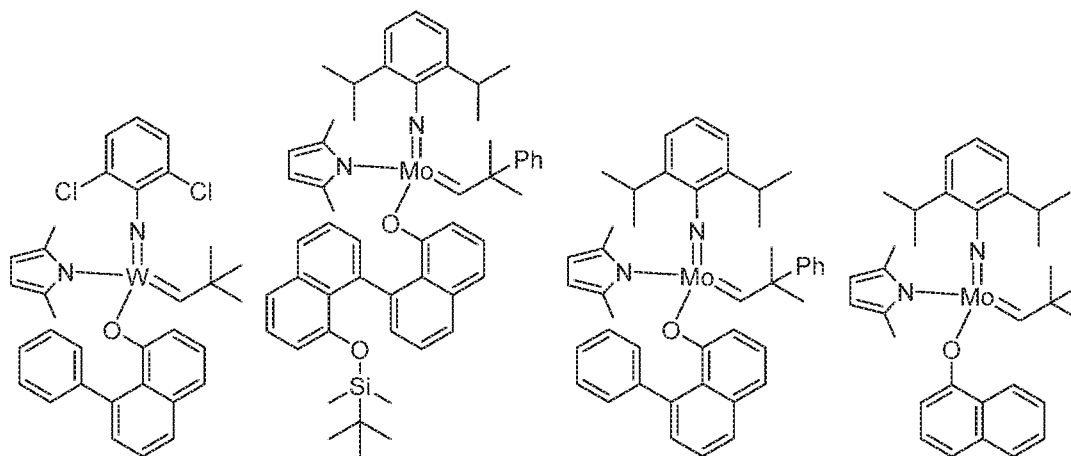
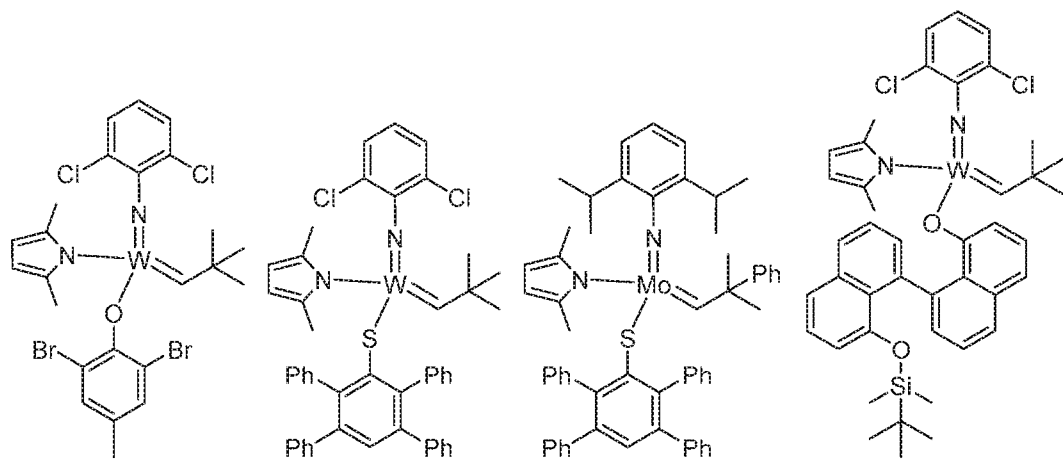


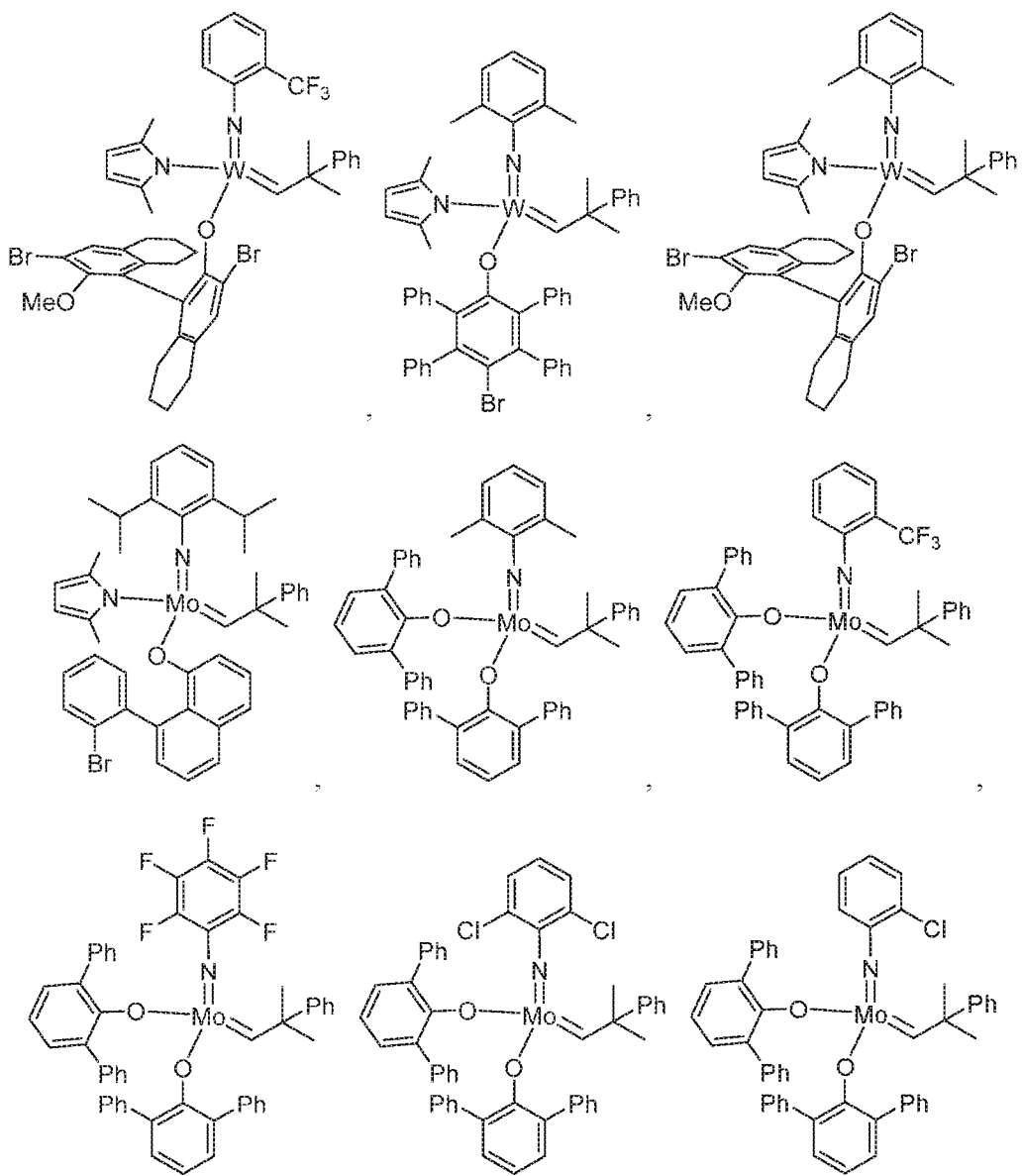


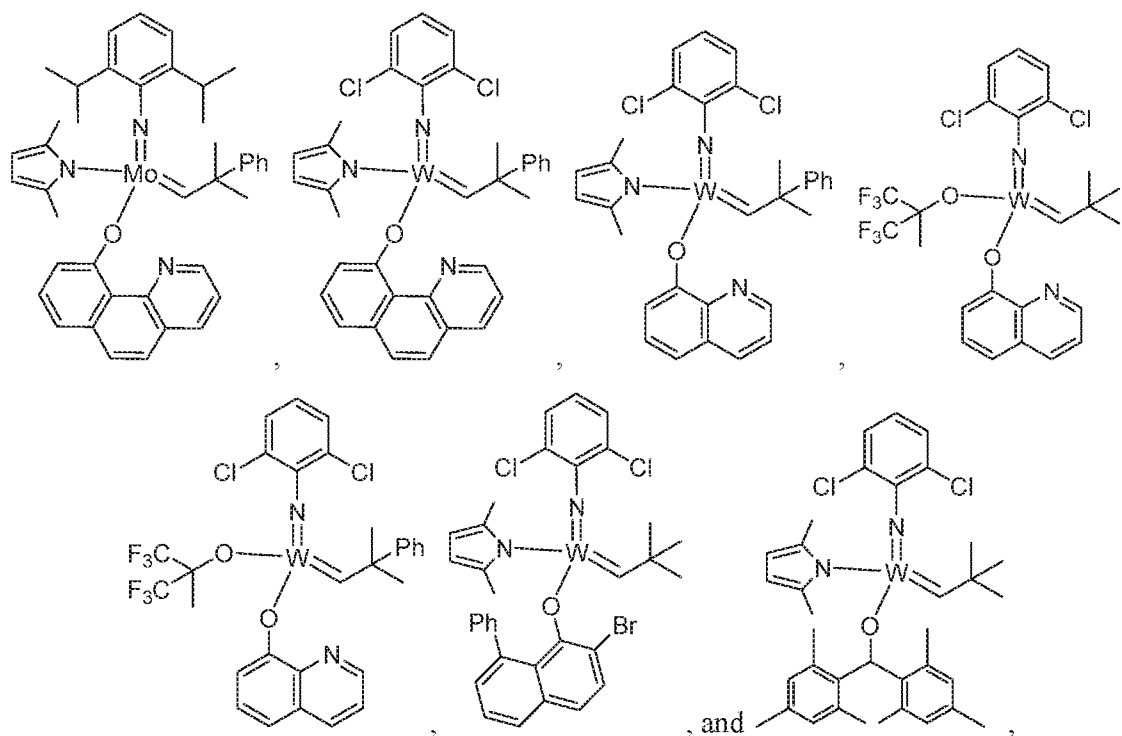






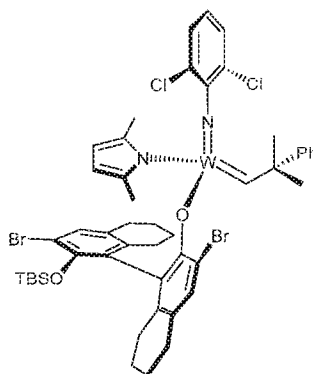




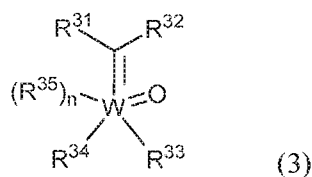


wherein “Me” is methyl, “Ph” is phenyl, “*i*-Pr” is isopropyl, “Mes” is mesityl (*i.e.*, 2,4,6-trimethylphenyl), and “TBS” is *tert*-butyldimethylsilyl.

5 [0168] In some embodiments, the metathesis catalyst is



[0169] In some embodiments, the catalyst is a compound of Formula 3:



wherein:

10 each of  $R^{31}$  and  $R^{32}$  is independently R, -OR, -SR, -N(R)<sub>2</sub>, -OC(O)R, -SOR, -SO<sub>2</sub>R, -SO<sub>2</sub>N(R)<sub>2</sub>, -C(O)N(R)<sub>2</sub>, -NRC(O)R, or -NRSO<sub>2</sub>R;

each of R<sup>33</sup> and R<sup>34</sup> is independently halogen, R, -N(R)<sub>2</sub>, -NRC(O)R, -NRC(O)OR, -NRC(O)N(R)<sub>2</sub>, -NRSO<sub>2</sub>R, -NRSO<sub>2</sub>N(R)<sub>2</sub>, -NROR, NR<sub>3</sub>, -OR, a phosphorus-containing ligand, or an optionally substituted group selected from:

- 5 a 5-6 membered monocyclic heteroaryl ring having at least one nitrogen and 0-3 additional heteroatoms independently selected from nitrogen, oxygen, or sulfur,
- a 4-7 membered saturated or partially unsaturated heterocyclic ring having at least one nitrogen and 0-2 additional heteroatoms independently selected from nitrogen, oxygen, or sulfur,
- 10 a 7-10 membered bicyclic saturated or partially unsaturated heterocyclic ring having at least one nitrogen and 0-4 additional heteroatoms independently selected from nitrogen, oxygen, or sulfur, and
- an 8-10 membered bicyclic heteroaryl ring having at least one nitrogen and 0-4 additional heteroatoms independently selected from nitrogen, oxygen, or sulfur;
- 15

each R is independently hydrogen or an optionally substituted group selected from:

- phenyl,
- ferrocene,
- 20 C<sub>1-20</sub> aliphatic,
- C<sub>1-20</sub> heteroaliphatic having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur,
- a 3-7 membered saturated or partially unsaturated carbocyclic ring,
- an 8-10 membered bicyclic saturated, partially unsaturated or aryl ring,
- 25 a 5-6 membered monocyclic heteroaryl ring having 1-4 heteroatoms independently selected from nitrogen, oxygen, or sulfur,
- a 4-7 membered saturated or partially unsaturated heterocyclic ring having 1-3 heteroatoms independently selected from nitrogen, oxygen, or sulfur,
- a 7-10 membered bicyclic saturated or partially unsaturated heterocyclic ring
- 30 having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur; and
- an 8-10 membered bicyclic heteroaryl ring having 1-5 heteroatoms independently selected from nitrogen, oxygen, or sulfur;

or two or three R groups on the same nitrogen atom are taken together with the nitrogen to form an optionally substituted 3-12 membered saturated, partially unsaturated, or aryl ring having 0-5 additional heteroatoms not including the same nitrogen atom independently selected from nitrogen, oxygen, or sulfur;

5 or two R groups on the same oxygen atom are taken together with the oxygen to form an optionally substituted 3-12 membered saturated, partially unsaturated, or aryl ring having 0-5 additional heteroatoms not including the same oxygen atom independently selected from nitrogen, oxygen, or sulfur;

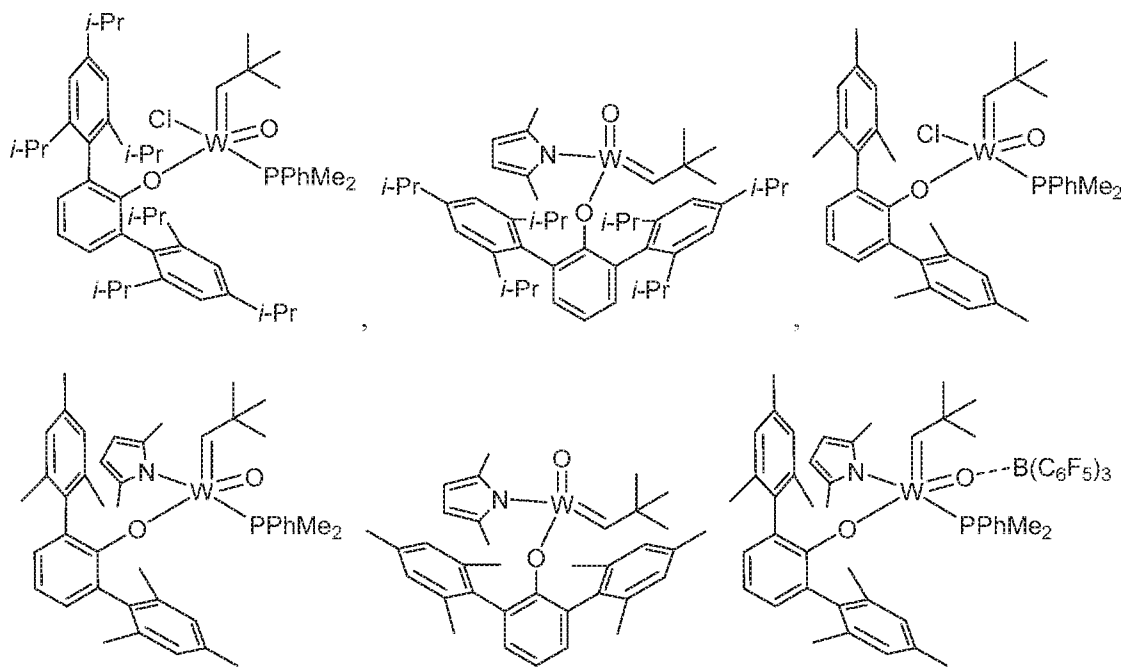
n is 0, 1, or 2;

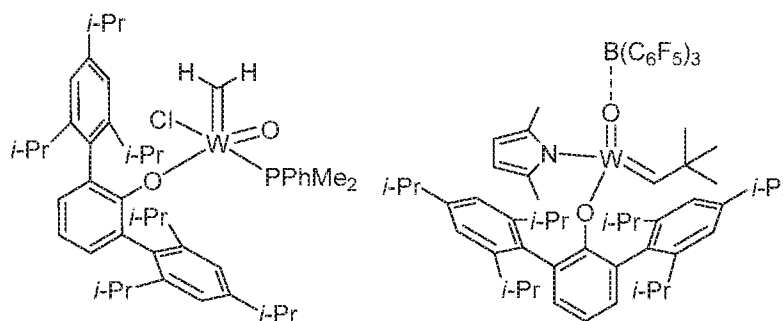
10 each R<sup>35</sup> is independently a monodentate ligand, or two R<sup>35</sup> are taken together with their intervening atoms to form an optionally substituted bidentate group; and

two or more of R<sup>31</sup>, R<sup>32</sup>, R<sup>33</sup>, R<sup>34</sup> and R<sup>35</sup> may be taken together with their intervening atoms to form an optionally substituted polydentate ligand.

[0170] In some embodiments, the metathesis catalyst has a structure according to Formula 3 and the metathesis product comprises a Z olefin.

[0171] In some embodiments, the catalyst is selected from:





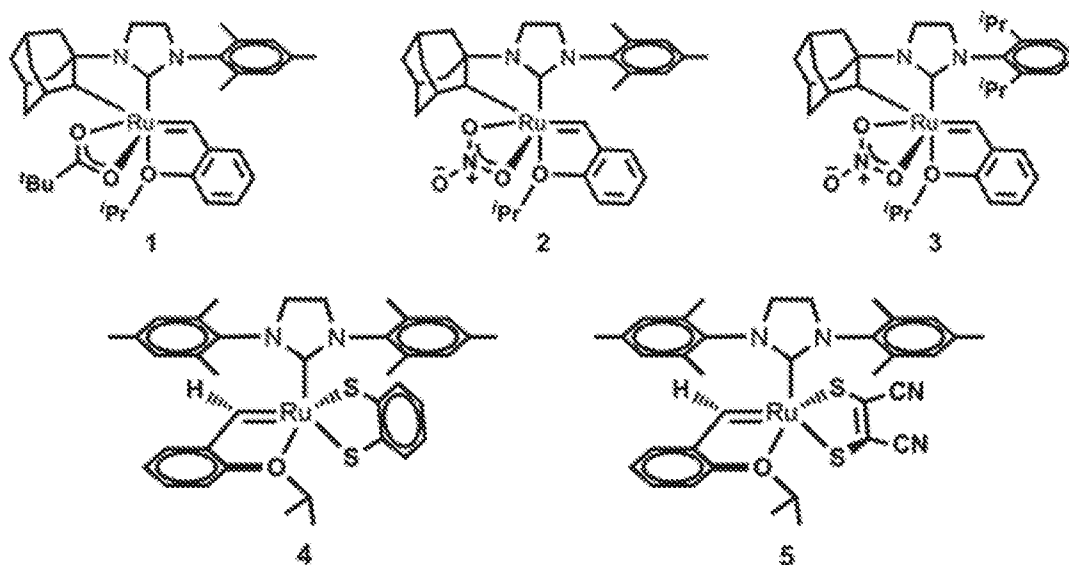
W(O)(CH-*t*-Bu)(Ph<sub>2</sub>Pyr)(OHMT); W(O)(CH-*t*-Bu)(Ph<sub>2</sub>Pyr)(OHIPT); W(O)(CH-*t*-Bu)  
 [N(C<sub>6</sub>F<sub>5</sub>)<sub>2</sub>](OHMT)(PPhMe<sub>2</sub>); W(O)(CH-*t*-Bu)(PMe<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub>; W(O)(CH-*t*-Bu)(O-2,6-  
 Ph<sub>2</sub>C<sub>6</sub>H<sub>3</sub>)<sub>2</sub>(PMe<sub>3</sub>); W(O)(CH-*t*-Bu)(Cl)(OHIPT); W(O)(CH-*t*-Bu)(PMe<sub>2</sub>Ph)<sub>2</sub>Cl<sub>2</sub>; W(O)  
 5 (CHCMe<sub>2</sub>Ph)Cl<sub>2</sub>(PMe<sub>2</sub>Ph)<sub>2</sub>; W[OB(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub>](CH-*t*-Bu)(Me<sub>2</sub>Pyr)(OHMT); W(O)(CH-*t*-Bu)[N-  
 (C<sub>6</sub>F<sub>5</sub>)<sub>2</sub>](OHMT); W(O)(CH-*t*-Bu)(OHMT)<sub>2</sub>; W(O)(CH-*t*-Bu)(OHIPT)<sub>2</sub>; W(O)(CH-*t*-  
 Bu)(Me<sub>2</sub>Pyr)(DFTO)(PPhMe<sub>2</sub>); W(O)(CH-*t*-Bu)(Me<sub>2</sub>Pyr)(DFTO); W(O)(CHCMe<sub>2</sub>Ph)  
 (Me<sub>2</sub>Pyr)(DFTO)(PPhMe<sub>2</sub>); W(O)(CHCMe<sub>2</sub>Ph)(Me<sub>2</sub>Pyr)(DFTO); W(O)(CH-*t*-Bu)[N-  
 (C<sub>6</sub>F<sub>5</sub>)<sub>2</sub>](DFTO); and W(O)(CH-*t*-Bu)(DFTO)<sub>2</sub>; wherein OHMT is O-2,6-  
 10 dimesitylphenoxide; OHIPT is O-2,6-(2,4,6-triisopropylphenyl)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>; DFTO is 2,6-  
 pentafluorophenylphenoxide; Ph<sub>2</sub>Pyr is 2,5-diphenylpyrrol-1-yl; and Me<sub>2</sub>Pyr is 2,5-  
 dimethylpyrrol-1-yl.

**[0172]** Other metathesis catalysts can be used in the methods of the invention. In general,  
 any metathesis catalyst stable under the reaction conditions and nonreactive with the  
 15 functional groups present on the reactant shown in Schemes 3 through 8 may be used with the  
 present invention. Such catalysts are, for example, those described by Grubbs (Grubbs, R.H.,  
 "Synthesis of large and small molecules using olefin metathesis catalysts." *PMSE Prepr.*,  
 2012), herein incorporated by reference in its entirety. Depending on the desired isomer of  
 the olefin, a cis-selective metathesis catalyst may be used, for example one of those described  
 20 by Shahane *et al.* (Shahane, S., *et al. ChemCatChem*, 2013. 5(12): p. 3436-3459), herein  
 incorporated by reference in its entirety. Specific catalysts 1-5 exhibiting cis-selectivity are  
 shown below (Scheme 5) and have been described previously (Khan, R.K., *et al. J. Am.*  
*Chem. Soc.*, 2013. 135(28): p. 10258-61; Hartung, J. *et al. J. Am. Chem. Soc.*, 2013. 135(28):  
 p. 10183-5.; Rosebrugh, L.E., *et al. J. Am. Chem. Soc.*, 2013. 135(4): p. 1276-9.; Marx, V.M.,  
 25 *et al. J. Am. Chem. Soc.*, 2013. 135(1): p. 94-7.; Herbert, M.B., *et al. Angew. Chem. Int. Ed.*  
*Engl.*, 2013. 52(1): p. 310-4; Keitz, B.K., *et al. J. Am. Chem. Soc.*, 2012. 134(4): p. 2040-3.;



Keitz, B.K., *et al. J. Am. Chem. Soc.*, 2012. 134(1): p. 693-9.; Endo, K. *et al. J. Am. Chem. Soc.*, 2011. 133(22): p. 8525-7).

Scheme 5



5

[0173] Additional Z-selective catalysts are described in (Cannon and Grubbs 2013; Bronner *et al.* 2014; Hartung *et al.* 2014; Pribisko *et al.* 2014; Quigley and Grubbs 2014) and are herein incorporated by reference in their entirety. Such metathesis catalysts include, but are not limited to, neutral ruthenium or osmium metal carbene complexes that possess metal centers that are formally in the +2 oxidation state, have an electron count of 16, are penta-coordinated, and are of the general formula  $LL'AA'M=CRbRc$  or  $LL'AA'M=(C\equiv)nCRbRc$  (Pederson and Grubbs 2002); wherein

M is ruthenium or osmium;

L and L' are each independently any neutral electron donor ligand and preferably selected from phosphine, sulfonated phosphine, phosphite, phosphinite, phosphonite, arsine, stibnite, ether, amine, amide, imine, sulfoxide, carboxyl, nitrosyl, pyridine, thioether, or heterocyclic carbenes; and

A and A' are anionic ligands independently selected from halogen, hydrogen, C<sub>1</sub>-C<sub>20</sub> alkyl, aryl, C<sub>1</sub>-C<sub>20</sub> alkoxide, aryloxy, C<sub>2</sub>-C<sub>20</sub> alkoxycarbonyl, arylcarboxylate, C<sub>1</sub>-C<sub>20</sub> carboxylate, arylsulfonyl, C<sub>1</sub>-C<sub>20</sub> alkylsulfonyl, C<sub>1</sub>-C<sub>20</sub> alkylsulfinyl; each ligand optionally being substituted with C<sub>1</sub>-C<sub>5</sub> alkyl, halogen, C<sub>1</sub>-C<sub>5</sub> alkoxy; or with a phenyl group that is optionally substituted with halogen, C<sub>1</sub>-C<sub>5</sub> alkyl, or C<sub>1</sub>-C<sub>5</sub> alkoxy; and A and A' together may optionally comprise a bidentate ligand; and

$R_b$  and  $R_c$  are independently selected from hydrogen,  $C_1$ - $C_{20}$  alkyl, aryl,  $C_1$ - $C_{20}$  carboxylate,  $C_1$ - $C_{20}$  alkoxy, aryloxy,  $C_1$ - $C_{20}$  alkoxy carbonyl,  $C_1$ - $C_{20}$  alkylthio,  $C_1$ - $C_{20}$  alkylsulfonyl and  $C_1$ - $C_{20}$  alkylsulfinyl, each of  $R_b$  and  $R_c$  optionally substituted with  $C_1$ - $C_5$  alkyl, halogen,  $C_1$ - $C_5$  alkoxy or with a phenyl group that is optionally substituted with halogen,  $C_1$ - $C_5$  alkyl, or  $C_1$ - $C_5$  alkoxy.

[0174] Other metathesis catalysts such as “well defined catalysts” can also be used. Such catalysts include, but are not limited to, Schrock's molybdenum metathesis catalyst, 2,6-diisopropylphenylimido neophylidenemolybdenum (VI) bis(hexafluoro-*t*-butoxide), described by Grubbs *et al.* (*Tetrahedron* 1998, 54: 4413-4450) and Basset's tungsten metathesis catalyst described by Couturier, J. L. *et al.* (*Angew. Chem. Int. Ed. Engl.* 1992, 31: 628).

[0175] Catalysts useful in the methods of the invention also include those described by Peryshkov, *et al.* *J. Am. Chem. Soc.* 2011, 133: 20754-20757; Wang, *et al.* *Angewandte Chemie*, 2013, 52: 1939-1943; Yu, *et al.* *J. Am. Chem. Soc.*, 2012, 134: 2788-2799; Halford. *Chem. Eng. News*, 2011, 89 (45): 11; Yu, *et al.* *Nature*, 2011, 479: 88-93; Lee. *Nature*, 2011, 471: 452-453; Meek, *et al.* *Nature*, 2011: 471, 461-466; Flook, *et al.* *J. Am. Chem. Soc.* 2011, 133: 1784-1786; Zhao, *et al.* *Org. Lett.*, 2011, 13(4): 784-787; Ondi, *et al.* “High activity, stabilized formulations, efficient synthesis and industrial use of Mo- and W-based metathesis catalysts” *XiMo Technology Updates*, 2015: [http://www.ximo-inc.com/files/ximo/uploads/download/Summary\\_\\_3.11.15.pdf](http://www.ximo-inc.com/files/ximo/uploads/download/Summary__3.11.15.pdf); Schrock, *et al.* *Macromolecules*, 2010: 43, 7515-7522; Peryshkov, *et al.* *Organometallics* 2013: 32, 5256-5259; Gerber, *et al.* *Organometallics* 2013: 32, 5573-5580; Marinescu, *et al.* *Organometallics* 2012: 31, 6336-6343; Wang, *et al.* *Angew. Chem. Int. Ed.* 2013: 52, 1939 - 1943; Wang, *et al.* *Chem. Eur. J.* 2013: 19, 2726-2740; Townsend *et al.* *J. Am. Chem. Soc.* 2012: 134, 11334-11337; and Johns *et al.* *Org. Lett.* 2016: 18, 772-775.

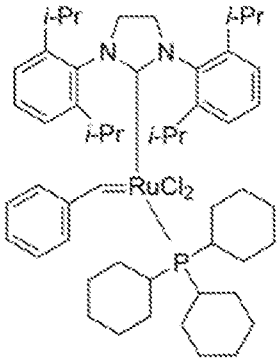
[0176] Catalysts useful in the methods of the invention also include those described in International Pub. No. WO 2014/155185; International Pub. No. WO 2014/172534; U.S. Pat. Appl. Pub. No. 2014/0330018; International Pub. No. WO 2015/003815; and International Pub. No. WO 2015/003814.

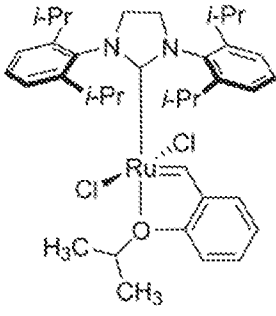
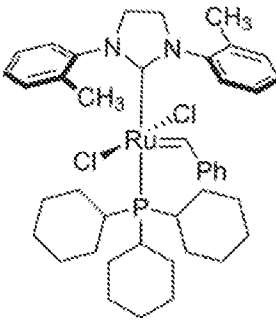
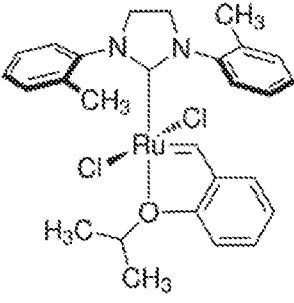
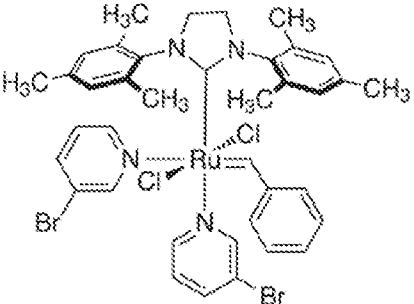
[0177] Catalysts useful in the methods of the invention also include those described in U.S. Pat. No. 4,231,947; U.S. Pat. No. 4,245,131; U.S. Pat. No. 4,427,595; U.S. Pat. No. 4,681,956; U.S. Pat. No. 4,727,215; International Pub. No. WO 1991/009825; U.S. Pat. No.

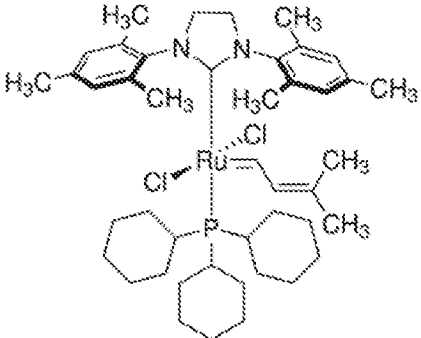
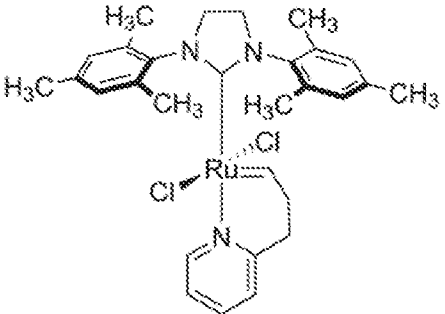
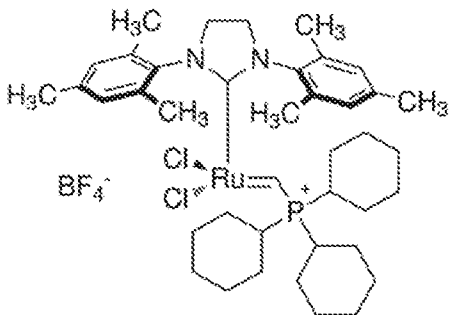
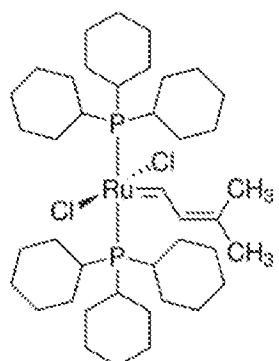
5,0877,10; U.S. Pat. No. 5,142,073; U.S. Pat. No. 5,146,033; International Pub. No. WO 1992/019631; U.S. Pat. No. 6,121,473; U.S. Pat. No. 6,346,652; U.S. Pat. No. 8,987,531; U.S. Pat. Appl. Pub. No. 2008/0119678; International Pub. No. WO 2008/066754; International Pub. No. WO 2009/094201; U.S. Pat. Appl. Pub. No. 2011/0015430; U.S. Pat. Appl. Pub. No. 2011/0065915; U.S. Pat. Appl. Pub. No. 2011/0077421; International Pub. No. WO 2011/040963; International Pub. No. WO 2011/097642; U.S. Pat. Appl. Pub. No. 2011/0237815; U.S. Pat. Appl. Pub. No. 2012/0302710; International Pub. No. WO 2012/167171; U.S. Pat. Appl. Pub. No. 2012/0323000; U.S. Pat. Appl. Pub. No. 2013/0116434; International Pub. No. WO 2013/070725; U.S. Pat. Appl. Pub. No. 2013/0274482; U.S. Pat. Appl. Pub. No. 2013/0281706; International Pub. No. WO 2014/139679; International Pub. No. WO 2014/169014; U.S. Pat. Appl. Pub. No. 2014/0330018; and U.S. Pat. Appl. Pub. No. 2014/0378637.

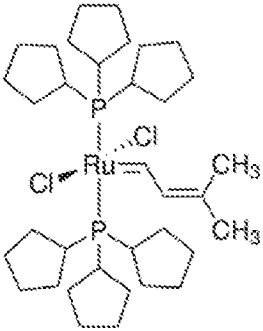
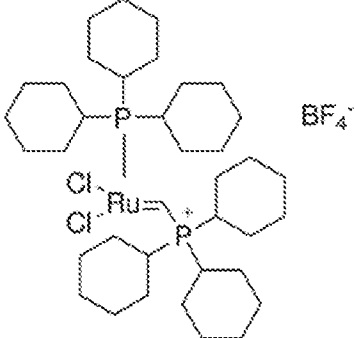
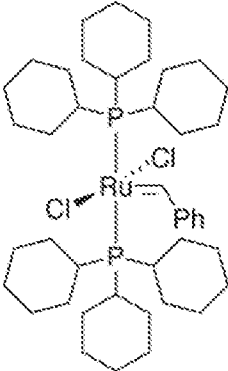
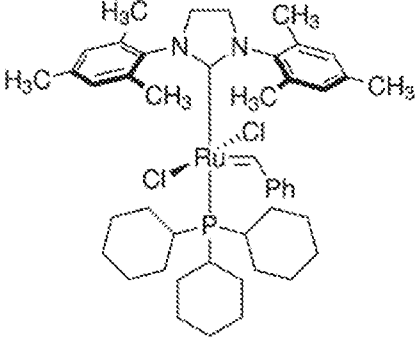
[0178] Catalysts useful in the methods of the invention also include those described in International Pub. No. WO 2007/075427; U.S. Pat. Appl. Pub. No. 2007/0282148; International Pub. No. WO 2009/126831; International Pub. No. WO 2011/069134; U.S. Pat. Appl. Pub. No. 2012/0123133; U.S. Pat. Appl. Pub. No. 2013/0261312; U.S. Pat. Appl. Pub. No. 2013/0296511; International Pub. No. WO 2014/134333; and U.S. Pat. Appl. Pub. No. 2015/0018557.

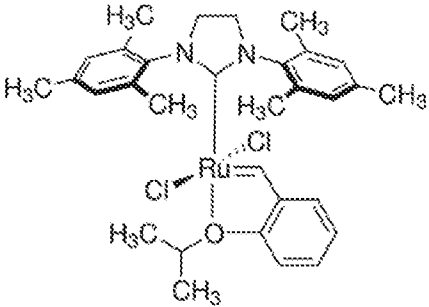
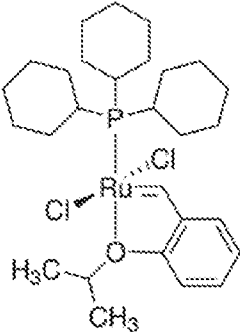
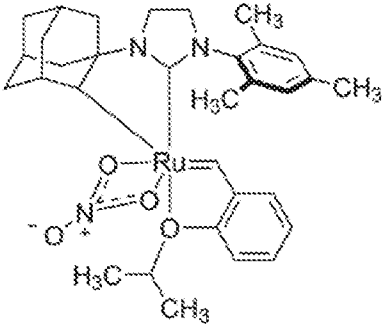
[0179] Catalysts useful in the methods of the invention also include those set forth in the following table:

Structure	Name
	dichloro[1,3-bis(2,6-isopropylphenyl)-2-imidazolidinylidene](benzylidene)(tricyclohexylphosphine)ruthenium(II)

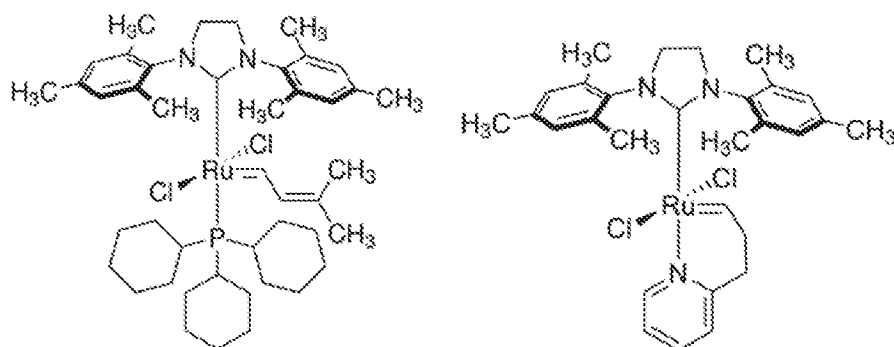
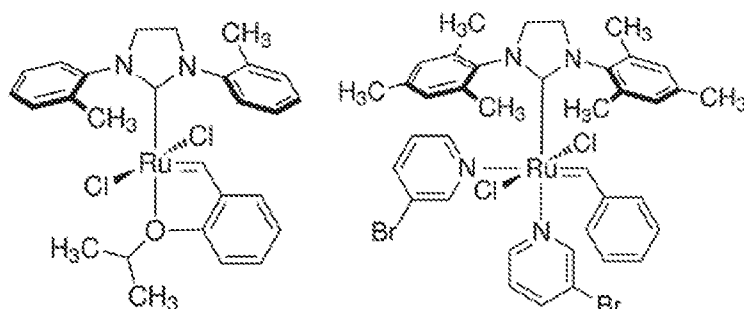
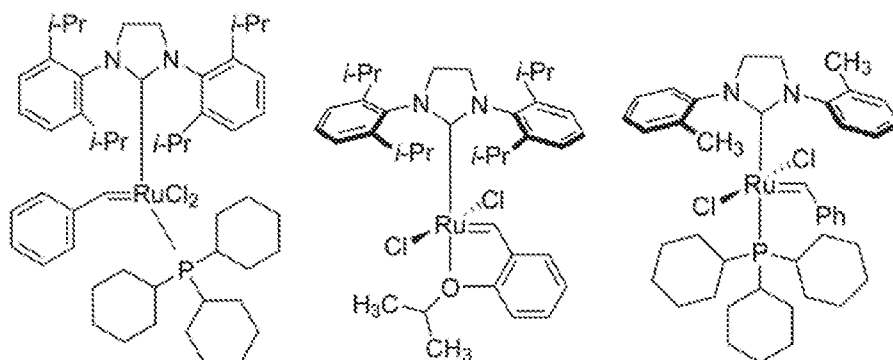
Structure	Name
	<p>dichloro[1,3-bis(2,6-isopropylphenyl)-2-imidazolidinylidene](2-isopropoxyphenylmethylene)ruthenium(II)</p>
	<p>dichloro[1,3-bis(2-methylphenyl)-2-imidazolidinylidene](benzylidene)(tricyclohexylphosphine)ruthenium(II)</p>
	<p>dichloro[1,3-bis(2-methylphenyl)-2-imidazolidinylidene](2-isopropoxyphenylmethylene)ruthenium(II)</p>
	<p>dichloro[1,3-bis(2,4,6-trimethylphenyl)-2-imidazolidinylidene](benzylidene)bis(3-bromopyridine)ruthenium(II)</p>

Structure	Name
	<p>dichloro[1,3-bis(2,4,6-trimethylphenyl)-2-imidazolidinylidene](3-methyl-2-butenylidene) (tricyclohexylphosphine) ruthenium(II)</p>
	<p>dichloro[1,3-bis(2,4,6-trimethylphenyl)-2-imidazolidinylidene][3-(2-pyridinyl)propylidene]ruthenium(II)</p>
	<p>dichloro[1,3-bis(2,4,6-trimethylphenyl)-2-imidazolidinylidene][(tricyclohexylphosphoryl)methylidene]ruthenium(II) tetrafluoroborate</p>
	<p>dichloro(3-methyl-2-butenylidene) bis(tricyclohexylphosphine)ruthenium(II)</p>

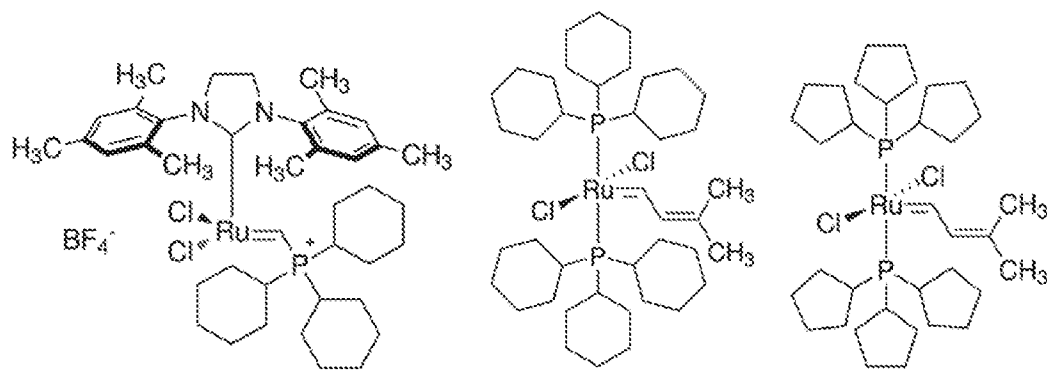
Structure	Name
	<p>dichloro(3-methyl-2-butenylidene) bis(tricyclopentylphosphine)ruthenium(II)</p>
	<p>dichloro(tricyclohexylphosphine)[(tricyclohexylphosphoranyl)methylidene]ruthenium(II) tetrafluoroborate</p>
	<p>bis(tricyclohexylphosphine) benzylidene ruthenium(IV) dichloride</p>
	<p>[1,3-bis-(2,4,6-trimethylphenyl)-2- imidazolidinylidene]dichloro(phenylmethylene)(tricyclohexylphosphine)ruthenium</p>

Structure	Name
	<p>(1,3-bis-(2,4,6-trimethylphenyl)-2-imidazolidinylidene)dichloro(<i>o</i>-isopropoxyphenylmethylene)ruthenium</p>
	<p>dichloro(<i>o</i>-isopropoxyphenylmethylene)(tricyclohexylphosphine)ruthenium(II)</p>
	<p>[2-(1-methylethoxy-<i>O</i>)phenylmethyl-<i>C</i>](nitrate-<i>O,O'</i>){<i>rel</i>-(2<i>R</i>,5<i>R</i>,7<i>R</i>)-adamantane-2,1-diy}[3-(2,4,6-trimethylphenyl)-1-imidazolidinyl-2-ylidene]}ruthenium</p>

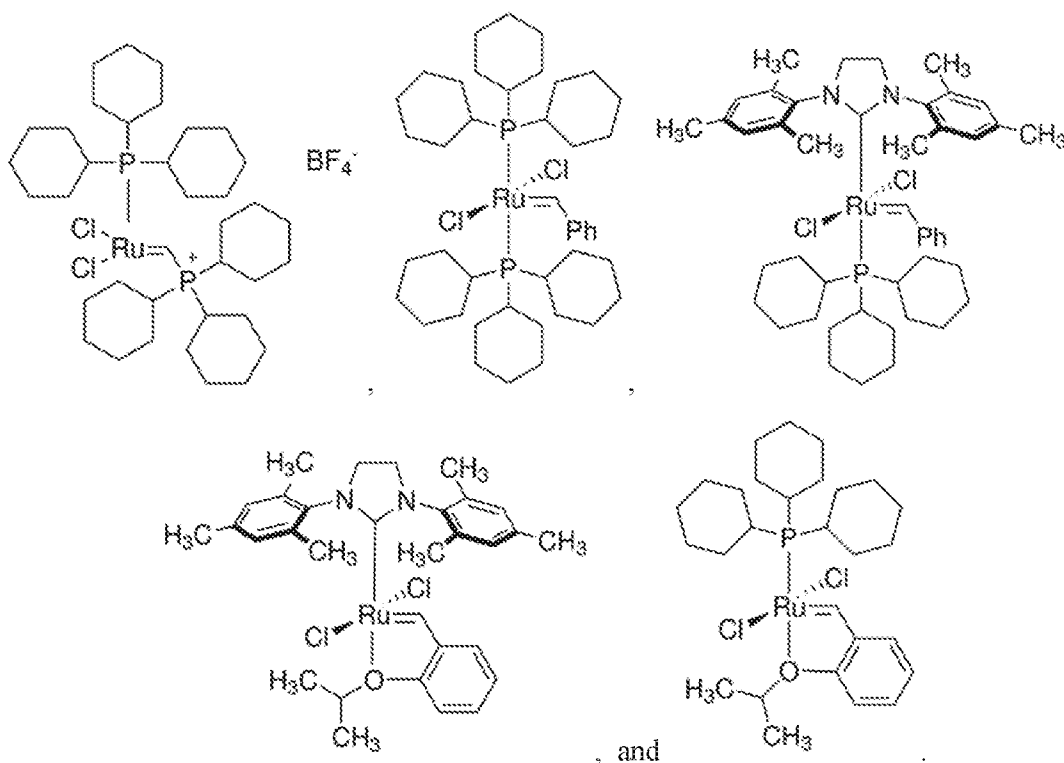
[0180] In some embodiments, the metathesis product comprises an *E* olefin, and the metathesis catalyst is selected from the group consisting of:



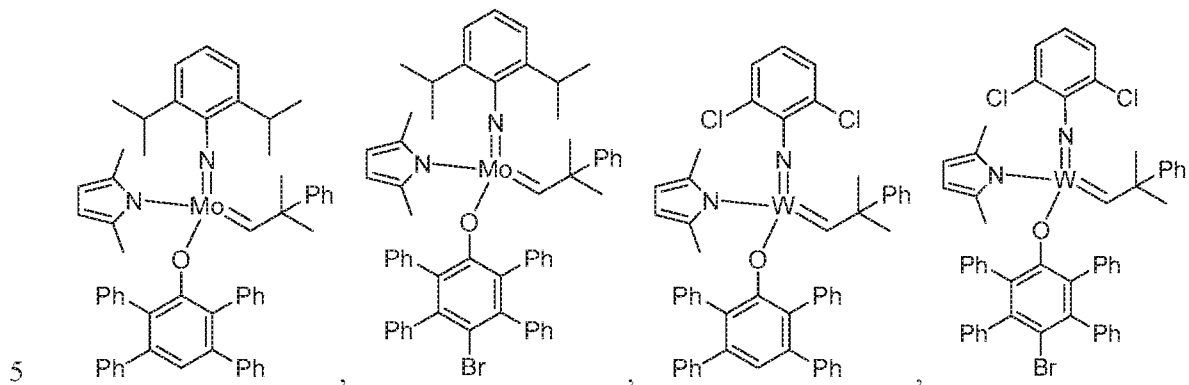
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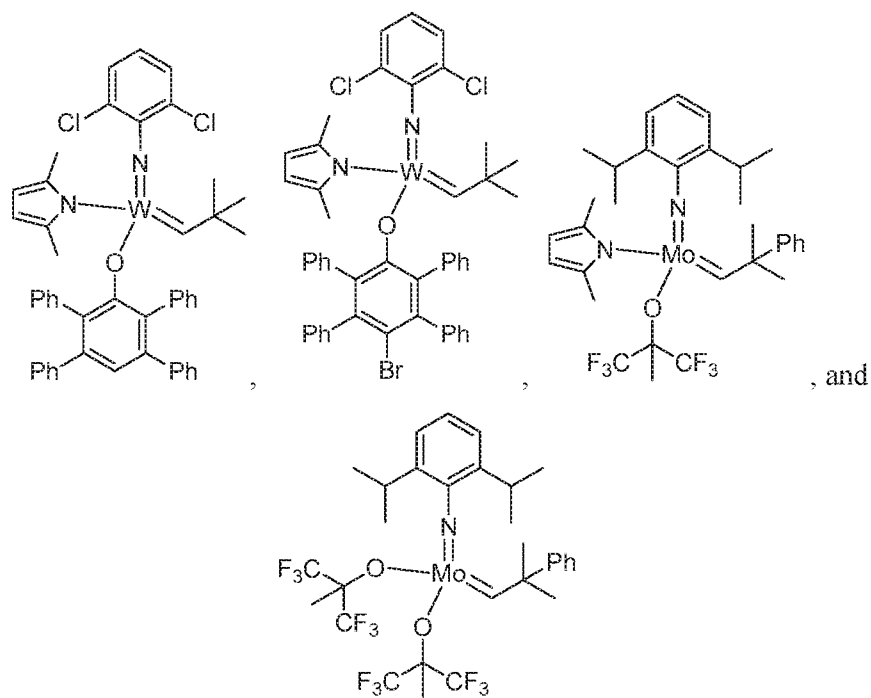




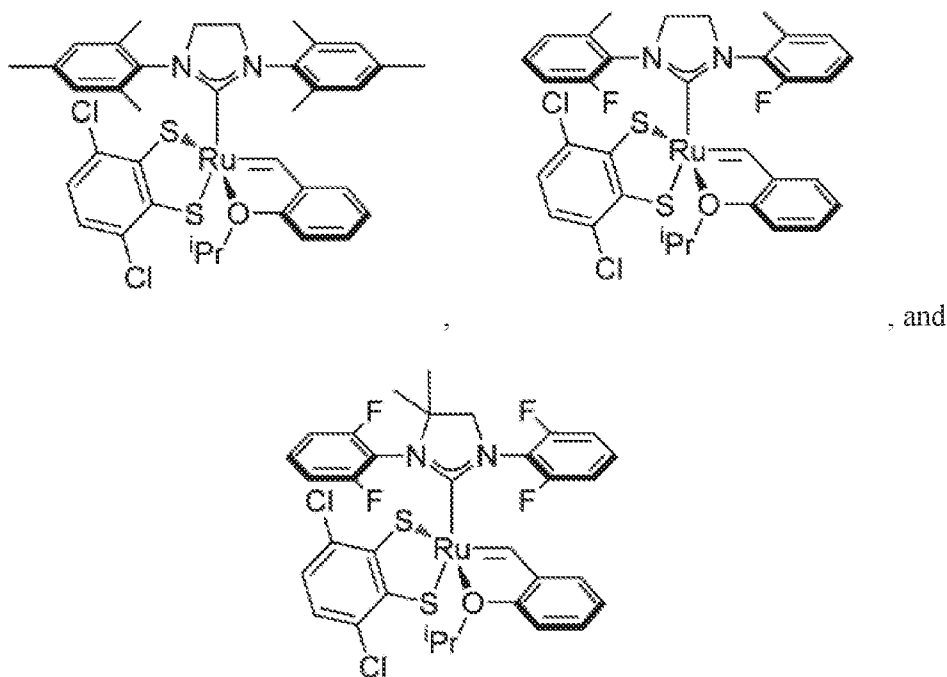


[0181] In some embodiments, the metathesis product comprises an *E* olefin, and the metathesis catalyst is selected from the group consisting of:





[0182] In some embodiments, the metathesis product comprises an *E* olefin, and the metathesis catalyst is selected from the group consisting of:



[0183] Catalysts useful in the methods of the invention also include those described in U.S. Pat. Appl. Pub. No. 2008/0009598; U.S. Pat. Appl. Pub. No. 2008/0207911; U.S. Pat. Appl.

Pub. No. 2008/0275247; U.S. Pat. Appl. Pub. No. 2011/0040099; U.S. Pat. Appl. Pub. No. 2011/0282068; and U.S. Pat. Appl. Pub. No. 2015/0038723.

[0184] Catalysts useful in the methods of the invention include those described in International Pub. No. WO 2007/140954; U.S. Pat. Appl. Pub. No. 2008/0221345; 5 International Pub. No. WO 2010/037550; U.S. Pat. Appl. Pub. No. 2010/0087644; U.S. Pat. Appl. Pub. No. 2010/0113795; U.S. Pat. Appl. Pub. No. 2010/0174068; International Pub. No. WO 2011/091980; International Pub. No. WO 2012/168183; U.S. Pat. Appl. Pub. No. 2013/0079515; U.S. Pat. Appl. Pub. No. 2013/0144060; U.S. Pat. Appl. Pub. No. 2013/0211096; International Pub. No. WO 2013/135776; International Pub. No. WO 10 2014/001291; International Pub. No. WO 2014/067767; U.S. Pat. Appl. Pub. No. 2014/0171607; and U.S. Pat. Appl. Pub. No. 2015/0045558.

#### Metathesis Reaction Conditions

[0185] The catalyst is typically provided in the reaction mixture in a sub-stoichiometric amount (*e.g.*, catalytic amount). In certain embodiments, that amount is in the range of about 15 0.001 to about 50 mol % with respect to the limiting reagent of the chemical reaction, depending upon which reagent is in stoichiometric excess. In some embodiments, the catalyst is present in less than or equal to about 40 mol % relative to the limiting reagent. In some embodiments, the catalyst is present in less than or equal to about 30 mol % relative to the limiting reagent. In some embodiments, the catalyst is present in less than about 20 mol %, 20 less than about 10 mol %, less than about 5 mol %, less than about 2.5 mol %, less than about 1 mol %, less than about 0.5 mol %, less than about 0.1 mol %, less than about 0.015 mol %, less than about 0.01 mol %, less than about 0.0015 mol %, or less, relative to the limiting reagent. In some embodiments, the catalyst is present in the range of about 2.5 mol % to 25 about 5 mol %, relative to the limiting reagent. In some embodiments, the reaction mixture contains about 0.5 mol% catalyst. In the case where the molecular formula of the catalyst complex includes more than one metal, the amount of the catalyst complex used in the reaction may be adjusted accordingly.

[0186] In some cases, the methods described herein can be performed in the absence of solvent (*e.g.*, neat). In some cases, the methods can include the use of one or more solvents. 30 Examples of solvents that may be suitable for use in the invention include, but are not limited to, benzene, *p*-cresol, toluene, xylene, diethyl ether, glycol, diethyl ether, petroleum ether, hexane, cyclohexane, pentane, methylene chloride, chloroform, carbon tetrachloride, dioxane,

tetrahydrofuran (THF), dimethyl sulfoxide, dimethylformamide, hexamethyl-phosphoric triamide, ethyl acetate, pyridine, triethylamine, picoline, and the like, as well as mixtures thereof. In some embodiments, the solvent is selected from benzene, toluene, pentane, methylene chloride, and THF. In certain embodiments, the solvent is benzene.

5 [0187] In some embodiments, the method is performed under reduced pressure. This may be advantageous in cases where a volatile byproduct, such as ethylene, may be produced during the course of the metathesis reaction. For example, removal of the ethylene byproduct from the reaction vessel may advantageously shift the equilibrium of the metathesis reaction towards formation of the desired product. In some embodiments, the method is performed at  
10 a pressure of about less than 760 torr. In some embodiments, the method is performed at a pressure of about less than 700 torr. In some embodiments, the method is performed at a pressure of about less than 650 torr. In some embodiments, the method is performed at a pressure of about less than 600 torr. In some embodiments, the method is performed at a pressure of about less than 550 torr. In some embodiments, the method is performed at  
15 a pressure of about less than 500 torr. In some embodiments, the method is performed at a pressure of about less than 450 torr. In some embodiments, the method is performed at a pressure of about less than 400 torr. In some embodiments, the method is performed at a pressure of about less than 350 torr. In some embodiments, the method is performed at a pressure of about less than 300 torr. In some embodiments, the method is performed at a  
20 pressure of about less than 250 torr. In some embodiments, the method is performed at a pressure of about less than 200 torr. In some embodiments, the method is performed at a pressure of about less than 150 torr. In some embodiments, the method is performed at a pressure of about less than 100 torr. In some embodiments, the method is performed at a  
25 pressure of about less than 90 torr. In some embodiments, the method is performed at a pressure of about less than 80 torr. In some embodiments, the method is performed at a pressure of about less than 70 torr. In some embodiments, the method is performed at a pressure of about less than 60 torr. In some embodiments, the method is performed at a pressure of about less than 50 torr. In some embodiments, the method is performed at a  
30 pressure of about less than 40 torr. In some embodiments, the method is performed at a pressure of about less than 30 torr. In some embodiments, the method is performed at a pressure of about less than 20 torr. In some embodiments, the method is performed at a pressure of about 20 torr.

[0188] In some embodiments, the method is performed at a pressure of about 19 torr. In some embodiments, the method is performed at a pressure of about 18 torr. In some embodiments, the method is performed at a pressure of about 17 torr. In some embodiments, the method is performed at a pressure of about 16 torr. In some embodiments, the method is performed at a pressure of about 15 torr. In some embodiments, the method is performed at a pressure of about 14 torr. In some embodiments, the method is performed at a pressure of about 13 torr. In some embodiments, the method is performed at a pressure of about 12 torr. In some embodiments, the method is performed at a pressure of about 11 torr. In some embodiments, the method is performed at a pressure of about 10 torr. In some embodiments, the method is performed at a pressure of about 10 torr. In some embodiments, the method is performed at a pressure of about 9 torr. In some embodiments, the method is performed at a pressure of about 8 torr. In some embodiments, the method is performed at a pressure of about 7 torr. In some embodiments, the method is performed at a pressure of about 6 torr. In some embodiments, the method is performed at a pressure of about 5 torr. In some embodiments, the method is performed at a pressure of about 4 torr. In some embodiments, the method is performed at a pressure of about 3 torr. In some embodiments, the method is performed at a pressure of about 2 torr. In some embodiments, the method is performed at a pressure of about 1 torr. In some embodiments, the method is performed at a pressure of less than about 1 torr.

[0189] In some embodiments, the two metathesis reactants are present in equimolar amounts. In some embodiments, the two metathesis reactants are not present in equimolar amounts. In certain embodiments, the two reactants are present in a molar ratio of about 20:1, 19:1, 18:1, 17:1, 16:1, 15:1, 14:1, 13:1, 12:1, 11:1, 10:1, 9:1, 8:1, 7:1, 6:1, 5:1, 4:1, 3:1, 2:1, 1:1, 1:2, 1:3, 1:4, 1:5, 1:6, 1:7, 1:8, 1:9, 1:10, 1:11, 1:12, 1:13, 1:14, 1:15, 1:16, 1:17, 1:18, 1:19, or 1:20. In certain embodiments, the two reactants are present in a molar ratio of about 10:1. In certain embodiments, the two reactants are present in a molar ratio of about 7:1. In certain embodiments, the two reactants are present in a molar ratio of about 5:1. In certain embodiments, the two reactants are present in a molar ratio of about 2:1. In certain embodiments, the two reactants are present in a molar ratio of about 1:10. In certain embodiments, the two reactants are present in a molar ratio of about 1:7. In certain embodiments, the two reactants are present in a molar ratio of about 1:5. In certain embodiments, the two reactants are present in a molar ratio of 1:2.

[0190] In some embodiments, one molar equivalent of the olefin is contacted with one molar equivalent of the metathesis reaction partner. In some embodiments, about 1.5, 2, 2.5, or 3 molar equivalents of the olefin is contacted with one molar equivalent of the metathesis reaction partner. In some embodiments, about 1.5 molar equivalents of the olefin is contacted with one molar equivalent of the metathesis reaction partner.

[0191] In general, the reactions with many of the metathesis catalysts disclosed herein provide yields better than 15%, *e.g.*, better than 50%, better than 75%, or better than 90%. In addition, the reactants and products are chosen to provide at least a 5°C difference, *e.g.*, a greater than 20°C difference, or a greater than 40°C difference in boiling points. Additionally, the use of metathesis catalysts allows for much faster product formation than byproduct, and it can be desirable to run these reactions as quickly as practical. In particular, the reactions are performed in less than about 24 hours, *e.g.*, less than 12 hours, or less than 8 hours, or less than 4 hours. Advantageously, the methods of the invention provide metathesis products on a scale ranging from a few milligrams to hundreds of kilograms or more. For example, the methods can be conducted using around 1-10 grams of the olefin according to Formula I, or around 10-100 grams of the olefin according to Formula I, or around 100-500 grams of the olefin according to Formula I, or around 500-1000 grams of the olefin according to Formula I. The methods can be conducted using at least 1, 5, 10, 25, 50, 100, or 1,000 kilograms of starting material. The metathesis reactions can be conducted using a metathesis reactor as described, for example, in WO 2011/046872, which reactor can be operated in conjunction with one or more downstream separation units for separating and/or recycling particular product or byproduct streams (*e.g.*, an olefin stream, a C<sub>2</sub>-C<sub>3</sub> compound stream, or a C<sub>3</sub>-C<sub>5</sub> compound stream). The metathesis reactor and separation unit(s) can be operated in conjunction with one or more adsorbent beds to facilitate the separation of the metathesized products from the catalyst, as well as washing and drying units for purification of desired products. The metathesis, reduction, and acylation reactions can be conducted to provide products on the scale of metric tons.

[0192] One of skill in the art will appreciate that the time, temperature and solvent can depend on each other, and that changing one can require changing the others to prepare the metathesis products in the methods of the invention. The metathesis steps can proceed at a variety of temperatures and times. In general, reactions in the methods of the invention are conducted using reaction times of several minutes to several days. For example, reaction times of from about 12 hours to about 7 days can be used. In some embodiments, reaction

times of 1-5 days can be used. In some embodiments, reaction times of from about 10 minutes to about 10 hours can be used. In general, reactions in the methods of the invention are conducted at a temperature of from about 0 °C to about 200 °C. For example, reactions can be conducted at 15-100 °C. In some embodiments, reaction can be conducted at 20-80  
5 °C. In some embodiments, reactions can be conducted at 100-150 °C.

[0193] The olefins, fatty alcohols, fatty acid esters, and other materials used in the methods of the invention can be obtained from any suitable source. In some embodiments, the metathesis reaction partners used in the methods of the invention are obtained from a natural oil and/or a derivative thereof. Representative examples of natural oils for use in accordance  
10 with the present teachings include but are not limited to vegetable oils, algal oils, animal fats, tall oils (*e.g.*, by-products of wood pulp manufacture), derivatives of these oils, and the like, and combinations thereof. Representative examples of vegetable oils for use in accordance with the present teachings include but are not limited to canola oil, rapeseed oil, coconut oil, corn oil, cottonseed oil, olive oil, palm oil, peanut oil, safflower oil, sesame oil, soybean oil,  
15 sunflower oil, high oleic sunflower oil, linseed oil, palm kernel oil, tung oil, jatropha oil, jojoba oil, mustard oil, pennycress oil, camelina oil, hemp oil, castor oil, and the like, and combinations thereof. Representative examples of animal fats for use in accordance with the present teachings include but are not limited to lard, tallow, poultry fat, yellow grease, brown grease, fish oil, and the like, and combinations thereof. The natural oil can be refined,  
20 bleached, and/or deodorized.

[0194] Representative examples of natural oil derivatives for use in accordance with the method of the invention include, but are not limited to, gums, phospholipids, soapstock, acidulated soapstock, distillate or distillate sludge, fatty acids, fatty acid esters (*e.g.*, non-limiting examples such as 2-ethylhexyl ester, *etc.*), hydroxy-substituted variations thereof,  
25 and the like, and combinations thereof. In some embodiments, the natural oil derivative comprises an ester. In some embodiments, the derivative is selected from the group consisting of a monoacylglyceride (MAG), a diacylglyceride (DAG), a triacylglyceride (TAG), and combinations thereof. In some embodiments, the natural oil derivative comprises a fatty acid methyl ester (FAME) derived from the glyceride of the natural oil.

[0195] In some embodiments, a feedstock includes canola or soybean oil, *e.g.*, refined, bleached, and/or deodorized soybean oil (*i.e.*, RBD soybean oil). Soybean oil typically contains about 95% weight or greater (*e.g.*, 99% weight or greater) triglycerides of fatty

acids. Major fatty acids in the polyol esters of soybean oil include saturated fatty acids, including palmitic acid (hexadecanoic acid) and stearic acid (octadecanoic acid), and unsaturated fatty acids, including oleic acid (9-octadecenoic acid), linoleic acid (9, 12-octadecadienoic acid), and linolenic acid (9, 12, 15-octadecatrienoic acid).

5 [0196] In some embodiments, materials to be reacted in a metathesis reaction—including those derived from natural oils—will contain one or more contaminants with the potential to adversely affect the performance of a metathesis catalyst. Such contaminants can be referred to as “catalyst poisons” or “catalyst poisoning contaminants.” The contaminant levels can be reduced according to the methods described herein. In some embodiments, the material  
10 comprises a plurality of contaminants and the method comprises reducing levels of two or more of the contaminants. In some embodiments, the material comprises a plurality of contaminants and the method comprises reducing levels of three or more of the contaminants. In some embodiments, the material comprises a plurality of contaminants and the method comprises reducing levels of four or more of the contaminants. In some embodiments, the  
15 material comprises a plurality of contaminants and the method comprises reducing levels of five or more of the contaminants.

[0197] Representative contaminants include but are not limited to water, peroxides, peroxide decomposition products, hydroperoxides, protic materials, polar materials, Lewis basic catalyst poisons, and the like, and combinations thereof. It is to be understood that some  
20 contaminants may properly be classified in multiple categories (*e.g.*, an alcohol can be considered both a protic material and a polar material). It is to be further understood that different catalysts may have different susceptibilities to a particular contaminant, and that a contaminant that adversely affects the performance of one catalyst (*e.g.*, a ruthenium-based catalyst) may or may not affect (to a similar extent or to any extent whatsoever) a different  
25 catalyst (*e.g.*, a molybdenum-based catalyst).

[0198] Representative protic materials that may be found as contaminants in a substrate that is to be reacted in a metathesis reaction include but are not limited to materials having a hydrogen atom bonded to oxygen (*e.g.*, carboxylic acids, alcohols, and the like) and/or a hydrogen atom bonded to nitrogen (*e.g.*, primary amines, secondary amines, and the like). In  
30 some embodiments, particularly though not exclusively in natural oil substrates, a protic material contaminant may comprise a carboxylic acid functional group, a hydroxyl functional group, or a combination thereof. In some embodiments, the protic material is selected from



the group consisting of free fatty acids, hydroxyl-containing materials, MAGs, DAGs, and the like, and combinations thereof.

[0199] Representative polar materials that may be found as contaminants in a substrate that is to be reacted in a metathesis reaction include but are not limited to heteroatom-containing materials such as oxygenates. In some embodiments, the polar material is selected from the group consisting of alcohols, aldehydes, ethers, and the like, and combinations thereof.

[0200] Representative Lewis basic catalyst poisons that may be found as contaminants in a substrate that is to be reacted in a metathesis reaction include but are not limited to heteroatom-containing materials. In some embodiments, the Lewis basic catalyst poisons are selected from the group consisting of N-containing materials, P-containing materials, S-containing materials, and the like, and combinations thereof.

[0201] Reaction materials containing contaminants can be treated with one or more conditioning agents that mitigate potentially adverse effects of one or more of the contaminants. Conditioning agents that can be used in the methods of the invention (individually, or in combination sequentially or simultaneously) include heat, molecular sieves, alumina (aluminum oxide), silica gel, montmorillonite clay, fuller's earth, bleaching clay, diatomaceous earth, zeolites, kaolin, activated metals (*e.g.*, Cu, Mg, and the like), acid anhydrides (*e.g.*, acetic anhydride and the like), activated carbon (*i.e.*, activated charcoal), soda ash, metal hydrides (*e.g.*, alkaline earth metal hydrides such as  $\text{CaH}_2$  and the like), metal sulfates (*e.g.*, alkaline earth metal sulfates such as calcium sulfate, magnesium sulfate, and the like; alkali metal sulfates such as potassium sulfate, sodium sulfate, and the like; and other metal sulfates such as aluminum sulfate, potassium magnesium sulfate, and the like), metal halides (*e.g.*, alkali earth metal halides such as potassium chloride and the like), metal carbonates (*e.g.*, calcium carbonate, sodium carbonate, and the like), metal silicates (*e.g.*, magnesium silicate and the like), phosphorous pentoxide, metal aluminum hydrides (*e.g.*, alkali metal aluminum hydrides such as  $\text{LiAlH}_4$ ,  $\text{NaAlH}_4$ , and the like), alkyl aluminum hydrides (*e.g.*, DIBALH), metal borohydrides (*e.g.*, alkali metal borohydrides such as  $\text{LiBH}_4$ ,  $\text{NaBH}_4$ , and the like), organometallic reagents (*e.g.*, Grignard reagents; organolithium reagents such as *n*-butyl lithium, *t*-butyl lithium, *sec*-butyl lithium; trialkyl aluminums such as triethyl aluminum, tributyl aluminum, triisobutyl aluminum, triisopropyl aluminum, trioctyl aluminum, and the like, metal amides (*e.g.*, lithium diisopropyl amide, metal

bis(trimethylsilyl)amides such as KHMDS, and the like), palladium on carbon (Pd/C) catalysts, and combinations thereof.

[0202] In some embodiments, the conditioning agent is a metal alkyl compound. In some embodiments, the metal, M, can be lithium, sodium, potassium, magnesium, calcium, zinc, cadmium, aluminum, or gallium. Examples of suitable alkyl radicals, R, include, but are not limited to, methyl, ethyl, butyl, hexyl, decyl, tetradecyl, and eicosyl. Examples of metal alkyl compounds include, but are not limited to,  $Mg(CH_3)_2$ ,  $Mg(C_2H_5)_2$ ,  $Mg(C_2H_5)(C_4H_9)$ ,  $Mg(C_4H_9)_2$ ,  $Mg(C_6H_{13})_2$ ,  $Mg(C_{12}H_{25})_2$ ,  $Zn(CH_3)_2$ ,  $Zn(C_2H_5)_2$ ,  $Zn(C_4H_9)_2$ ,  $Zn(C_4H_9)(C_8H_{17})$ ,  $Zn(C_6H_{13})_2$ ,  $Zn(C_6H_5)_2$ ,  $Al(C_2H_5)_3$ ,  $Al(CH_3)_3$ ,  $Al(n-C_4H_9)_3$ ,  $Al(C_8H_{17})_3$ ,  $Al(iso-C_4H_9)_3$ ,  $Al(C_{12}H_{25})_3$ , and combinations thereof. Metal alkyl compounds also include substances having one or more halogen or hydride groups, such as ethylaluminum dichloride, diethylaluminum chloride, diethylaluminum hydride, Grignard reagents, diisobutylaluminum hydride, and the like.

[0203] In some embodiments, the treating of the metathesis reaction material (*e.g.*, a natural oil or a natural oil derivative) can include contacting the reaction material with a metal alkyl compound and, either simultaneously or separately, contacting the reaction material with a hydride-containing compound. In some embodiments, where the reaction material is contacted simultaneously with the metal alkyl compound and the hydride-containing compound, the hydride-containing compounds can be included in the metal alkyl compound. For example, in some instances, processes used to make certain metal alkyl compounds, such as trialkyl aluminum compounds, can lead to the formation of a certain concentration of hydride-containing compounds. In other embodiments, however, the metal alkyl compounds can be combined with one or more hydride-containing compounds. Or, in some embodiments, the metathesis reaction material can be treated by the hydride-containing compounds in a separate treatment step, which can be performed before, after, or both before and after, treatment of the reaction material with the metal alkyl compounds.

[0204] Any suitable hydride-containing compounds can be used. In some embodiments, the hydride-containing compounds are selected from the group consisting of metal aluminum hydrides (*e.g.*, alkali metal aluminum hydrides such as  $LiAlH_4$ ,  $NaAlH_4$ , and the like), alkyl aluminum hydrides (*e.g.*, DIBALH), and combinations thereof. In some embodiments, the hydride-containing compound is an alkyl aluminum hydride, such as DIBALH.

[0205] In some embodiments, contacting the metathesis reaction material with the hydride-containing compound occurs in the same step as contacting the reaction material with the metal alkyl compound. In some embodiments, the weight-to-weight ratio of the metal alkyl compound to the hydride-containing compound in the treatment composition is from 2:1, or from 5:1, or from 10:1, or from 15:1, or from 20:1 to 1000:1. In some embodiments, the weight-to-weight ratio of the metal alkyl compound to the hydride-containing compound in the treatment composition is at least 2:1, or at least 5:1, or at least 10:1, or at least 15:1, or at least 20:1.

[0206] In certain instances, the efficacy of the metathesis catalyst can be improved (e.g., the turnover number can be increased or the overall catalyst loading may be decreased) through slow addition of the catalyst to a substrate. The overall catalyst loading can be decreased by at least 10%, at least 20%, or at least 30% when administered slowly to achieve the same turnover number as a single, full batch loading. The slow addition of overall catalyst loading can include adding fractional catalyst loadings to the reaction materials at an average rate of approximately 10 ppm by weight of catalyst per hour (ppmwt/hr), 5 ppmwt/hr, 1 ppmwt/hr, 0.5 ppmwt/hr, 0.1 ppmwt/hr, 0.05 ppmwt/hr, or 0.01 ppmwt/hr. In some embodiments, the catalyst is slowly added at a rate of between about 0.01-10 ppmwt/hr, 0.05-5 ppmwt/hr, or 0.1-1 ppmwt/hr. The slow addition of the catalyst can be conducted in batch loadings at frequencies of every 5 minutes, 15 minutes, 30 minutes, 1 hour, 2 hours, 4 hours, 12 hours, or 1 day. In other embodiments, the slow addition is conducted in a continuous addition process.

### Pheromone Products

[0207] As described above, a number of the fatty olefin derivatives obtained via the methods of the invention can be used as insect pheromones or pheromone precursor materials. The precursor materials and pheromone products include, for example, the compounds listed in Table 1 and Table 6. The method can be used for synthesizing one or more of the pheromones listed in Table 7.

Table 7. Pheromone products.

Name	Name	Name
(E)-2-Decen-1-ol	(Z,Z)-5,9-Tridecadienyl acetate	(Z)-10-Hexadecenal
(E)-2-Decenyl acetate	(Z,Z)-7,11-Tridecadienyl acetate	(E)-11-Hexadecen-1-ol

Name	Name	Name
(E)-2-Decenal	(E,Z,Z)-4,7,10-Tridecatrienyl acetate	(E)-11-Hexadecenyl acetate
(Z)-2-Decen-1-ol	(E)-3-Tetradecen-1-ol	(E)-11-Hexadecenal
(Z)-2-Decenyl acetate	(E)-3-Tetradecenyl acetate	(Z)-11-Hexadecen-1-ol
(Z)-2-Decenal	(Z)-3-Tetradecen-1-ol	(Z)-11-Hexadecenyl acetate
(E)-3-Decen-1-ol	(Z)-3-Tetradecenyl acetate	(Z)-11-Hexadecenal
(Z)-3-Decenyl acetate	(E)-5-Tetradecen-1-ol	(Z)-12-Hexadecenyl acetate
(Z)-3-Decen-1-ol	(E)-5-Tetradecenyl acetate	(Z)-12-Hexadecenal
(Z)-4-Decen-1-ol	(E)-5-Tetradecenal	(E)-14-Hexadecenal
(E)-4-Decenyl acetate	(Z)-5-Tetradecen-1-ol	(Z)-14-Hexadecenyl acetate
(Z)-4-Decenyl acetate	(Z)-5-Tetradecenyl acetate	(E,E)-1,3-Hexadecadien-1-ol
(Z)-4-Decenal	(Z)-5-Tetradecenal	(E,Z)-4,6-Hexadecadien-1-ol
(E)-5-Decen-1-ol	(E)-6-Tetradecenyl acetate	(E,Z)-4,6-Hexadecadienyl acetate
(E)-5-Decenyl acetate	(Z)-6-Tetradecenyl acetate	(E,Z)-4,6-Hexadecadienal
(Z)-5-Decen-1-ol	(E)-7-Tetradecen-1-ol	(E,Z)-6,11-Hexadecadienyl acetate
(Z)-5-Decenyl acetate	(E)-7-Tetradecenyl acetate	(E,Z)-6,11-Hexadecadienal
(Z)-5-Decenal	(Z)-7-Tetradecen-1-ol	(Z,Z)-7,10-Hexadecadien-1-ol
(E)-7-Decenyl acetate	(Z)-7-Tetradecenyl acetate	(Z,Z)-7,10-Hexadecadienyl acetate
(Z)-7-Decenyl acetate	(Z)-7-Tetradecenal	(Z,E)-7,11-Hexadecadien-1-ol
(E)-8-Decen-1-ol	(E)-8-Tetradecenyl acetate	(Z,E)-7,11-Hexadecadienyl acetate
(E,E)-2,4-Decadienal	(Z)-8-Tetradecen-1-ol	(Z,E)-7,11-Hexadecadienal
(E,Z)-2,4-Decadienal	(Z)-8-Tetradecenyl acetate	(Z,Z)-7,11-Hexadecadien-1-ol
(Z,Z)-2,4-Decadienal	(Z)-8-Tetradecenal	(Z,Z)-7,11-Hexadecadienyl acetate
(E,E)-3,5-Decadienyl acetate	(E)-9-Tetradecen-1-ol	(Z,Z)-7,11-Hexadecadienal
(Z,E)-3,5-Decadienyl acetate	(E)-9-Tetradecenyl acetate	(Z,Z)-8,10-Hexadecadienyl acetate
(Z,Z)-4,7-Decadien-1-ol	(Z)-9-Tetradecen-1-ol	(E,Z)-8,11-Hexadecadienal
(Z,Z)-4,7-Decadienyl acetate	(Z)-9-Tetradecenyl acetate	(E,E)-9,11-Hexadecadienal
(E)-2-Undecenyl acetate	(Z)-9-Tetradecenal	(E,Z)-9,11-Hexadecadienyl acetate
(E)-2-Undecenal	(E)-10-Tetradecenyl acetate	(E,Z)-9,11-Hexadecadienal
(Z)-5-Undecenyl acetate	(Z)-10-Tetradecenyl acetate	(Z,E)-9,11-Hexadecadienal

Name	Name	Name
(Z)-7-Undecenyl acetate	(E)-11-Tetradecen-1-ol	(Z,Z)-9,11-Hexadecadienal
(Z)-8-Undecenyl acetate	(E)-11-Tetradecenyl acetate	(E,E)-10,12-Hexadecadien-1-ol
(Z)-9-Undecenyl acetate	(E)-11-Tetradecenol	(E,E)-10,12-Hexadecadienyl acetate
(E)-2-Dodecenal	(Z)-11-Tetradecen-1-ol	(E,E)-10,12-Hexadecadienal
(Z)-3-Dodecen-1-ol	(Z)-11-Tetradecenyl acetate	(E,Z)-10,12-Hexadecadien-1-ol
(E)-3-Dodecenyl acetate	(Z)-11-Tetradecenol	(E,Z)-10,12-Hexadecadienyl acetate
(Z)-3-Dodecenyl acetate	(E)-12-Tetradecenyl acetate	(E,Z)-10,12-Hexadecadienal
(E)-4-Dodecenyl acetate	(Z)-12-Tetradecenyl acetate	(Z,E)-10,12-Hexadecadienyl acetate
(E)-5-Dodecen-1-ol	(E,E)-2,4-Tetradecadienal	(Z,E)-10,12-Hexadecadienal
(E)-5-Dodecenyl acetate	(E,E)-3,5-Tetradecadienyl acetate	(Z,Z)-10,12-Hexadecadienal
(Z)-5-Dodecen-1-ol	(E,Z)-3,5-Tetradecadienyl acetate	(E,E)-11,13-Hexadecadien-1-ol
(Z)-5-Dodecenyl acetate	(Z,E)-3,5-Tetradecadienyl acetate	(E,E)-11,13-Hexadecadienyl acetate
(Z)-5-Dodecenol	(E,Z)-3,7-Tetradecadienyl acetate	(E,E)-11,13-Hexadecadienal
(E)-6-Dodecen-1-ol	(E,Z)-3,8-Tetradecadienyl acetate	(E,Z)-11,13-Hexadecadien-1-ol
(Z)-6-Dodecenyl acetate	(E,Z)-4,9-Tetradecadienyl acetate	(E,Z)-11,13-Hexadecadienyl acetate
(E)-6-Dodecenol	(E,Z)-4,9-Tetradecadienal	(E,Z)-11,13-Hexadecadienal
(E)-7-Dodecen-1-ol	(E,Z)-4,10-Tetradecadienyl acetate	(Z,E)-11,13-Hexadecadien-1-ol
(E)-7-Dodecenyl acetate	(E,E)-5,8-Tetradecadienal	(Z,E)-11,13-Hexadecadienyl acetate
(E)-7-Dodecenol	(Z,Z)-5,8-Tetradecadien-1-ol	(Z,E)-11,13-Hexadecadienal
(Z)-7-Dodecen-1-ol	(Z,Z)-5,8-Tetradecadienyl acetate	(Z,Z)-11,13-Hexadecadien-1-ol
(Z)-7-Dodecenyl acetate	(Z,Z)-5,8-Tetradecadienal	(Z,Z)-11,13-Hexadecadienyl acetate
(Z)-7-Dodecenol	(E,E)-8,10-Tetradecadien-1-ol	(Z,Z)-11,13-Hexadecadienal
(E)-8-Dodecen-1-ol	(E,E)-8,10-Tetradecadienyl acetate	(E,E)-10,14-Hexadecadienal
(E)-8-Dodecenyl acetate	(E,E)-8,10-Tetradecadienal	(Z,E)-11,14-Hexadecadienyl acetate
(E)-8-Dodecenol	(E,Z)-8,10-Tetradecadienyl acetate	(E,E,Z)-4,6,10-Hexadecatrien-1-ol

Name	Name	Name
(Z)-8-Dodecen-1-ol	(E,Z)-8,10-Tetradecadienal	(E,E,Z)-4,6,10-Hexadecatrienyl acetate
(Z)-8-Dodecanyl acetate	(Z,E)-8,10-Tetradecadien-1-ol	(E,Z,Z)-4,6,10-Hexadecatrien-1-ol
(E)-9-Dodecen-1-ol	(Z,E)-8,10-Tetradecadienyl acetate	(E,Z,Z)-4,6,10-Hexadecatrienyl acetate
(E)-9-Dodecanyl acetate	(Z,Z)-8,10-Tetradecadienal	(E,E,Z)-4,6,11-Hexadecatrienyl acetate
(E)-9-Dodecenal	(E,E)-9,11-Tetradecadienyl acetate	(E,E,Z)-4,6,11-Hexadecatrienal
(Z)-9-Dodecen-1-ol	(E,Z)-9,11-Tetradecadienyl acetate	(Z,Z,E)-7,11,13-Hexadecatrienal
(Z)-9-Dodecanyl acetate	(Z,E)-9,11-Tetradecadien-1-ol	(E,E,E)-10,12,14-Hexadecatrienyl acetate
(Z)-9-Dodecenal	(Z,E)-9,11-Tetradecadienyl acetate	(E,E,E)-10,12,14-Hexadecatrienal
(E)-10-Dodecen-1-ol	(Z,E)-9,11-Tetradecadienal	(E,E,Z)-10,12,14-Hexadecatrienyl acetate
(E)-10-Dodecanyl acetate	(Z,Z)-9,11-Tetradecadien-1-ol	(E,E,Z)-10,12,14-Hexadecatrienal
(E)-10-Dodecenal	(Z,Z)-9,11-Tetradecadienyl acetate	(E,E,Z,Z)-4,6,11,13-Hexadecatetraenal
(Z)-10-Dodecen-1-ol	(Z,Z)-9,11-Tetradecadienal	(E)-2-Heptadecenal
(Z)-10-Dodecanyl acetate	(E,E)-9,12-Tetradecadienyl acetate	(Z)-2-Heptadecenal
(E,Z)-3,5-Dodecadienyl acetate	(Z,E)-9,12-Tetradecadien-1-ol	(E)-8-Heptadecen-1-ol
(Z,E)-3,5-Dodecadienyl acetate	(Z,E)-9,12-Tetradecadienyl acetate	(E)-8-Heptadecanyl acetate
(Z,Z)-3,6-Dodecadien-1-ol	(Z,E)-9,12-Tetradecadienal	(Z)-8-Heptadecen-1-ol
(E,E)-4,10-Dodecadienyl acetate	(Z,Z)-9,12-Tetradecadien-1-ol	(Z)-9-Heptadecenal
(E,E)-5,7-Dodecadien-1-ol	(Z,Z)-9,12-Tetradecadienyl acetate	(E)-10-Heptadecanyl acetate
(E,E)-5,7-Dodecadienyl acetate	(E,E)-10,12-Tetradecadien-1-ol	(Z)-11-Heptadecen-1-ol
(E,Z)-5,7-Dodecadien-1-ol	(E,E)-10,12-Tetradecadienyl acetate	(Z)-11-Heptadecanyl acetate
(E,Z)-5,7-Dodecadienyl acetate	(E,E)-10,12-Tetradecadienal	(E,E)-4,8-Heptadecadienyl acetate
(E,Z)-5,7-Dodecadienal	(E,Z)-10,12-Tetradecadienyl acetate	(Z,Z)-8,10-Heptadecadien-1-ol
(Z,E)-5,7-Dodecadien-1-ol	(Z,E)-10,12-Tetradecadienyl acetate	(Z,Z)-8,11-Heptadecadienyl acetate
(Z,E)-5,7-Dodecadienyl acetate	(Z,Z)-10,12-Tetradecadien-1-ol	(E)-2-Octadecanyl acetate

Name	Name	Name
(Z,E)-5,7-Dodecadienal	(Z,Z)-10,12-Tetradecadienyl acetate	(E)-2-Octadecenal
(Z,Z)-5,7-Dodecadienyl acetate	(E,Z,Z)-3,8,11-Tetradecatrienyl acetate	(Z)-2-Octadecenyl acetate
(Z,Z)-5,7-Dodecadienal	(E)-8-Pentadecen-1-ol	(Z)-2-Octadecenal
(E,E)-7,9-Dodecadienyl acetate	(E)-8-Pentadecenyl acetate	(E)-9-Octadecen-1-ol
(E,Z)-7,9-Dodecadien-1-ol	(Z)-8-Pentadecen-1-ol	(E)-9-Octadecenyl acetate
(E,Z)-7,9-Dodecadienyl acetate	(Z)-8-Pentadecenyl acetate	(E)-9-Octadecenal
(E,Z)-7,9-Dodecadienal	(Z)-9-Pentadecenyl acetate	(Z)-9-Octadecen-1-ol
(Z,E)-7,9-Dodecadien-1-ol	(E)-9-Pentadecenyl acetate	(Z)-9-Octadecenyl acetate
(Z,E)-7,9-Dodecadienyl acetate	(Z)-10-Pentadecenyl acetate	(Z)-9-Octadecenal
(Z,Z)-7,9-Dodecadien-1-ol	(Z)-10-Pentadecenal	(E)-11-Octadecen-1-ol
(Z,Z)-7,9-Dodecadienyl acetate	(E)-12-Pentadecenyl acetate	(E)-11-Octadecenal
(E,E)-8,10-Dodecadien-1-ol	(Z)-12-Pentadecenyl acetate	(Z)-11-Octadecen-1-ol
(E,E)-8,10-Dodecadienyl acetate	(Z,Z)-6,9-Pentadecadien-1-ol	(Z)-11-Octadecenyl acetate
(E,E)-8,10-Dodecadienal	(Z,Z)-6,9-Pentadecadienyl acetate	(Z)-11-Octadecenal
(E,Z)-8,10-Dodecadien-1-ol	(Z,Z)-6,9-Pentadecadienal	(E)-13-Octadecenyl acetate
(E,Z)-8,10-Dodecadienyl acetate	(E,E)-8,10-Pentadecadienyl acetate	(E)-13-Octadecenal
(E,Z)-8,10-Dodecadienal	(E,Z)-8,10-Pentadecadien-1-ol	(Z)-13-Octadecen-1-ol
(Z,E)-8,10-Dodecadien-1-ol	(E,Z)-8,10-Pentadecadienyl acetate	(Z)-13-Octadecenyl acetate
(Z,E)-8,10-Dodecadienyl acetate	(Z,E)-8,10-Pentadecadienyl acetate	(Z)-13-Octadecenal
(Z,E)-8,10-Dodecadienal	(Z,Z)-8,10-Pentadecadienyl acetate	(E)-14-Octadecenal
(Z,Z)-8,10-Dodecadien-1-ol	(E,Z)-9,11-Pentadecadienal	(E,Z)-2,13-Octadecadien-1-ol
(Z,Z)-8,10-Dodecadienyl acetate	(Z,Z)-9,11-Pentadecadienal	(E,Z)-2,13-Octadecadienyl acetate
(Z,E,E)-3,6,8-Dodecatrien-1-ol	(Z)-3-Hexadecenyl acetate	(E,Z)-2,13-Octadecadienal
(Z,Z,E)-3,6,8-Dodecatrien-1-ol	(E)-5-Hexadecen-1-ol	(Z,E)-2,13-Octadecadienyl acetate
(E)-2-Tridecenyl acetate	(E)-5-Hexadecenyl acetate	(Z,Z)-2,13-Octadecadien-1-ol

Name	Name	Name
(Z)-2-Tridecenyl acetate	(Z)-5-Hexadecen-1-ol	(Z,Z)-2,13-Octadecadienyl acetate
(E)-3-Tridecenyl acetate	(Z)-5-Hexadecenyl acetate	(E,E)-3,13-Octadecadienyl acetate
(E)-4-Tridecenyl acetate	(E)-6-Hexadecenyl acetate	(E,Z)-3,13-Octadecadienyl acetate
(Z)-4-Tridecenyl acetate	(E)-7-Hexadecen-1-ol	(E,Z)-3,13-Octadecadienal
(Z)-4-Tridecenal	(E)-7-Hexadecenyl acetate	(Z,E)-3,13-Octadecadienyl acetate
(E)-6-Tridecenyl acetate	(E)-7-Hexadecenal	(Z,Z)-3,13-Octadecadienyl acetate
(Z)-7-Tridecenyl acetate	(Z)-7-Hexadecen-1-ol	(Z,Z)-3,13-Octadecadienal
(E)-8-Tridecenyl acetate	(Z)-7-Hexadecenyl acetate	(E,E)-5,9-Octadecadien-1-ol
(Z)-8-Tridecenyl acetate	(Z)-7-Hexadecenal	(E,E)-5,9-Octadecadienyl acetate
(E)-9-Tridecenyl acetate	(E)-8-Hexadecenyl acetate	(E,E)-9,12-Octadecadien-1-ol
(Z)-9-Tridecenyl acetate	(E)-9-Hexadecen-1-ol	(Z,Z)-9,12-Octadecadienyl acetate
(Z)-10-Tridecenyl acetate	(E)-9-Hexadecenyl acetate	(Z,Z)-9,12-Octadecadienal
(E)-11-Tridecenyl acetate	(E)-9-Hexadecenal	(Z,Z)-11,13-Octadecadienal
(Z)-11-Tridecenyl acetate	(Z)-9-Hexadecen-1-ol	(E,E)-11,14-Octadecadienal
(E,Z)-4,7-Tridecadienyl acetate	(Z)-9-Hexadecenyl acetate	(Z,Z)-13,15-Octadecadienal
(Z,Z)-4,7-Tridecadien-1-ol	(Z)-9-Hexadecenal	(Z,Z,Z)-3,6,9-Octadecatrienyl acetate
(Z,Z)-4,7-Tridecadienyl acetate	(E)-10-Hexadecen-1-ol	(E,E,E)-9,12,15-Octadecatrien-1-ol
(E,Z)-5,9-Tridecadienyl acetate	(E)-10-Hexadecenal	(Z,Z,Z)-9,12,15-Octadecatrienyl acetate
(Z,E)-5,9-Tridecadienyl acetate	(Z)-10-Hexadecenyl acetate	(Z,Z,Z)-9,12,15-Octadecatrienal

[0208] In certain embodiments, the invention provides a method for synthesizing a fatty olefin derivative as described above wherein the fatty olefin derivative is selected from (E)-7-dodecenal; (Z)-10-dodecenyl acetate; (Z)-10-hexadecenyl acetate; (Z)-10-pentadecenal; (Z)-10-pentadecenyl acetate; (Z)-10-tetradecenyl acetate; (Z)-10-tridecenyl acetate; (Z)-7-decenyl acetate; (Z)-7-dodecenyl acetate; (Z)-7-hexadecenal; (Z)-7-hexadecenyl acetate; (Z)-7-tetradecenal; (Z)-7-tetradecenyl acetate; (Z)-7-undecenyl acetate; (Z)-9-dodecenal; (Z)-9-dodecenyl acetate; (Z)-9-hexadecenal; (Z)-9-hexadecenyl acetate; (Z)-9-pentadecenyl acetate; (Z)-9-tetradecenal; (Z)-9-tetradecenyl acetate; (Z)-9-tetradecenyl formate; (Z)-9-tetradecenyl



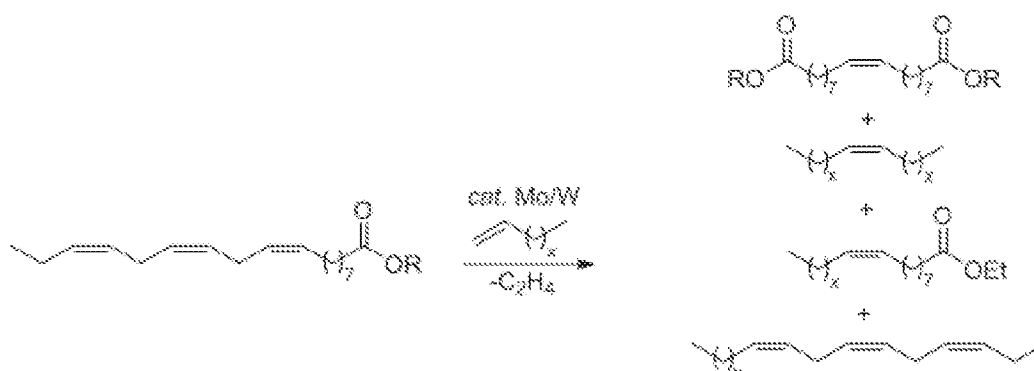
nitrate; (Z)-9-tridecenyl acetate; (Z)-9-undecenyl acetate; (E)-11-tetradecen-1-ol; (E)-11-tetradecenyl acetate; (E)-5-decen-1-ol; (E)-5-decenyl acetate; (E)-8-dodecen-1-ol; (E)-8-dodecenyl acetate; (Z)-11-hexadecen-1-ol; (Z)-11-hexadecenal; (Z)-11-hexadecenyl acetate; (Z)-11-tetradecen-1-ol; (Z)-11-tetradecenyl acetate; (Z)-13-octadecen-1-ol; (Z)-13-octadecenal; (Z)-3-hexanol; (Z)-3-nonen-1-ol; (Z)-5-decen-1-ol; (Z)-5-decenyl acetate; (Z)-7-dodecen-1-ol; (Z)-7-hexadecen-1-ol; (Z)-8-dodecen-1-ol; (Z)-8-dodecenyl acetate; (Z)-9-dodecen-1-ol; (Z)-9-hexadecen-1-ol; and (Z)-9-tetradecen-1-ol. In some such embodiments, the fatty olefin derivative is a pheromone.

[0209] In some embodiments, the fatty olefin derivative is selected from (E)-7-dodecenal; (Z)-10-dodecenyl acetate; (Z)-10-hexadecenyl acetate; (Z)-10-pentadecenal; (Z)-10-pentadecenyl acetate; (Z)-10-tetradecenyl acetate; (Z)-10-tridecenyl acetate; (Z)-7-decenyl acetate; (Z)-7-dodecenyl acetate; (Z)-7-hexadecenal; (Z)-7-hexadecenyl acetate; (Z)-7-tetradecenal; (Z)-7-tetradecenyl acetate; (Z)-7-undecenyl acetate; (Z)-9-dodecenal; (Z)-9-dodecenyl acetate; (Z)-9-hexadecenal; (Z)-9-hexadecenyl acetate; (Z)-9-pentadecenyl acetate; (Z)-9-tetradecenal; (Z)-9-tetradecenyl acetate; (Z)-9-tetradecenyl formate; (Z)-9-tetradecenyl nitrate; (Z)-9-tridecenyl acetate; and (Z)-9-undecenyl acetate. In some such embodiments, the fatty olefin derivative is a pheromone.

[0210] In some embodiments, the fatty olefin derivative is selected from (E)-7-dodecenal; (Z)-10-dodecenyl acetate; (Z)-10-hexadecenyl acetate; (Z)-10-pentadecenal; (Z)-10-pentadecenyl acetate; (Z)-10-tetradecenyl acetate; (Z)-10-Tridecenyl acetate; (Z)-7-decenyl acetate; (Z)-7-hexadecenyl acetate; (Z)-7-tetradecenal; (Z)-7-tetradecenyl acetate; (Z)-7-undecenyl acetate; (Z)-9-dodecenal; (Z)-9-pentadecenyl acetate; (Z)-9-tetradecenal; (Z)-9-tetradecenyl formate; (Z)-9-tetradecenyl nitrate; (Z)-9-tridecenyl acetate; and (Z)-9-undecenyl acetate. In some such embodiments, the fatty olefin derivative is a pheromone.

[0211] As described above, the methods of the invention can also be used for the synthesis of polyene derivatives, including polyene pheromones. See, for example, Scheme 6.

Scheme 6



[0212] Polyene derivatives include dienes, trienes, and tetraenes. The double bonds in the polyenes can be Z double bonds or E double bonds. Dienes that can be prepared using the methods of the invention include, but are not limited to, (6Z,9Z)-heptadeca-6,9-diene; (6Z,9Z)-octadeca-6,9-diene; (6Z,9Z)-nonadeca-6,9-diene; (6Z,9Z)-eicosa-6,9-diene; (6Z,9Z)-henicosa-6,9-diene; (6Z,9Z)-docosa-6,9-diene; and (6Z,9Z)-tricoso-6,9-diene. The dienes can be used as pheromones.

[0213] Trienes that can be prepared using the methods of the invention include, but are not limited to, (3Z,6Z,9Z)-heptadeca-3,6,9-triene; (3Z,6Z,9Z)-octadeca-3,6,9-triene; (3Z,6Z,9Z)-nonadeca-3,6,9-triene; (3Z,6Z,9Z)-eicosa-3,6,9-triene; (3Z,6Z,9Z)-henicosa-3,6,9-triene; (3Z,6Z,9Z)-docosa-3,6,9-triene; (3Z,6Z,9Z)-tricoso-3,6,9-triene; (4E,6Z,9Z)-heptadeca-4,6,9-triene; (4E,6Z,9Z)-octadeca-4,6,9-triene; (4E,6Z,9Z)-nonadeca-4,6,9-triene; (4E,6Z,9Z)-eicosa-4,6,9-triene; (4E,6Z,9Z)-henicosa-4,6,9-triene; (4E,6Z,9Z)-docosa-4,6,9-triene; and (4E,6Z,9Z)-tricoso-4,6,9-triene. The trienes can be used as pheromones.

[0214] Tetraenes that can be prepared using the methods of the invention include, but are not limited to, (3Z,6Z,9Z)-heptadeca-1,3,6,9-tetraene; (3Z,6Z,9Z)-octadeca-1,3,6,9-tetraene; (3Z,6Z,9Z)-nonadeca-1,3,6,9-tetraene; (3Z,6Z,9Z)-eicosa-1,3,6,9-tetraene; (3Z,6Z,9Z)-henicosa-1,3,6,9-tetraene; (3Z,6Z,9Z)-docosa-1,3,6,9-tetraene; (3Z,6Z,9Z)-tricoso-1,3,6,9-tetraene; (3Z,6Z,9Z,11E/Z)-heptadeca-3,6,9,11-tetraene; (3Z,6Z,9Z,11E/Z)-octadeca-3,6,9,11-tetraene; (3Z,6Z,9Z,11E/Z)-nonadeca-3,6,9,11-tetraene; (3Z,6Z,9Z,11E/Z)-eicosa-3,6,9,11-tetraene; (3Z,6Z,9Z,11E/Z)-henicosa-3,6,9,11-tetraene; (3Z,6Z,9Z,11E/Z)-docosa-3,6,9,11-tetraene; and (3Z,6Z,9Z,11E/Z)-tricoso-3,6,9,11-tetraene. The tetraenes can be used as pheromones.

[0215] Polyene derivatives include oxidized polyenes such as ketones and epoxides. Examples of ketone polyene derivatives include, but are not limited to: (6Z,9Z)-heptadeca-6,9-dien-3-one; (6Z,9Z)-octadeca-6,9-dien-3-one; (6Z,9Z)-nonadeca-6,9-dien-3-one; (6Z,9Z)-eicosa-6,9-dien-3-one; (6Z,9Z)-heneicosa-6,9-dien-3-one; (6Z,9Z)-docosa-6,9-dien-3-one; and (6E,9E)-tricoso-6,9-dien-3-one. Examples of polyene epoxide derivatives include, but are not limited to 3Z,6Z-9R,10S-epoxy-heneicosadiene, 3Z,6Z-9R,10S-epoxy-docosadiene, and the like. The ketone polyene derivatives and the polyene epoxide derivatives can be used as pheromones. The structure, taxonomic distribution, mechanisms of action, and biosynthetic pathways of polyene pheromones (including polyene epoxides) are described by Millar (*Annu. Rev. Entomol.* 2000. 45:575-604).

### **Pheromone Compositions and Uses Thereof**

[0216] Pheromones prepared according to the methods of the invention can be formulated for use as insect control compositions. The pheromone compositions can include a carrier, and/or be contained in a dispenser. The carrier can be, but is not limited to, an inert liquid or solid.

[0217] Examples of solid carriers include but are not limited to fillers such as kaolin, bentonite, dolomite, calcium carbonate, talc, powdered magnesia, Fuller's earth, wax, gypsum, diatomaceous earth, rubber, plastic, silica and China clay. Examples of liquid carriers include, but are not limited to, water; alcohols, such as ethanol, butanol or glycol, as well as their ethers or esters, such as methylglycol acetate; ketones, such as acetone, cyclohexanone, methylethyl ketone, methylisobutylketone, or isophorone; alkanes such as hexane, pentane, or heptanes; aromatic hydrocarbons, such as xylenes or alkyl naphthalenes; mineral or vegetable oils; aliphatic chlorinated hydrocarbons, such as trichloroethane or methylene chloride; aromatic chlorinated hydrocarbons, such as chlorobenzenes; water-soluble or strongly polar solvents such as dimethylformamide, dimethyl sulfoxide, or N-methylpyrrolidone; liquefied gases; and mixtures thereof. Baits or feeding stimulants can also be added to the carrier.

[0218] Pheromone compositions can be formulated so as to provide slow release into the atmosphere, and/or so as to be protected from degradation following release. For example, the pheromone compositions can be included in carriers such as microcapsules, biodegradable flakes and paraffin wax-based matrices.

[0219] Pheromone compositions can contain other pheromones or attractants provided that the other compounds do not substantially interfere with the activity of the composition. The pheromone compositions can also include insecticides. Examples of suitable insecticides include, but are not limited to, buprofezin, pyriproxyfen, flonicamid, acetamiprid, 5 dinotefuran, clothianidin, acephate, malathion, quinolphos, chloropyrifos, profenophos, bendiocarb, bifenthrin, chlorpyrifos, cyfluthrin, diazinon, pyrethrum, fenpropathrin, kinoprene, insecticidal soap or oil, and mixtures thereof.

[0220] Pheromone compositions can be used in conjunction with a dispenser for release of the composition in a particular environment. Any suitable dispenser known in the art can be 10 used. Examples of such dispensers include but are not limited to bubble caps comprising a reservoir with a permeable barrier through which pheromones are slowly released, pads, beads, tubes rods, spirals or balls composed of rubber, plastic, leather, cotton, cotton wool, wood or wood products that are impregnated with the pheromone composition. For example, polyvinyl chloride laminates, pellets, granules, ropes or spirals from which the pheromone 15 composition evaporates, or rubber septa. One of skill in the art will be able to select suitable carriers and/or dispensers for the desired mode of application, storage, transport or handling.

[0221] A variety of pheromones, including those set forth in Table 1 can be prepared according to the methods of the invention and formulated as described above. For example, the methods of the invention can be used to prepare peach twig borer (PTB) sex pheromone, 20 which is a mixture of (E)-dec-5-en-1-ol (17%) and (E)-dec-5-en-1-yl acetate (83%). The PTB sex pheromone can be used in conjunction with a sustained pheromone release device having a polymer container containing a mixture of the PTB sex pheromone and a fatty acid ester (such as a sebacate, laurate, palmitate, stearate or arachidate ester) or a fatty alcohol (such as undecanol, dodecanol, tridecanol, tridecenol, tetradecanol, tetradecenol, 25 tetradecadienol, pentadecanol, pentadecenol, hexadecanol, hexadecenol, hexadecadienol, octadecanol and octadecadienol). The polymer container can be a tube, an ampule, or a bag made of a polyolefin or an olefin component-containing copolymer. Sex pheromones of other pest insects such the cotton bollworm (*Helicoverpa armigera*), fall army worm (*Spodoptera frugiperda*), oriental fruit moth (*Grapholita molesta*) and leaf roller 30 (*Tortricidae*) can be used in this type of sustained pheromone release device. The sex pheromones typically include one or more aliphatic acetate compounds having from 10 to 16 carbon atoms (*e.g.*, decyl acetate, decenyl acetate, decadienyl acetate, undecyl acetate, undecenyl acetate, dodecyl acetate, dodecenyl acetate, dodecadienyl acetate, tridecyl acetate,

tridecanyl acetate, tridecadienyl acetate, tetradecyl acetate, tetradecenyl acetate, tetradecadienyl acetate, and the like) and/or one or more aliphatic aldehyde compounds having from 10 to 16 carbon atoms (e.g., 7-hexadecenal, 11-hexadecenal, 13-octadecenal, and the like).

5 [0222] Pheromones prepared according to the methods of the invention, as well as compositions containing the pheromones, can be used to control the behavior and/or growth of insects in various environments. The pheromones can be used, for example, to attract or repel male or female insects to or from a particular target area. The pheromones can be used to attract insects away from vulnerable crop areas. The pheromones can also be used  
10 example to attract insects as part of a strategy for insect monitoring, mass trapping, lure/attract-and-kill or mating disruption.

[0223] Mass trapping involves placing a high density of traps in a crop to be protected so that a high proportion of the insects are removed before the crop is damaged. Lure/attract-and-kill techniques are similar except once the insect is attracted to a lure, it is subjected to a  
15 killing agent. Where the killing agent is an insecticide, a dispenser can also contain a bait or feeding stimulant that will entice the insects to ingest an effective amount of the insecticide.

[0224] It will be appreciated by a person skilled in the art that a variety of different traps are possible. Suitable examples of such traps include water traps, sticky traps, and one-way traps. Sticky traps come in many varieties. One example of a sticky trap is of cardboard  
20 construction, triangular or wedge-shaped in cross-section, where the interior surfaces are coated with a non-drying sticky substance. The insects contact the sticky surface and are caught. Water traps include pans of water and detergent that are used to trap insects. The detergent destroys the surface tension of the water, causing insects that are attracted to the pan, to drown in the water. One-way traps allow an insect to enter the trap but prevent it from  
25 exiting. The traps of the invention can be colored brightly, to provide additional attraction for the insects.

[0225] The trap is positioned in an area infested (or potentially infested) with insects. Generally, the trap is placed on or close to a tree or large plant and the pheromone attracts the insects to the trap. The insects can then be caught, immobilized and/or killed within the trap,  
30 for example, by the killing agent present in the trap.

[0226] Pheromones prepared according to the methods of the invention can also be used to disrupt mating. Strategies of mating disruption include confusion, trail-masking and false-

trail following. Constant exposure of insects to a high concentration of a pheromone can prevent male insects from responding to normal levels of the pheromone released by female insects. Trail-masking uses a pheromone to destroy the trail of pheromones released by females. False-trail following is carried out by laying numerous spots of a pheromone in high concentration to present the male with many false trails to follow. When released in sufficiently high quantities, the male insects are unable to find the natural source of the sex pheromones (the female insects) so that mating cannot occur.

[0227] Insect populations can be surveyed or monitored by counting the number of insects in a target area (*e.g.*, the number of insects caught in a trap). Inspection by a horticulturist can provide information about the life stage of a population. Knowing where insects are, how many of them there are, and their life stage enables informed decisions to be made as to where and when insecticides or other treatments are warranted. For example, a discovery of a high insect population can necessitate the use of methods for removal of the insect. Early warning of an infestation in a new habitat can allow action to be taken before the population becomes unmanageable. Conversely, a discovery of a low insect population can lead to a decision that it is sufficient to continue monitoring the population. Insect populations can be monitored regularly so that the insects are only controlled when they reach a certain threshold. This provides cost-effective control of the insects and reduces the environmental impact of the use of insecticides.

[0228] As will be apparent to one of skill in the art, the amount of a pheromone or pheromone composition used for a particular application can vary depending on several factors such as the type and level of infestation; the type of composition used; the concentration of the active components; how the composition is provided, for example, the type of dispenser used; the type of location to be treated; the length of time the method is to be used for; and environmental factors such as temperature, wind speed and direction, rainfall and humidity. Those of skill in the art will be able to determine an effective amount of a pheromone or pheromone composition for use in a given application.

#### IV. EXAMPLES

##### Example 1. Cross-metathesis of dec-9-en-1-yl acetate with hex-1-ene.

[0229] Prior to introduction of the metathesis catalyst, dec-9-en-1-yl acetate (CAS # 50816-18-7) and hex-1-ene (CAS # 592-41-6) are treated with either aluminum oxide ( $\text{Al}_2\text{O}_3$ ) or a trialkylaluminum as described in U.S. Pat. No. 9,388,097 to reduce moisture, peroxides, and

other potential catalyst poisons to a level suitable for conducting the metathesis reaction. In a nitrogen-filled glovebox, a 20 mL scintillation vial is charged with a magnetic stir bar, 1.00 g of pretreated dec-9-en-1-yl acetate and 1.27 g of pretreated hex-1-ene. The vial is closed with a perforated septum and placed in an aluminum heating block regulated at 40 °C atop a hotplate/magnetic stirrer where the stirring rate is fixed at 500 rpm. A solution of 1-({3,3'-dibromo-2'-[(tert-butyl)dimethylsilyl]oxy}-5H,5'H,6H,6'H,7H,7'H,8H,8'H-[1,1'-binaphthalene]-2-yl}oxy)-1-(2,5-dimethylpyrrol-1-yl)-1-(2-methyl-2-phenylpropylidene)-N-phenyltungstenimine (CAS # 1628041-76-8) catalyst in dry and degassed toluene is prepared by weighing 10 mg of the catalyst into a 1 mL volumetric flask and diluting to the calibration mark with solvent. Using a gas tight microliter syringe, 57 µL of the catalyst solution (0.57 mg, 0.025 wt%, 0.0025 mol%) is withdrawn from the volumetric flask and added to the reaction mixture. After four hours, the vial is removed from the glovebox and the reaction mixture is analyzed by GC-MS. The GC-MS data indicates that (Z)-tetradec-9-en-1-yl acetate is formed in high yield.

15 **Example 2. Cross-metathesis of methyl dec-9-enoate with oct-1-ene.**

[0230] Prior to introduction of the metathesis catalyst, methyl dec-9-enoate (CAS # 25601-41-6) and oct-1-ene (CAS # 111-66-0) are treated to reduce moisture, peroxides and other potential catalyst poisons to a level suitable for conducting the metathesis reaction as described in U.S. Pat. No. 9,388,097. In a nitrogen-filled glovebox, a 20 mL scintillation vial is charged with a magnetic stir bar, 1.00 g of pretreated methyl dec-9-enoate and 1.83 g of pretreated oct-1-ene. The vial is closed with a perforated septum and placed in an aluminum heating block regulated at 40 °C atop a hotplate/magnetic stirrer where the stirring rate is fixed at 500 rpm. A solution of 1-({3,3'-dibromo-2'-[(tert-butyl)dimethylsilyl]oxy}-5H,5'H,6H,6'H,7H,7'H,8H,8'H-[1,1'-binaphthalene]-2-yl}oxy)-1-(2,5-dimethylpyrrol-1-yl)-1-(2-methyl-2-phenylpropylidene)-N-phenyltungstenimine (CAS # 1628041-76-8) catalyst in dry and degassed toluene is prepared by weighing 10 mg of the catalyst into a 1 mL volumetric flask and diluting to the calibration mark with solvent. Using a gas tight microliter syringe, 71 µL of the catalyst solution (0.71 mg cat., 0.025 wt%, 0.0029 mol%) is withdrawn from the volumetric flask and added reaction mixture. After four hours the vial is removed from the glovebox and the reaction mixture is analyzed by GC-MS. The GC-MS data indicates that methyl (Z)-hexadec-9-enoate is formed in high yield.

**Example 3. Reduction of methyl hexadec-9-enoate with sodium bis(2-methoxyethoxy) aluminumhydride.**

[0231] In an oven-dried, nitrogen-flushed flask sealed with a rubber septum and containing a magnetic stir bar is added 0.47 g *N*-methylpiperazine (CAS # 109-01-3) and 10 mL of dry, degassed toluene. The flask is submerged in an ice bath and, with magnetic stirring, 1.48 g of a 70% solution of sodium bis(2-methoxyethoxy)aluminumhydride (CAS # 22722-98-1) in toluene is added dropwise. In a separate oven dried, nitrogen-flushed flask sealed with a rubber septum is added 1.00 g of methyl hexadec-9-enoate, prepared through the process detailed in Example 2, and 20 mL of dry, degassed toluene. The flask is then submerged in an ice bath and stirrer via an external magnetic stirrer. After stirring for one hour, the *N*-methylpiperazine/sodium bis(2-methoxyethoxy)aluminumhydride mixture is added dropwise via a cannula to the toluene solution of ester. The resulting mixture is stirred at ice-bath temperature for one hour and then brought to ambient temperature and stirred for an additional hour. The reaction is quenched by addition of 20 mL of deionized water and then extracted with 20 mL of EtOAc. The organic layer is washed with 20 mL of deionized water, dried over sodium sulfated and then concentrated *in vacuo*. The product is analyzed by GC-MS, indicating that (*Z*)-hexadec-9-enal is formed in high yield.

**Example 4. Preparation of Eicosa-3,6,9-triene, a polyene pheromone.**

[0232] Prior to introduction of metathesis catalysts, linseed oil (CAS # 8001-26-1) and dodec-1-ene (CAS # 112-41-4) are treated to reduce moisture, peroxides and other potential catalyst poisons to the desired level. In a nitrogen-filled glovebox, a 20 mL scintillation vial is charged with a magnetic stir bar, 1.00 g of pretreated linseed oil and 0.481 g of pretreated dec-1-ene. The vial is closed with a perforated septum and placed in an aluminum heating block regulated at 40 °C atop a hotplate/magnetic stirrer where the stirring rate is fixed at 500 rpm. A solution of 1-({3,3'-dibromo-2'-[(*tert*-butyldimethylsilyl)oxy]-5H,5'H,6H,6'H,7H,7'H,8H,8'H-[1,1'-binaphthalene]-2-yl}oxy)-1-(2,5-dimethylpyrrol-1-yl)-1-(2-methyl-2-phenylpropylidene)-*N*-phenyltungstenimine (CAS # 1628041-76-8) in dry and degassed toluene is prepared by weighing 10 mg of the catalyst into a 1 mL volumetric flask and diluting to the calibration mark with solvent. Using a gas tight microliter syringe, 37  $\mu$ L (0.37 mg cat., 0.025 wt%, 0.0071 mol%) of the catalyst solution is withdrawn from the volumetric flask and added reaction mixture. After one hour the vial is removed from the glovebox. The reaction mixture is transesterified with methanol using sodium methoxide as a



catalyst prior to analysis by GC-MS. The transesterified reaction mixture contains the desired eicosa-3,6,9-triene product (CAS # 134370-60-8), as well as small amounts of 1,18-dimethyl octadec-9-enedioate (CAS # 13481-97-5), methyl eicos-9-enoate (CAS # 10340-21-3), docos-11-ene (CAS # 62978-77-2), and cyclohexa-1,4-diene (CAS # 628-41-1).

5 **Example 5. Metathesis catalyst screening for the Z-selective cross-metathesis of methyl dec-9-enoate and hex-1-ene.**

[0233] In a nitrogen-filled glovebox, a 30 mL glass vial was charged a with a magnetic stir bar and 2.70 g of an equimolar mixture of methyl dec-9-enoate and hex-1-ene previously treated with activated basic alumina to reduce levels of moisture, peroxide and protic  
10 impurities in the method described in US 14/209,686. To the olefin mixture was added 0.0025 mol% of a molybdenum or tungsten metathesis catalysts as a toluene solution. The vial was then closed with a perforated cap and the reaction mixtures were stirred by means of a magnetic hotplate stirrer for a total of four hours after the addition of catalyst. Aliquots of the reaction mixture were taken at one and four hours after the addition of catalyst and  
15 analyzed to determine 9-DAME conversion (%) and methyl (Z)-tetradec-9-enoate selectivity (%) (Table 8) by GC-MS/FID after using the equations below in conjunction with external calibration curves obtained for the analytes of interest. GC chromatograms were recorded using a Shimadzu GC2010 Plus instrument equipped with an Agilent DB-23 capillary column with a length of 30 m, an inner diameter of 0.25 mm and a film thickness of 0.25  $\mu$ m.  
20 Nitrogen was used as the carrier gas and the total flow of gas through the column was 61.9 mL/min. Injections were split at a 1:30 ratio with the carrier gas and the injector of the instrument was maintained at a constant temperature of 240 °C. The oven temperature was held at 35 °C during the injection and for the following five minutes, then raised to 100 °C at a rate of 35 °C/min, raised further to 130 °C at a rate of 7 °C/min, raised again to 240 °C at a  
25 rate of 35 °C/min and finally held at this terminal temperature for 3.71 minutes for a total run length of approx. 18 minutes.

$$\begin{aligned} & \text{Methyl Dec} - 9 - \text{enoate Conversion (\%)} \\ & = 1 - \left( \frac{\text{Final mol Methyl Dec} - 9 - \text{enoate}}{\text{Initial mol Methyl Dec} - 9 - \text{enoate}} \right) \times 100 \end{aligned}$$

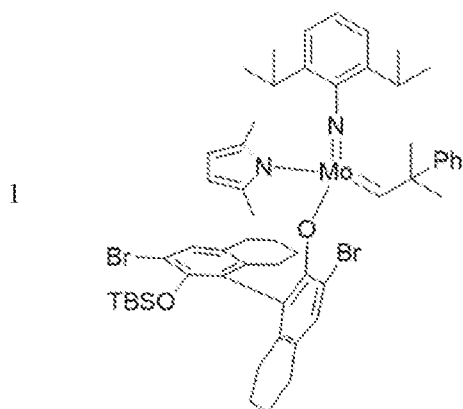
Methyl (Z) – Tetradec – 9 – enoate Selectivity (%)

$$= \left( \frac{\text{mol Methyl (Z) – Tetradec – 9 – enoate}}{\text{mol Methyl (Z) – Tetradec – 9 – enoate} + \text{mol Methyl (E) – Tetradec – 9 – enoate}} \right) \times 100$$

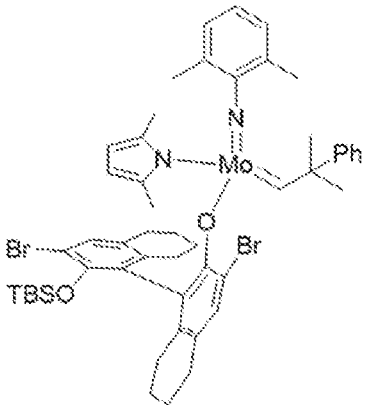
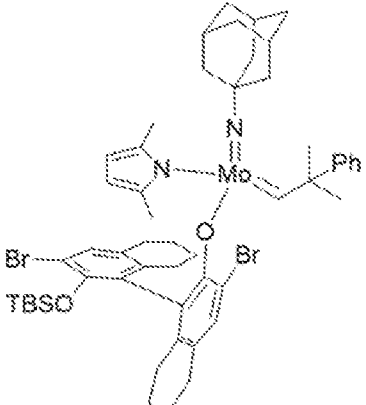
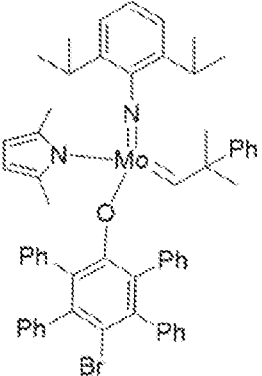
Table 8

Catalyst	4 Hour Reaction Length		24 Hour Reaction Length	
	Methyl Dec-9-enoate Conversion (%)	Methyl (Z)-Tetradec-9-enoate Selectivity (%)	Methyl Dec-9-enoate Conversion (%)	Methyl (Z)-Tetradec-9-enoate Selectivity (%)
1	40	91	73	90
2	56	94	70	93
3	67	95	68	95
4	51	16	52	16
5	21	95	28	94
6	47	94	54	94
7	<0.1	Not Determined	<0.1	Not Determined
8	<0.1	Not Determined	<0.1	Not Determined
9	15	95	17	95
10	52	93	60	93

Catalyst	Structure	Formula
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C<sub>54</sub>H<sub>70</sub>Br<sub>2</sub>MoN<sub>2</sub>O<sub>2</sub>Si

Catalyst	Structure	Formula
2		$C_{50}H_{62}Br_2MoN_2O_2Si$
3		$C_{52}H_{68}Br_2MoN_2O_2Si$
4		$C_{52}H_{68}Br_2MoN_2OSi$

Catalyst	Structure	Formula
5		C <sub>50</sub> H <sub>59</sub> FMoN <sub>2</sub> O
6		C <sub>46</sub> H <sub>52</sub> Br <sub>2</sub> Cl <sub>2</sub> N <sub>2</sub> O <sub>3</sub> SiW
7		C <sub>48</sub> H <sub>56</sub> NO <sub>2</sub> PW
8		C <sub>54</sub> H <sub>52</sub> NO <sub>2</sub> PW

Catalyst	Structure	Formula
9		C <sub>50</sub> H <sub>60</sub> MoN <sub>2</sub> O
10		C <sub>54</sub> H <sub>50</sub> N <sub>2</sub> O <sub>W</sub>

Ph = phenyl, C<sub>6</sub>H<sub>5</sub>; Mes = 2,4,6-trimethylphenyl, 2,4,6-Me<sub>3</sub>C<sub>6</sub>H<sub>2</sub>; TBS = *tert*-butyldimethylsilyl, SiMe<sub>2</sub>(*t*-Bu)

**Example 6. Synthesis and Isolation of Methyl (Z)-Tetradec-9-enoate via Cross-metathesis of methyl dec-9-enoate and hex-1-ene.**

[0234] Into a glass vessel equipped with an agitator, thermometer and reflux condenser,  
 5 were charged 500 g of methyl dec-9-enoate (2.71 mol) and 480 g of hex-1-ene (5.70 mol).  
 To the thoroughly homogenized feedstocks a solution of triethylaluminum in toluene (3.82 g,  
 0.0335 mol, 0.389 mol%) was added in one portion. After agitating at 500 rpm for an hour at  
 23-25 °C, the temperature of the feedstock was raised to 40-41 °C. 0.121 g (0.00128 mol%,  
 123 ppmwt) of tungsten, [(1R)-3,3'-dibromo-2'-[[1,1-dimethylethyl]dimethylsilyl]oxy]-5,5',  
 10 6,6',7,7',8,8'-octahydro[1,1'-binaphthalen]-2-olato-κO][2,6-dichlorobenzenaminato(2-)-κN](2,  
 5-dimethyl-1H-pyrrol-1-yl)[(2-methoxyphenyl)methylene]-, (T-4)- (CAS # 1817807-15-0)  
 was added in four portions to control the rate of ethylene generation and the reaction was  
 allowed to proceed for three hours. After that time GC-FID analysis showed the reaction  
 proceed in 57% Methyl Dec-9-enoate Conversion and 96% Methyl (Z)-tetradec-9-enoate  
 15 Selectivity. To the cooled (25-30°C) reaction mixture was added 10 mL of methanol (H<sub>2</sub>O =  
 0.035-0.038 w%). The mixture was stirred at ambient temperature for 15-20 minutes. The

aliquot was then removed from the reactor and filtered through a plug comprising a lower 0.5 cm layer of diatomaceous earth and an upper 1.0 cm layer of silica gel. The filter cake was washed with 7×100mL MTBE. The volume of the colorless and clear filtrate was concentrated under reduced pressure in a 45 °C water bath at a pressure of 40 mbar to obtain the crude product as a colorless liquid. The crude material was vacuum distilled (0.2-1 mbar) using a short path distillation apparatus and 166 g (25% overall yield) of methyl (Z)-tetradec-9-enoate was collected at a head temperature of 95-97 °C and pressure of 0.4 mbar.

**Example 7. Reduction of methyl (Z)-tetradec-9-enoate to (Z)-tetradec-9-en-1-ol using sodium bis(2-methoxyethoxy) aluminumhydride.**

[0235] In an oven dried, nitrogen-flushed flask sealed with a rubber septum and containing a magnetic stir bar was added 240 g (0.831 mol 'AlH<sub>2</sub>', 1.2 eq.) of a 70% solution of sodium bis(2-methoxyethoxy)aluminumhydride (CAS # 22722-98-1) in toluene. The flask is then submerged in an ice bath and stirred via an external magnetic stirrer and 166 g (0.691 mol) of methyl (Z)-tetradec-9-enoate, prepared through the process detailed in Example 6, was slowly added. The resulting mixture is stirred at ice-bath temperature for one hour and then brought to ambient temperature and stirred for an additional hour. The reaction mixture was then quenched with 10 mL deionized water and acidified with 15 w/w% aqueous sulfuric acid until the pH of the aqueous layer was 4. The obtained slurry was filtered through diatomaceous earth and the filter cake was rinsed with 2×150 mL of toluene. The two phases of the mother liquor were separated. The aqueous layer was washed with additional 300 mL of toluene. The combined organic phases were washed with 1500 mL deionized water. All volatile components were removed by *in vacuo* and the product dried via azeotropic distillation with additional toluene to yield 144 g (0.678 mol, 98% yield).

**Example 8. Synthesis of (Z)-tetradec-9-en-1-yl acetate through esterification of (Z)-tetradec-9-en-1-ol to with acetic anhydride.**

[0236] In an oven dried, nitrogen-flushed flask sealed with a rubber septum and containing a magnetic stir bar was added 144 g (0.678 mol) of (Z)-tetradec-9-en-1-ol, prepared through the method detailed in Example 7, 75.9 g of acetic anhydride (0.743 mol) and 5.50 g of sodium acetate (0.067 mol, 0.1 eq.). The reaction mixture was then heated to 60 °C for one hour, cooled and then washed consecutively with water and a sodium carbonate solution, yielding 160 g (0.629 mol, 92% yield) of (Z)-tetradec-9-en-1-yl acetate as a colorless liquid.

**Example 9. Acetylation of 7-octen-1-ol with acetic anhydride.**

[0237] 7-octen-1-ol (46.49 g, 363 mmol), first purified via vacuum distillation (72 °C/8 mbar), was charged into a three-necked, round-bottomed flask equipped with a thermometer, a reflux condenser and a magnetic stirrer bar. The top of the condenser was connected to a Schlenk line and the whole apparatus was flushed with nitrogen. Acetic anhydride (44.29 g, 434 mmol) and anhydrous sodium acetate (3.25 g, 39.7 mmol) were added to the flask. The mixture was stirred at 68 °C for 4 hours. GC showed complete conversion. 200 mL of DCM was added to the reaction mixture and mixed with water (100 mL). NaHCO<sub>3</sub> (25g) was carefully and portion-wise added to adjust the pH of the aqueous phase to 6. The organic phase was separated and extracted with saturated solution of NaHCO<sub>3</sub> (pH~8-9) then with 100 mL of water (pH~7). The separated DCM fraction was dried over Na<sub>2</sub>SO<sub>4</sub> (60 g) and Na<sub>2</sub>CO<sub>3</sub> (6 g) for one night. Organic phase was collected filtered, solid was washed with DCM and hexane. Volatiles were removed on rotary evaporator and the crude product further dried at 60 °C/10 mbar for 4 hours. The material was then vacuum distilled a (79-80 °C/10mbar) to yield 51.53 g (83% yield) of a colorless liquid was obtained.

**Example 10. Cross-metathesis of oct-7-en-1-yl acetate with hex-1-ene.**

[0238] In a nitrogen-filled glovebox, a 20 mL scintillation vial was charged with a magnetic stir bar, 1.315 g of oct-7-en-1-yl acetate (CAS # 5048-35-1) and finally 0.685 g of hex-1-ene (1.05 equivalents). The vial was then closed with a perforated septum. The feedstock was treated with 69 µL of a 25 wt% solution of triethylaluminum in toluene (14.4 mg AlEt<sub>3</sub>, 0.720 wt%, 0.803 mol%) and the mixture stirred via an external magnetic stirrer at room temperature for four hours. To the mixture was then added 0.002 mol% (0.35 mg, 0.0177 wt%) of tungsten [(1R)-3,3'-dibromo-2'-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5', 6,6',7,7',8,8'-octahydro[1,1'-binaphthalen]-2-olato-κO][[2,6-dichlorobenzenaminato(2-)-κN](2, 5-dimethyl-1H-pyrrol-1-yl)][(2-methoxyphenyl)methylene]-, (T-4)- (CAS # 1817807-15-0) as a solution in benzene. At the time after the additional of catalyst specified in the table below, an aliquot of the reaction mixture was removed from the glovebox and analyzed by GC-MS/FID. The results of the GC-MS/FID analysis of these samples is presented in the table below:

Time After Catalyst Addition (h)	Approximate Conversion of Oct-7-en-1-yl Acetate to Dodec-7-en-1-yl Acetate (%)	Approximate (Z)-Dodec-7-en-1-yl Acetate Content (%)
1	34	97
4	37	97
6	38	97
24	38	97

**Example 11. Cross-metathesis of oct-7-en-1-yl acetate with hex-1-ene.**

[0239] Prior to conducting the procedure below, the oct-7-en-1-yl acetate was further purified through a second vacuum distillation to remove additional catalyst deactivating impurities. In a nitrogen-filled glovebox, a 20 mL scintillation vial was charged with a magnetic stir bar, 1.338 g of oct-7-en-1-yl acetate (CAS # 5048-35-1) and finally 0.662 g of hex-1-ene. The vial was then closed with a perforated septum. The feedstock was treated with 7.4  $\mu$ L of a 25 wt% solution of triethylaluminum in toluene (1.54 mg AlEt<sub>3</sub>, 0.0769 wt%, 0.0857 mol%) and the mixture stirred via an external magnetic stirrer at room temperature for four hours. To the mixture was then added 0.002 mol% (0.35 mg, 0.0177 wt%) of tungsten [(1R)-3,3'-dibromo-2'-[[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5,5',6,6',7,7',8,8'-octahydro[1,1'-binaphthalen]-2-olato- $\kappa$ O]][2,6-dichlorobenzenaminato(2-)- $\kappa$ N](2,5-dimethyl-1H-pyrrol-1-yl)](2-methoxyphenyl)methylene]-, (T-4)- (CAS # 1817807-15-0) was added as a solution in benzene. At the time after the additional of catalyst specified in the table below, an aliquot of the reaction mixture was removed from the glovebox and analyzed by GC-MS/FID. The results of the GC-MS/FID analysis of these samples is presented in the table below:

Time After Catalyst Addition (h)	Approximate Conversion of Oct-7-en-1-yl Acetate to Dodec-7-en-1-yl Acetate (%)	Approximate (Z)-Dodec-7-en-1-yl Acetate Content (%)
1	47	97
2	62	97
4	72	96
8	80	96
72	83	96



**Example 12. Reduction of methyl dec-9-enoate to dec-9-en-1-ol using sodium bis(2-methoxyethoxy) aluminumhydride.**

[0240] In an oven dried, nitrogen-flushed flask sealed with a rubber septum and containing a magnetic stir bar was added 96.0 mL (353 mmol 'AlH<sub>2</sub>', 1.3 eq.) of a 70% solution of sodium bis(2-methoxyethoxy)aluminumhydride (CAS # 22722-98-1) in toluene. The flask is then submerged in an ice bath and stirred via an external magnetic stirrer and 50 g (271 mmol) of methyl dec-9-enoate was slowly added so as to maintain the temperature of the reaction mixture below 15 °C. The resulting mixture is stirred at ice-bath temperature for one hour and then brought to ambient temperature and stirred for an additional hour. The reaction mixture was then quenched with 10 mL deionized water and acidified with 15 w/w% aqueous sulfuric acid until the pH of the aqueous layer was 4. The obtained slurry was filtered through diatomaceous earth and the filter cake was rinsed with 2×50 mL of toluene. The two phases of the mother liquor were separated. The aqueous layer was washed with additional 100 mL of toluene. The combined organic phases were washed with 50 mL deionized water. All volatile components were removed by *in vacuo* and the product dried via azeotropic distillation with additional toluene to yield 42.9 g of a colorless oil. This oil was later determined to contain 96.0 wt% of dec-9-en-ol (97.1% yield) by GC-MS/FID analysis.

**Example 13. Acetylation of 9-decen-1-ol.**

[0241] 9-Decen-1-ol (50.0 g, 320 mmol), prepared through the method of Example 13, was charged into a three-necked, round-bottomed flask equipped with a thermometer, a reflux condenser and a magnetic stirrer bar. The top of the condenser was connected to a Schlenk line and the whole apparatus was flushed with nitrogen. Acetic anhydride (33 mL, 352 mmol, 1.1 eq.) and anhydrous sodium acetate 2.6 g, 32 mmol) were added to the flask. The mixture was stirred at 68 °C for 4 hours. GC showed complete conversion. 100 mL of DCM was added to the reaction mixture and mixed with water (100 mL). NaHCO<sub>3</sub> (25g) was carefully and portion-wise added to adjust the pH of the aqueous phase to 6. The organic phase was separated and extracted with saturated solution of NaHCO<sub>3</sub> (pH~8-9) then with 100 mL of water (pH~7). The separated DCM fraction was dried over Na<sub>2</sub>SO<sub>4</sub> (60 g) and Na<sub>2</sub>CO<sub>3</sub> (6 g) for one night. Organic phase was collected filtered, solid was washed with DCM and hexane. All volatile components were removed on rotary evaporator to yield 63.6 g of a colorless oil. This oil was later determined to contain 95.8 wt% of dec-9-en-ol (95.6% yield).

**Example 14. Cross-metathesis of dec-9-en-1-yl acetate with hex-1-ene.**

[0242] In a nitrogen-filled glovebox, a 20 mL scintillation vial was charged with a magnetic stir bar, 1.404 g of dec-9-en-1-yl acetate prepared through the method of Example 14 and finally 0.596 g of hex-1-ene. The vial was then closed with a perforated septum. The feedstock was treated with 42.7  $\mu$ L of a 25 wt% solution of triethylaluminum in toluene (0.9 mg AlEt<sub>3</sub>, 0.444 wt%, 0.541 mol%) and the mixture stirred via an external magnetic stirrer at room temperature for four hours. To the mixture was then added 0.002 mol% (0.32 mg, 0.0159 wt%) of tungsten [(1R)-3,3'-dibromo-2'-[[1,1-dimethylethyl]dimethylsilyl]oxy]-5,5',6,6',7,7',8,8'-octahydro[1,1'-binaphthalen]-2-olato- $\kappa$ O][2,6-dichlorobenzaminato(2-)- $\kappa$ N](2,5-dimethyl-1H-pyrrol-1-yl)[(2-methoxyphenyl)methylene]-, (T-4)- (CAS # 1817807-15-0) as a solution in benzene. At the time after the additional of catalyst specified in the table below, an aliquot of the reaction mixture was removed from the glovebox and analyzed by GC-MS/FID. The GC-MS/FID data indicated that 23.9% of the starting dec-9-en-1-yl acetate was converted to tetradec-9-en-1-yl acetate and in an E/Z ratio of 3/97.

**Example 15. Effect of metathesis catalyst loading on the Z-selective cross-metathesis of methyl dec-9-enoate and hex-1-ene.**

[0243] In a nitrogen-filled glovebox, five 30 mL scintillation vial wer charged with a magnetic stir bar, 2.70 g of an equimolar mixture of methyl dec-9-enoate and hex-1-ene. The vial was then closed with a perforated septum. The feedstock was treated with 11  $\mu$ L of a 25 wt% solution of triethylaluminum in toluene (2.3 mg AlEt<sub>3</sub>, 0.085 wt%, 0.1 mol%) and the mixture stirred via an external magnetic stirrer at room temperature for 18 hours. To the mixture was added the amount of tungsten [(1R)-3,3'-dibromo-2'-[[1,1-dimethylethyl]dimethylsilyl]oxy]-5,5',6,6',7,7',8,8'-octahydro[1,1'-binaphthalen]-2-olato- $\kappa$ O][2,6-dichlorobenzaminato(2-)- $\kappa$ N](2,5-dimethyl-1H-pyrrol-1-yl)[(2-methoxyphenyl)methylene]-, (T-4)- (CAS # 1817807-15-0) listed in the table below as a solution in benzene. At the time after the addition of catalyst specified in the table below, an aliquot of the reaction mixture was removed from the glovebox and analyzed by GC-MS/FID to determine '9-DAME Conversion (%)' and 'Methyl (Z)-tetradec-9-enoate Selectivity (%)' as described in Example 5.

Catalyst Loading (mol%)	Time (h)	Methyl Dec-9-enoate Conversion (%)	Methyl (Z)-Tetradec-9-enoate Selectivity (%)
0.0005	1	31	99
	4	58	98
	8	59	97
0.001	1	38	98
	4	76	97
	8	76	96
0.0015	1	54	98
	4	72	95
	8	75	94
0.002	1	66	98
	4	82	93
	8	84	90
0.0025	1	72	97
	4	84	91
	8	88	88

**Example 16. Cross-metathesis of oct-7-en-1-yl acetate with oct-1-ene.**

[0244] Using the method of Example 1, an equimolar amount of oct-7-en-1-yl acetate and oct-1-ene are charged into a 20 mL glass scintillation vial equipped with a magnetic stir bar inside of a nitrogen-filled glovebox. The mixture is then stirred by means of an external hotplate stirrer and is then treated with an alkyl aluminum reagent to reduce levels of moisture, peroxide and protic impurities as described in US 9,388,097. After sufficient time to ensure the removal of catalyst deactivating impurities to the desired level, the temperature of the substrate mixture is raised to the desired level and a sufficient quantity of a Z-selective group 6 metathesis catalyst to generate the desired level of 'Methyl Dec-9-enoate Conversion (%)', as defined in Example 5, is added to the pretreated substrates. After the required amount of time, the vial is removed from the glovebox and the reaction mixture is analyzed by GC-MS. The GC-MS data indicates that (Z)-tetradec-7-en-1-yl acetate is formed in high yield.

**Example 17. Cross-metathesis of oct-7-en-1-yl acetate with but-1-ene.**

[0245] Using the method of Example 1, an equimolar amount of oct-7-en-1-yl acetate and but-1-ene are charged into a glass pressure vessel equipped with a magnetic stir bar. The mixture is then stirred by means of an external hotplate stirrer and treated with an alkyl

aluminum reagent to reduce levels of moisture, peroxide and protic impurities as described in US 9,388,097. After sufficient time to ensure the removal of catalyst deactivating impurities to the desired level, the temperature of the substrate mixture is raised to the appropriate temperature and a sufficient quantity of a Z-selective group 6 metathesis catalyst to generate the desired level of 'Methyl Dec-9-enoate Conversion (%)', as defined in Example 5, is added to the pretreated substrates. After the required amount of time, the vial is removed from the glovebox and the reaction mixture is analyzed by GC-MS. The GC-MS data indicates that (Z)-dec-7-en-1-yl acetate is formed in high yield.

**Example 18. Cross-metathesis of dec-9-en-1-yl acetate with oct-1-ene.**

[0246] Using the method of Example 1, an equimolar amount of dec-9-en-1-yl acetate and oct-1-ene are charged into a 20 mL glass scintillation vial equipped with a magnetic stir bar inside of a nitrogen-filled glovebox. The mixture is then stirred by means of an external hotplate stirrer and is then treated with an alkyl aluminum reagent to reduce levels of moisture, peroxide and protic impurities as described in US 9,388,097. After sufficient time to ensure the removal of catalyst deactivating impurities to the desired level, the temperature of the substrate mixture is raised to the desired level and a sufficient quantity of a Z-selective group 6 metathesis catalyst to generate the desired level of 'Methyl Dec-9-enoate Conversion (%)', as defined in Example 5, is added to the pretreated substrates. After the required amount of time, the vial is removed from the glovebox and the reaction mixture is analyzed by GC-MS. The GC-MS data indicates that (Z)-hexadec-9-en-1-yl acetate is formed in high yield.

**Example 19. Cross-metathesis of dec-9-en-1-yl acetate with but-1-ene.**

[0247] Using the method of Example 1, an equimolar amount of dec-9-en-1-yl acetate and but-1-ene are charged into a glass pressure vessel equipped with a magnetic stir bar. The mixture is then stirred by means of an external hotplate stirrer and treated with an alkyl aluminum reagent to reduce levels of moisture, peroxide and protic impurities as described in US 9,388,097. After sufficient time to ensure the removal of catalyst deactivating impurities to the desired level, the temperature of the substrate mixture is raised to the desired level and a sufficient quantity of a Z-selective group 6 metathesis catalyst to generate the desired level of 'Methyl Dec-9-enoate Conversion (%)', as defined in Example 5, is added to the pretreated substrates. After the required amount of time, the vial is removed from the glovebox and the

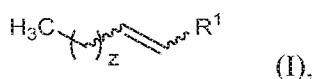
reaction mixture is analyzed by GC-MS. The GC-MS data indicates that (Z)-dodec-9-en-1-yl acetate is formed in high yield.

## V. EXEMPLARY EMBODIMENTS

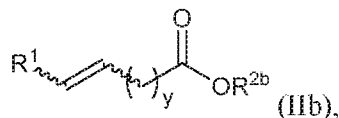
[0248] Exemplary embodiments provided in accordance with the presently disclosed subject matter include, but are not limited to, the claims and the following embodiments:

1. A method for synthesizing a fatty olefin derivative, the method comprising:

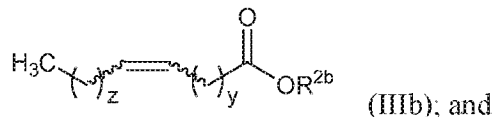
a) contacting an olefin according to Formula I



with a metathesis reaction partner according to Formula IIb



in the presence of a metathesis catalyst under conditions sufficient to form a metathesis product according to Formula IIIb:



b) converting the metathesis product to the fatty olefin derivative;

wherein:

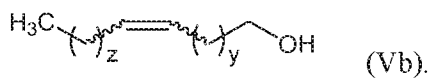
each  $\text{R}^1$  is independently selected from the group consisting of H,  $\text{C}_{1-18}$  alkyl, and  $\text{C}_{2-18}$  alkenyl;

$\text{R}^{2b}$  is  $\text{C}_{1-8}$  alkyl;

subscript y is an integer ranging from 0 to 17; and

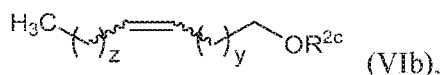
subscript z is an integer ranging from 0 to 17.

2. The method of embodiment 1, wherein converting the metathesis product to the fatty olefin derivative comprises reducing the metathesis product to form an alkenol according to Formula Vb:



3. The method of embodiment 2, wherein the alkenol is the fatty olefin derivative.

4. The method of embodiment 2, wherein converting the metathesis product to the fatty olefin derivative further comprises acylating the alkenol, thereby forming a fatty olefin derivative according to Formula VIb:

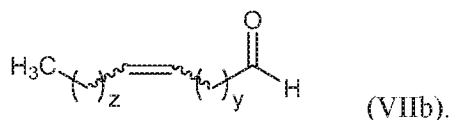


wherein  $\text{R}^{2c}$  is  $\text{C}_{1-6}$  acyl.

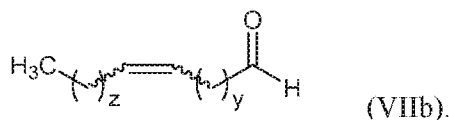
5. The method of any one of embodiments 1-3, wherein  $\text{R}^1$  is H,  $\text{R}^{2b}$  is methyl, subscript  $y$  is 7, and subscript  $z$  is 3.

6. The method of embodiment 4, wherein  $\text{R}^1$  is H,  $\text{R}^{2b}$  is methyl, subscript  $y$  is 7, subscript  $z$  is 3, and  $\text{R}^{2c}$  is acetyl.

7. The method of embodiment 2, wherein converting the metathesis product to the fatty olefin derivative further comprises oxidizing the alkenol, thereby forming a fatty olefin derivative according to Formula VIIb:

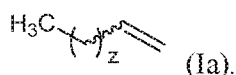


8. The method of embodiment 1, wherein converting the metathesis product to the fatty olefin derivative further comprises reducing the metathesis product, thereby forming a fatty olefin derivative according to Formula VIIb:

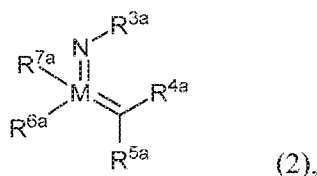


9. The method of embodiment 7 or embodiment 8, wherein  $\text{R}^1$  is H,  $\text{R}^{2b}$  is methyl, subscript  $y$  is 7, and subscript  $z$  is 3.

10. The method of any one of embodiments 1-9, wherein the olefin has a structure according to Formula Ia:



11. The method of embodiment 10, wherein subscript z is 3.
12. The method of any one of embodiments 1-11, wherein the metathesis product comprises a Z olefin.
13. The method of embodiment 12, wherein at least about 80% of the olefin is a Z olefin.
14. The method of embodiment 12, wherein at least about 90% of the olefin is a Z olefin.
15. The method of any one of embodiments 12-14, wherein the metathesis catalyst is a Z-selective molybdenum catalyst or a Z-selective tungsten catalyst.
16. The method of embodiment 15, wherein the metathesis catalyst has a structure according to Formula 2:



wherein:

M is Mo or W;

- 15  $R^{3a}$  is selected from the group consisting of aryl, heteroaryl, alkyl, heteroalkyl, cycloalkyl, and heterocycloalkyl, each of which is optionally substituted;

- $R^{4a}$  and  $R^{5a}$  are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted aryl, and optionally substituted heteroaryl;
- 20

$R^{7a}$  is selected from the group consisting of alkyl, alkoxy, heteroalkyl, aryl, aryloxy, heteroaryl, silylalkyl, and silyloxy, each of which is optionally substituted; and

$R^{6a}$  is  $R^{8a}$ -X-, wherein

X is O or S and  $R^{8a}$  is optionally substituted aryl; or

- 25 X is O and  $R^{8a}$  is  $SiR^{9a}R^{10a}R^{11a}$  or  $CR^{12a}R^{13a}R^{14a}$ , wherein  $R^{9a}$ ,  $R^{10a}$ ,  $R^{11a}$ ,  $R^{12a}$ ,  $R^{13a}$ , and  $R^{14a}$  are independently selected from the group consisting of optionally substituted alkyl and optionally substituted phenyl; or

$R^{6a}$  and  $R^{7a}$  are linked together and are bonded to M via oxygen.

17. The method of embodiment 16, wherein:

$R^{7a}$  is selected from the group consisting of alkyl, alkoxy, heteroalkyl, aryl, aryloxy, and heteroaryl, each of which is optionally substituted; and

X is O or S and  $R^{8a}$  is optionally substituted aryl; or

5 X is O and  $R^{8a}$  is  $CR^{12a}R^{13a}R^{14a}$ .

18. The method of embodiment 16, wherein

$R^{3a}$  is selected from the group consisting of 2,6-dimethylphenyl; 2,6-diisopropylphenyl; 2,6-dichlorophenyl; and adamant-1-yl;

$R^{4a}$  is selected from the group consisting of  $-C(CH_3)_2C_6H_5$  and  $-C(CH_3)_3$ ;

10  $R^{5a}$  is H;

$R^{7a}$  is selected from the group consisting of pyrrol-1-yl; 2,5-dimethyl-pyrrol-1-yl; triphenylsilyloxy; triisopropylsilyloxy; 2-phenyl-1,1,1,3,3,3-hexafluoro-prop-2-yloxy; 2-methyl-1,1,1,3,3,3-hexafluoro-prop-2-yloxy; 9-phenyl-fluorene-9-yloxy; 2,6-diphenyl-phenoxy; and *t*-butyloxy; and

15  $R^{6a}$  is  $R^{8a}-X-$ , wherein

X = O and

$R^{8a}$  is phenyl which bears two substituents in the ortho positions with respect to O, or which bears at least three substituents, from which two substituents are in the ortho positions with respect to O and one substituent is in the para position with respect to O; or

20  $R^{8a}$  is selected from the group consisting of optionally substituted 8-(naphthalene-1-yl)-naphthalene-1-yl; optionally substituted 8-phenylnaphthalene-1-yl; optionally substituted quinoline-8-yl; triphenylsilyl; triisopropylsilyl; triphenylmethyl; tri(4-methylphenyl)methyl; 9-phenyl-fluorene-9-yl; 2-phenyl-1,1,1,3,3,3-hexafluoro-prop-2-yl; 2-methyl-1,1,1,3,3,3-hexafluoro-prop-2-yl; and *t*-butyl.

25 19. The method of embodiment 18, wherein:

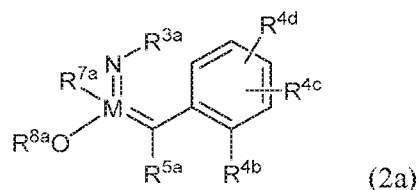
$R^{7a}$  is selected from the group consisting of pyrrol-1-yl; 2,5-dimethyl-pyrrol-1-yl; and

30  $R^{8a}$  is phenyl which bears two substituents in the ortho positions with respect to O, or which bears at least three substituents, from which two substituents are in the ortho positions with respect to O and one substituent is in the para position with respect to O; or

$R^{8a}$  is selected from the group consisting of optionally substituted 8-(naphthalene-1-yl)-naphthalene-1-yl and optionally substituted 8-phenylnaphthalene-1-yl.



20. The method of embodiment 16, wherein the metathesis catalyst has a structure according to Formula 2a:



wherein:

5  $R^{3a}$  is aryl, heteroaryl, alkyl, or cycloalkyl, each of which is optionally substituted;

$R^{7a}$  is pyrrolyl, imidazolyl, indolyl, pyrazolyl, azaindolyl, or indazolyl, each of which is optionally substituted;

$R^{8a}$  is optionally substituted aryl;

10  $R^{5a}$  is a hydrogen atom, alkyl, or alkoxy;

$R^{4b}$  is a hydrogen atom,  $-O-(C_{1-6}$  alkyl),  $-CH_2-O-(C_{1-6}$  alkyl), heteroalkoxy, or  $-N(C_{1-6}$  alkyl)<sub>2</sub>; and

$R^{4c}$  and  $R^{4d}$  are independently a hydrogen atom,  $C_{1-6}$  alkyl,  $C_{1-6}$  alkoxy, a halogen atom,  $-NO_2$ , an amide, or a sulfonamide.

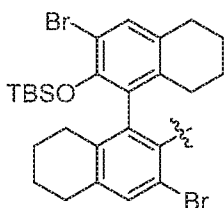
15 21. The method of embodiment 20, wherein:

$R^{7a}$  is pyrrolyl, imidazolyl, pyrazolyl, azaindolyl, or indazolyl, each of which is optionally substituted; and

$R^{5a}$  is a hydrogen atom.

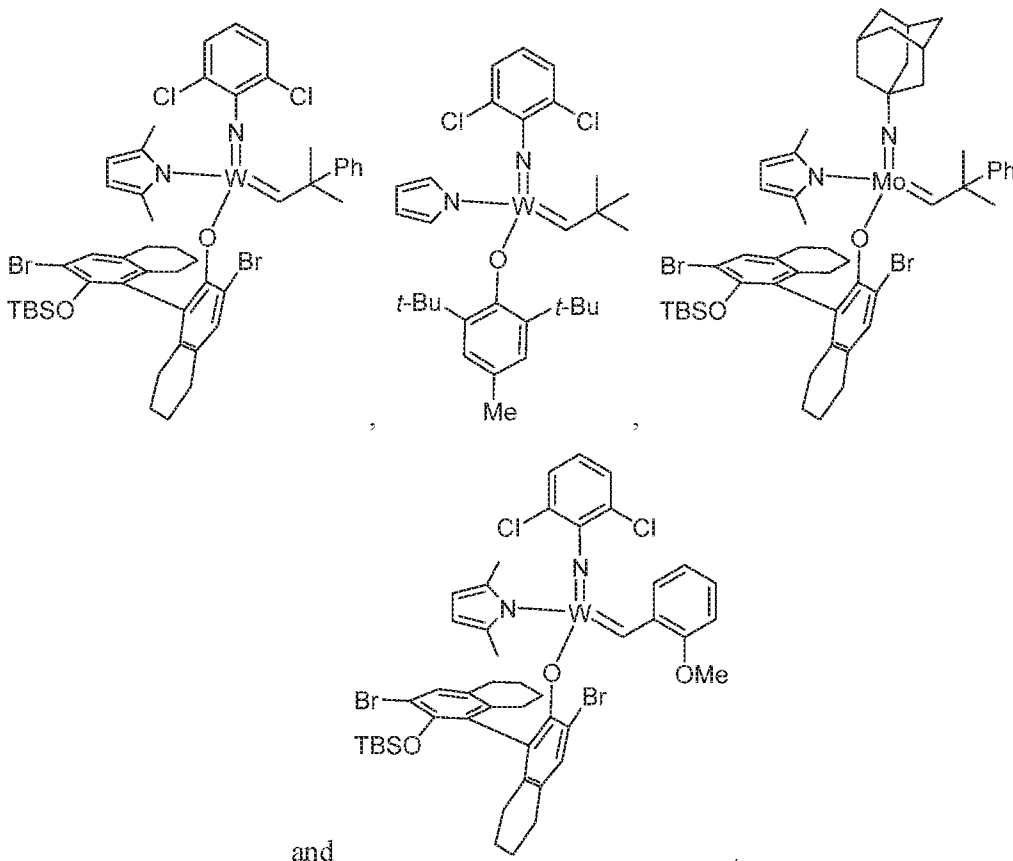
20 22. The method of embodiment 20, wherein  $R^{3a}$  is phenyl, 2,6-dichlorophenyl, 2,6-dimethylphenyl, 2,6-diisopropylphenyl, 2-trifluoromethylphenyl, pentafluorophenyl, tert-butyl, or 1-adamantyl.

23. The method of embodiment 20 or embodiment 22, wherein  $R^{8a}$  is



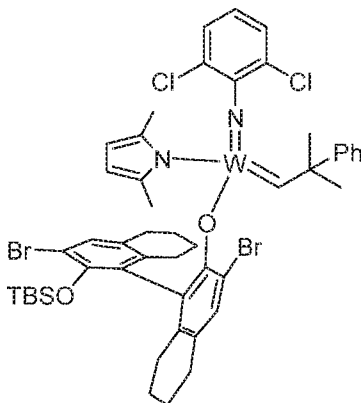
25 24. The method of any one of embodiments 20-23, wherein  $R^{4b}$  is methoxy,  $R^{4c}$  is hydrogen, and  $R^{4d}$  is hydrogen.

25. The method of embodiment 15, wherein the metathesis catalyst is selected from the group consisting of

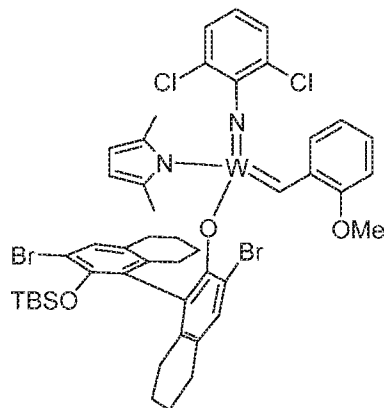


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26. The method of embodiment 25, wherein the metathesis catalyst is



27. The method of embodiment 25, wherein the metathesis catalyst is



28. The method of any one of embodiments 15-27, wherein the catalyst is present in an amount less than 0.01 mol% with respect to the olefin or to the metathesis reaction partner.

29. The method of any one of embodiments 1-10, wherein the metathesis product comprises an *E* olefin.

30. The method of embodiment 29, wherein greater than about 85% of the olefin is an *E* olefin.

31. The method of embodiment 29, wherein at least about 90% of the olefin is an *E* olefin.

32. The method of any one of embodiments 29-31, wherein the metathesis catalyst is an *E*-selective ruthenium catalyst.

33. The method of any one of embodiments 1-32, wherein the molar ratio of the olefin to the metathesis reaction partner ranges from about 1:1 to about 5:1.

34. The method of any one of embodiments 33, wherein the molar ratio of the olefin to the metathesis reaction partner ranges from about 2:1 to about 3:1.

35. The method of any one of embodiments 1-34, wherein the metathesis reaction partner is derived from a natural oil.

36. The method of embodiment 35, wherein the natural oil is selected from the group consisting of canola oil, rapeseed oil, coconut oil, corn oil, cottonseed oil, olive oil,

palm oil, peanut oil, safflower oil, sesame oil, soybean oil, sunflower oil, linseed oil, palm kernel oil, tung oil, jatropha oil, jojoba oil, mustard oil, pennycress oil, camelina oil, castor oil, and combinations thereof.

37. The method of embodiment 35 or 36, wherein the metathesis reaction partner comprises one or more catalyst-poisoning contaminants.

38. The method of embodiment 37, further comprising treating the metathesis reaction partner with a metal alkyl compound under conditions sufficient to reduce the concentration of at least one of the catalyst-poisoning contaminants, wherein the treating is conducted prior to contacting the olefin with the metathesis reaction partner.

39. The method of embodiment 1, wherein the olefin according to Formula I is a linear C<sub>3</sub>-C<sub>12</sub> alpha olefin, the metathesis reaction partner according to Formula IIb is a Δ<sup>9</sup>-unsaturated fatty acid alkyl ester, the metathesis catalyst is a Z-selective metathesis catalyst, and the metathesis product according to Formula IIIb is a C<sub>11</sub>-C<sub>20</sub> (Z)-9-unsaturated fatty acid alkyl ester.

40. The method of embodiment 39, wherein converting the metathesis product to the fatty olefin derivative comprises contacting the C<sub>11</sub>-C<sub>20</sub> (Z)-9-unsaturated fatty acid alkyl ester with a reducing agent under conditions sufficient to form a C<sub>11</sub>-C<sub>20</sub> (Z)-9-fatty alcohol.

41. The method of embodiment 40, wherein the reducing agent is sodium bis(2-methoxyethoxy)aluminum hydride.

42. The method of embodiment 40, wherein converting the metathesis product to the fatty olefin derivative further comprises contacting the C<sub>11</sub>-C<sub>20</sub> (Z)-9-fatty alcohol with an acylating agent in the presence of a base under conditions sufficient to form an acetate ester of the C<sub>11</sub>-C<sub>20</sub> (Z)-9-fatty alcohol.

43. The method of embodiment 42, wherein the acylating agent is acetic anhydride.

44. The method of embodiment 40, wherein converting the metathesis product to the fatty olefin derivative further comprises oxidizing the C<sub>11</sub>-C<sub>20</sub> (Z)-9-fatty alcohol to form a C<sub>11</sub>-C<sub>20</sub> (Z)-9-alkenal.
45. The method of embodiment 39, wherein converting the metathesis product to the fatty olefin derivative comprises contacting the C<sub>11</sub>-C<sub>20</sub> (Z)-9-fatty acid alkyl ester with a reducing agent under conditions sufficient to form a C<sub>11</sub>-C<sub>20</sub> (Z)-9-alkenal.
46. The method of embodiment 45, wherein the reducing agent is amine-modified sodium bis(2-methoxyethoxy)aluminumhydride.
47. The method of embodiment 1, wherein:  
the fatty acid derivative is (Z)-tetradec-9-en-1-yl acetate;  
the olefin according to Formula I is hex-1-ene,  
the metathesis reaction partner according to Formula IIb is a  $\Delta^9$ -unsaturated fatty acid alkyl ester,  
the metathesis catalyst is a Z-selective metathesis catalyst, and  
the metathesis product according to Formula IIIb is an alkyl ester of (Z)-9-tetradec-9-enoate; and  
wherein converting the metathesis product to the fatty olefin derivative comprises:  
contacting the alkyl ester of (Z)-9-tetradec-9-enoate with a reducing agent under conditions sufficient to form (Z)-tetradec-9-en-1-ol, and  
acylating the (Z)-tetradec-9-en-1-ol to form the (Z)-tetradec-9-en-1-yl acetate.
48. The method of embodiment 47, wherein the metathesis reaction partner according to Formula IIb is methyl 9-decenoate and the metathesis product is methyl (Z)-tetradec-9-enoate.
49. The method of embodiment 47, wherein the reducing agent is sodium bis(2-methoxyethoxy)aluminumhydride.
50. The method of embodiment 47, wherein acylating the (Z)-tetradec-9-en-1-ol comprises contacting the (Z)-tetradec-9-en-1-ol with an acylating agent in the presence of a base under conditions sufficient to form (Z)-tetradec-9-en-1-yl acetate.

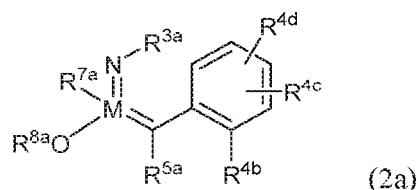
51. The method of embodiment 50, wherein the acylating agent is acetic anhydride.
52. The method of any one of embodiments 47-51, wherein the metathesis reaction partner according to Formula IIb is methyl 9-decenoate and the metathesis product is methyl (*Z*)-tetradec-9-enoate.
53. The method of embodiment 1, wherein:  
the fatty acid derivative is (*Z*)-tetradec-9-enal,  
the olefin according to Formula I is hex-1-ene,  
the metathesis reaction partner according to Formula IIb is a  $\Delta^9$ -unsaturated fatty acid alkyl ester,  
the metathesis catalyst is a *Z*-selective metathesis catalyst, and  
the metathesis product according to Formula IIIb is an alkyl ester of (*Z*)-9-tetradec-9-enoate; and  
wherein converting the metathesis product to the fatty olefin derivative comprises contacting the alkyl ester of (*Z*)-9-tetradec-9-enoate with a reducing agent under conditions sufficient to form the (*Z*)-tetradec-9-enal.
54. The method of embodiment 53, wherein the reducing agent is amine-modified sodium bis(2-methoxyethoxy) aluminumhydride.
55. The method of embodiment 53 or embodiment 54, wherein the  $\Delta^9$ -unsaturated fatty acid alkyl ester according to Formula IIg is methyl 9-decenoate and the metathesis product is methyl (*Z*)-tetradec-9-enoate.
56. The method of embodiment 1, wherein:  
the fatty acid derivative is (*Z*)-tetradec-9-enal,  
the olefin according to Formula I is hex-1-ene,  
the metathesis reaction partner according to Formula IIb is a  $\Delta^9$ -unsaturated fatty acid alkyl ester,  
the metathesis catalyst is a *Z*-selective metathesis catalyst, and  
the metathesis product according to Formula IIIb is an alkyl ester of (*Z*)-9-tetradec-9-enoate; and  
wherein converting the metathesis product to the fatty olefin derivative comprises

contacting the alkyl ester of (Z)-9-tetradec-9-enoate with a reducing agent under conditions sufficient to form (Z)-tetradec-9-en-1-ol, and oxidizing the (Z)-tetradec-9-en-1-ol to form the (Z)-tetradec-9-enal.

57. The method of embodiment 56, wherein the reducing agent is sodium bis(2-methoxyethoxy)aluminumhydride.

58. The method of embodiment 56 or embodiment 57, wherein the  $\Delta^9$ -unsaturated fatty acid alkyl ester according to Formula IIg is methyl 9-decenoate and the metathesis product is methyl (Z)-tetradec-9-enoate.

59. The method of any one of embodiments 39-58, wherein the metathesis catalyst has a structure according to Formula 2a:



wherein:

M is Mo or W;

15  $R^{3a}$  is aryl, heteroaryl, alkyl, or cycloalkyl, each of which is optionally substituted;

$R^{7a}$  is pyrrolyl, imidazolyl, indolyl, pyrazolyl, azaindolyl, or indazolyl, each of which is optionally substituted;

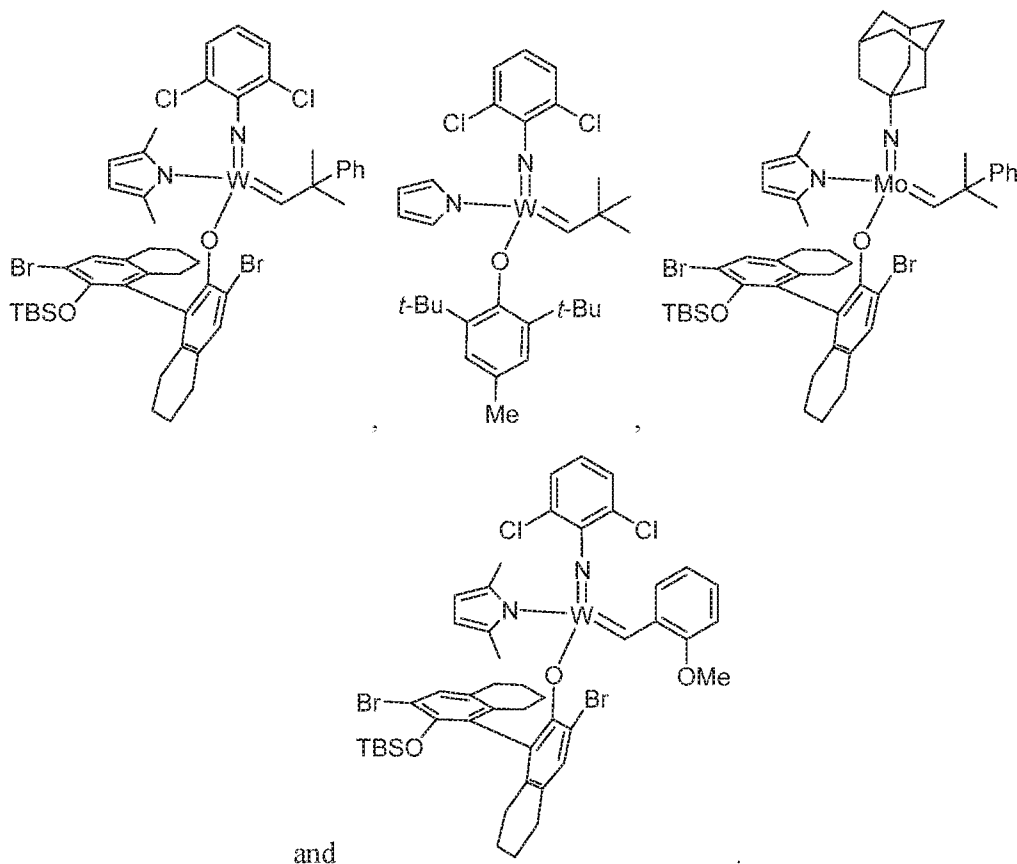
$R^{8a}$  is optionally substituted aryl;

$R^{5a}$  is a hydrogen atom, alkyl, or alkoxy;

20  $R^{4b}$  is a hydrogen atom,  $-O-(C_{1-6}$  alkyl),  $-CH_2-O-(C_{1-6}$  alkyl), heteroalkoxy, or  $-N(C_{1-6}$  alkyl)<sub>2</sub>; and

$R^{4c}$  and  $R^{4d}$  are independently a hydrogen atom,  $C_{1-6}$  alkyl,  $C_{1-6}$  alkoxy, a halogen atom,  $-NO_2$ , an amide, or a sulfonamide.

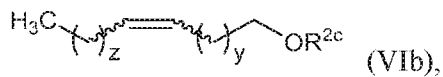
60. The method of embodiment 59, wherein the metathesis catalyst is selected from the group consisting of:



61. A fatty olefin derivative synthesized according to the method of any one of embodiments 1-60.

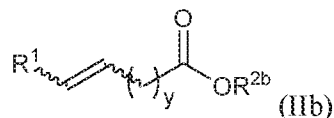
5 62. The fatty olefin derivative of embodiment 61, which is an insect pheromone.

63. A method for synthesizing a fatty olefin derivative according to Formula VIb:

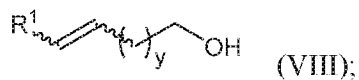


10 the method comprising:

i) reducing an alkyl ester according to Formula IIb

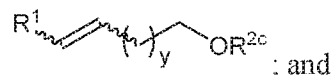


to form an alkenol according to Formula VIII





ii) acylating the alkenol to form an acylated alkenol according to Formula IX



iii) contacting the acylated alkenol with an olefin according to Formula I



5                in the presence of a metathesis catalyst under conditions sufficient to form the fatty olefin derivative; wherein:

$\text{R}^1$  is selected from the group consisting of H, C<sub>1-18</sub> alkyl, and C<sub>2-18</sub> alkenyl;

$\text{R}^{2b}$  is C<sub>1-8</sub> alkyl,

$\text{R}^{2c}$  is C<sub>1-6</sub> acyl,

10                subscript y is an integer ranging from 0 to 17;

                  subscript z is an integer ranging from 0 to 17; and

                  the metathesis catalyst is a tungsten catalyst or a molybdenum catalyst.

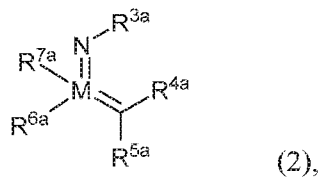
64.            The method of embodiment 63, wherein  $\text{R}^1$  is H,  $\text{R}^{2b}$  is methyl,  $\text{R}^{2c}$  is acetyl, subscript y is 7, and subscript z is 3.

15                65.            The method of embodiment 63 or embodiment 64, wherein the metathesis product comprises an E olefin.

66.            The method of embodiment 63 or embodiment 64, wherein the metathesis product comprises a Z olefin.

20                67.            The method of embodiment 66, wherein the metathesis catalyst is a Z-selective molybdenum catalyst or a Z-selective tungsten catalyst.

68.            The method of embodiment 67, wherein the metathesis catalyst has a structure according to Formula 2:



wherein:

25                M is Mo or W;

$R^{3a}$  is selected from the group consisting of aryl, heteroaryl, alkyl, heteroalkyl, cycloalkyl, and heterocycloalkyl, each of which is optionally substituted;

$R^{4a}$  and  $R^{5a}$  are independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted heteroalkyl, optionally substituted heteroalkenyl, optionally substituted aryl, and optionally substituted heteroaryl;

$R^{7a}$  is selected from the group consisting of alkyl, alkoxy, heteroalkyl, aryl, aryloxy, heteroaryl, silylalkyl, and silyloxy, each of which is optionally substituted; and

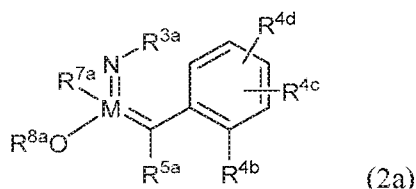
$R^{6a}$  is  $R^{8a}$ -X-, wherein

X is O or S and  $R^{8a}$  is optionally substituted aryl; or

X is O and  $R^{8a}$  is  $SiR^{9a}R^{10a}R^{11a}$  or  $CR^{12a}R^{13a}R^{14a}$ , wherein  $R^{9a}$ ,  $R^{10a}$ ,  $R^{11a}$ ,  $R^{12a}$ ,  $R^{13a}$ , and  $R^{14a}$  are independently selected from the group consisting of optionally substituted alkyl and optionally substituted phenyl; or

$R^{6a}$  and  $R^{7a}$  are linked together and are bonded to M via oxygen.

69. The method of embodiment 68, wherein the metathesis catalyst has a structure according to Formula 2a:



wherein:

$R^{3a}$  is aryl, heteroaryl, alkyl, or cycloalkyl, each of which is optionally substituted;

$R^{7a}$  is pyrrolyl, imidazolyl, indolyl, pyrazolyl, azaindolyl, or indazolyl, each of which is optionally substituted;

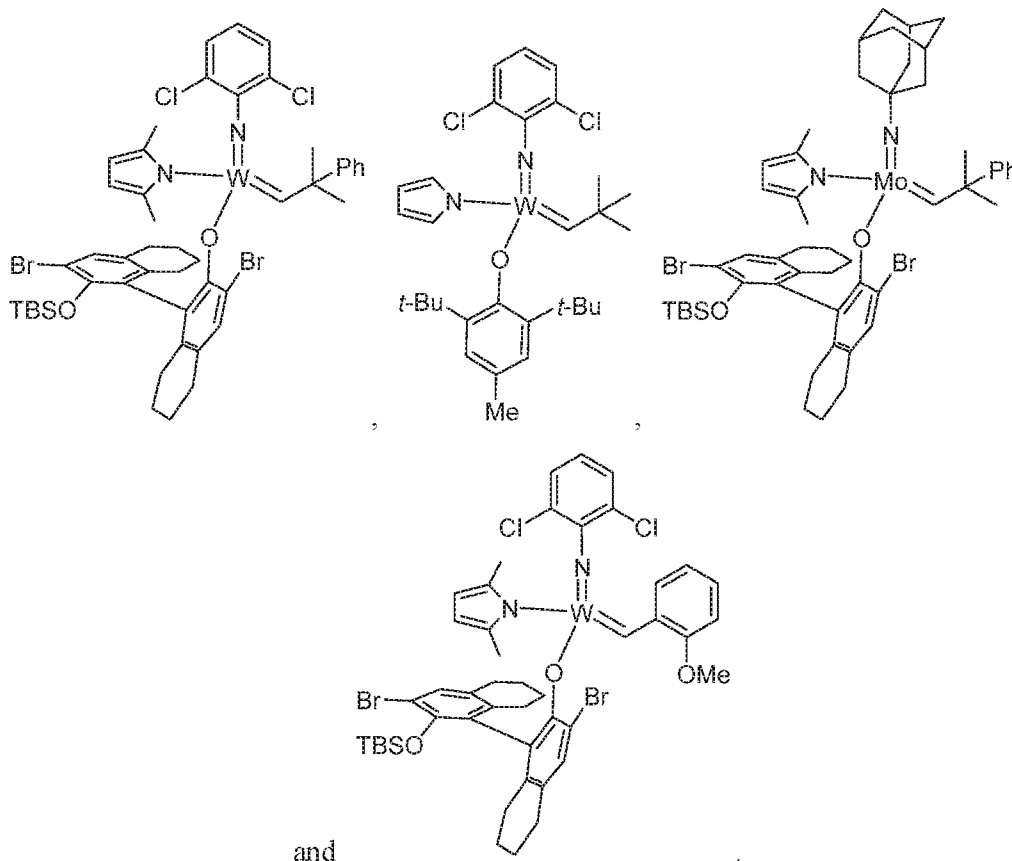
$R^{8a}$  is optionally substituted aryl;

$R^{5a}$  is a hydrogen atom, alkyl, or alkoxy;

$R^{4b}$  is a hydrogen atom,  $-O-(C_{1-6}$  alkyl),  $-CH_2-O-(C_{1-6}$  alkyl), heteroalkoxy, or  $-N(C_{1-6}$  alkyl)<sub>2</sub>; and

$R^{4c}$  and  $R^{4d}$  are independently a hydrogen atom,  $C_{1-6}$  alkyl,  $C_{1-6}$  alkoxy, a halogen atom,  $-NO_2$ , an amide, or a sulfonamide.

70. The method of embodiment 68 or embodiment 69, wherein the metathesis catalyst is selected from the group consisting of:



5

[0249] Although the foregoing has been described in some detail by way of illustration and example for purposes of clarity and understanding, one of skill in the art will appreciate that certain changes and modifications can be practiced within the scope of the appended claims.

10 All publications, patents, patent applications, and sequence accession numbers cited herein are hereby incorporated by reference in their entirety for all purposes.

WHAT IS CLAIMED IS:

1                   1.       A method for synthesizing a fatty olefin derivative, the method  
2 comprising:

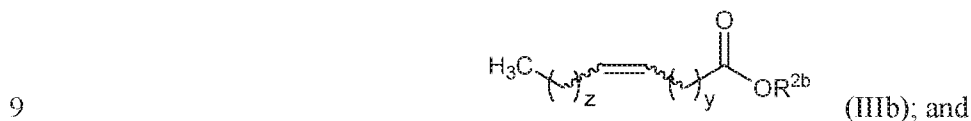
3                   a) contacting an olefin according to Formula I



5                   with a metathesis reaction partner according to Formula IIb



7                   in the presence of a metathesis catalyst under conditions sufficient to form a  
8 metathesis product according to Formula IIIb:



10                  b) converting the metathesis product to the fatty olefin derivative;  
11 wherein:

12                  each R<sup>1</sup> is independently selected from the group consisting of H, C<sub>1-18</sub> alkyl,  
13 and C<sub>2-18</sub> alkenyl;

14                  R<sup>2b</sup> is C<sub>1-8</sub> alkyl;

15                  subscript y is an integer ranging from 0 to 17; and

16                  subscript z is an integer ranging from 0 to 17.

1                   2.       The method of claim 1, wherein converting the metathesis product to  
2 the fatty olefin derivative comprises reducing the metathesis product to form an alkenol  
3 according to Formula Vb:



1                   3.       The method of claim 2, wherein the alkenol is the fatty olefin  
2 derivative.

1                   4.       The method of claim 2, wherein converting the metathesis product to  
2 the fatty olefin derivative further comprises acylating the alkenol, thereby forming a fatty  
3 olefin derivative according to Formula VIb:

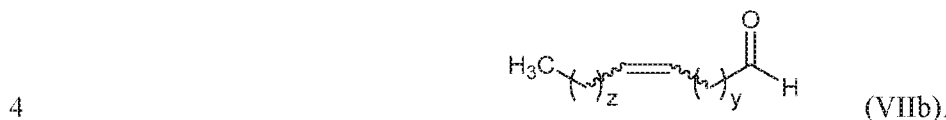


5 wherein R<sup>2c</sup> is C<sub>1-6</sub> acyl.

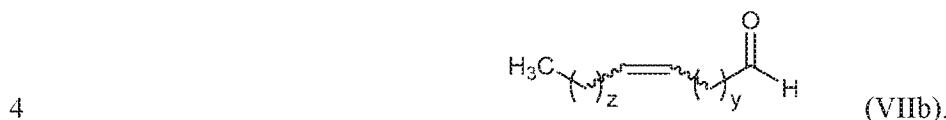
1 5. The method of claim 1, wherein R<sup>1</sup> is H, R<sup>2b</sup> is methyl, subscript y is 7,  
2 and subscript z is 3.

1 6. The method of claim 4, wherein R<sup>1</sup> is H, R<sup>2b</sup> is methyl, subscript y is 7,  
2 subscript z is 3, and R<sup>2c</sup> is acetyl.

1 7. The method of claim 2, wherein converting the metathesis product to  
2 the fatty olefin derivative further comprises oxidizing the alkenol, thereby forming a fatty  
3 olefin derivative according to Formula VIIIb:



1 8. The method of claim 1, wherein converting the metathesis product to  
2 the fatty olefin derivative further comprises reducing the metathesis product, thereby forming  
3 a fatty olefin derivative according to Formula VIIIb:



1 9. The method of claim 7, wherein R<sup>1</sup> is H, R<sup>2b</sup> is methyl, subscript y is 7,  
2 and subscript z is 3.

1 10. The method of claim 1, wherein the olefin has a structure according to  
2 Formula Ia:



1 11. The method of claim 10, wherein subscript z is 3.

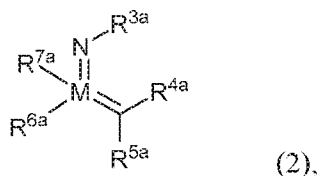
1 12. The method of claim 1, wherein the metathesis product comprises a Z  
2 olefin.

1 13. The method of claim 12, wherein at least about 80% of the olefin is a Z  
2 olefin.

1                   14.     The method of claim 12, wherein at least about 90% of the olefin is a Z  
2 olefin.

1                   15.     The method of claim 12, wherein the metathesis catalyst is a Z-  
2 selective molybdenum catalyst or a Z-selective tungsten catalyst.

1                   16.     The method of claim 15, wherein the metathesis catalyst has a structure  
2 according to Formula 2:



3

4                   wherein:

5                   M is Mo or W;

6                   R<sup>3a</sup> is selected from the group consisting of aryl, heteroaryl, alkyl, heteroalkyl,  
7 cycloalkyl, and heterocycloalkyl, each of which is optionally substituted;

8                   R<sup>4a</sup> and R<sup>5a</sup> are independently selected from the group consisting of hydrogen,  
9 optionally substituted alkyl, optionally substituted alkenyl, optionally substituted heteroalkyl,  
10 optionally substituted heteroalkenyl, optionally substituted aryl, and optionally substituted  
11 heteroaryl;

12                   R<sup>7a</sup> is selected from the group consisting of alkyl, alkoxy, heteroalkyl, aryl,  
13 aryloxy, heteroaryl, silylalkyl, and silyloxy, each of which is optionally substituted; and

14                   R<sup>6a</sup> is R<sup>8a</sup>-X-, wherein

15                   X is O or S and R<sup>8a</sup> is optionally substituted aryl; or

16                   X is O and R<sup>8a</sup> is SiR<sup>9a</sup>R<sup>10a</sup>R<sup>11a</sup> or CR<sup>12a</sup>R<sup>13a</sup>R<sup>14a</sup>, wherein R<sup>9a</sup>, R<sup>10a</sup>, R<sup>11a</sup>, R<sup>12a</sup>,  
17 R<sup>13a</sup>, and R<sup>14a</sup> are independently selected from the group consisting of optionally substituted  
18 alkyl and optionally substituted phenyl; or

19                   R<sup>6a</sup> and R<sup>7a</sup> are linked together and are bonded to M via oxygen.

1                   17.     The method of claim 16, wherein:

2                   R<sup>7a</sup> is selected from the group consisting of alkyl, alkoxy, heteroalkyl, aryl,  
3 aryloxy, and heteroaryl, each of which is optionally substituted; and

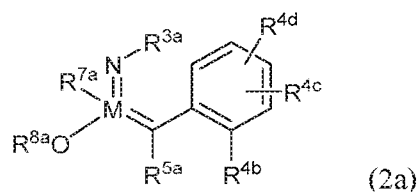
4                   X is O or S and R<sup>8a</sup> is optionally substituted aryl; or

5                   X is O and R<sup>8a</sup> is CR<sup>12a</sup>R<sup>13a</sup>R<sup>14a</sup>.

1                   18.     The method of claim 16, wherein  
2                   R<sup>3a</sup> is selected from the group consisting of 2,6-dimethylphenyl; 2,6-  
3 diisopropylphenyl; 2,6-dichlorophenyl; and adamant-1-yl;  
4                   R<sup>4a</sup> is selected from the group consisting of -C(CH<sub>3</sub>)<sub>2</sub>C<sub>6</sub>H<sub>5</sub> and -C(CH<sub>3</sub>)<sub>3</sub>;  
5                   R<sup>5a</sup> is H;  
6                   R<sup>7a</sup> is selected from the group consisting of pyrrol-1-yl; 2,5-dimethyl-pyrrol-1-  
7 yl; triphenylsilyloxy; triisopropylsilyloxy; 2-phenyl-1,1,1,3,3,3-hexafluoro-prop-2-yloxy; 2-  
8 methyl-1,1,1,3,3,3-hexafluoro-prop-2-yloxy; 9-phenyl-fluorene-9-yloxy; 2,6-diphenyl-  
9 phenoxy; and *t*-butyloxy; and  
10                  R<sup>6a</sup> is R<sup>8a</sup>-X-, wherein  
11                  X = O and  
12                  R<sup>8a</sup> is phenyl which bears two substituents in the ortho positions with respect  
13 to O, or which bears at least three substituents, from which two substituents are in the ortho  
14 positions with respect to O and one substituent is in the para position with respect to O; or  
15                  R<sup>8a</sup> is selected from the group consisting of optionally substituted  
16 8-(naphthalene-1-yl)-naphthalene-1-yl; optionally substituted 8-phenylnaphthalene-1-yl;  
17 optionally substituted quinoline-8-yl; triphenylsilyl; triisopropylsilyl; triphenylmethyl;  
18 tri(4-methylphenyl)methyl; 9-phenyl-fluorene-9-yl; 2-phenyl-1,1,1,3,3,3-hexafluoro-  
19 prop-2-yl; 2-methyl-1,1,1,3,3,3-hexafluoro-prop-2-yl; and *t*-butyl.

1                   19.     The method of claim 18, wherein:  
2                   R<sup>7a</sup> is selected from the group consisting of pyrrol-1-yl; 2,5-dimethyl-pyrrol-1-  
3 yl; and  
4                   R<sup>8a</sup> is phenyl which bears two substituents in the ortho positions with respect  
5 to O, or which bears at least three substituents, from which two substituents are in the ortho  
6 positions with respect to O and one substituent is in the para position with respect to O; or  
7                   R<sup>8a</sup> is selected from the group consisting of optionally substituted  
8 8-(naphthalene-1-yl)-naphthalene-1-yl and optionally substituted 8-phenylnaphthalene-1-yl.

1                   20.     The method of claim 16, wherein the metathesis catalyst has a structure  
2 according to Formula 2a:



3                   wherein:

4                   R<sup>3a</sup> is aryl, heteroaryl, alkyl, or cycloalkyl, each of which is optionally  
5 substituted;

6                   R<sup>7a</sup> is pyrrolyl, imidazolyl, indolyl, pyrazolyl, azaindolyl, or indazolyl, each of  
7 which is optionally substituted;

8                   R<sup>8a</sup> is optionally substituted aryl;

9                   R<sup>5a</sup> is a hydrogen atom, alkyl, or alkoxy;

10                  R<sup>4b</sup> is a hydrogen atom, -O-(C<sub>1-6</sub> alkyl), -CH<sub>2</sub>-O-(C<sub>1-6</sub> alkyl), heteroalkoxy, or  
11 -N(C<sub>1-6</sub> alkyl)<sub>2</sub>; and

12                  R<sup>4c</sup> and R<sup>4d</sup> are independently a hydrogen atom, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, a  
13 halogen atom, -NO<sub>2</sub>, an amide, or a sulfonamide.  
14

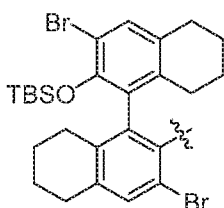
1                   21.     The method of claim 20, wherein:

2                   R<sup>7a</sup> is pyrrolyl, imidazolyl, pyrazolyl, azaindolyl, or indazolyl, each of which  
3 is optionally substituted; and

4                   R<sup>5a</sup> is a hydrogen atom.

1                   22.     The method of claim 20, wherein R<sup>3a</sup> is phenyl, 2,6-dichlorophenyl,  
2 2,6-dimethylphenyl, 2,6-diisopropylphenyl, 2-trifluoromethylphenyl, pentafluorophenyl, tert-  
3 butyl, or 1-adamantyl.

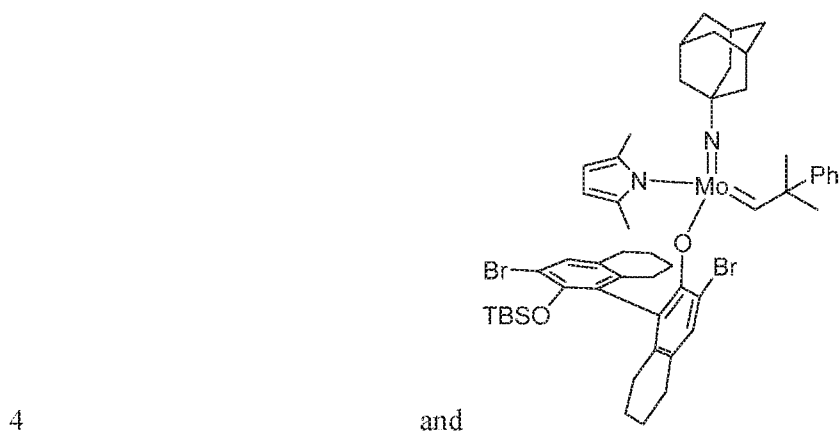
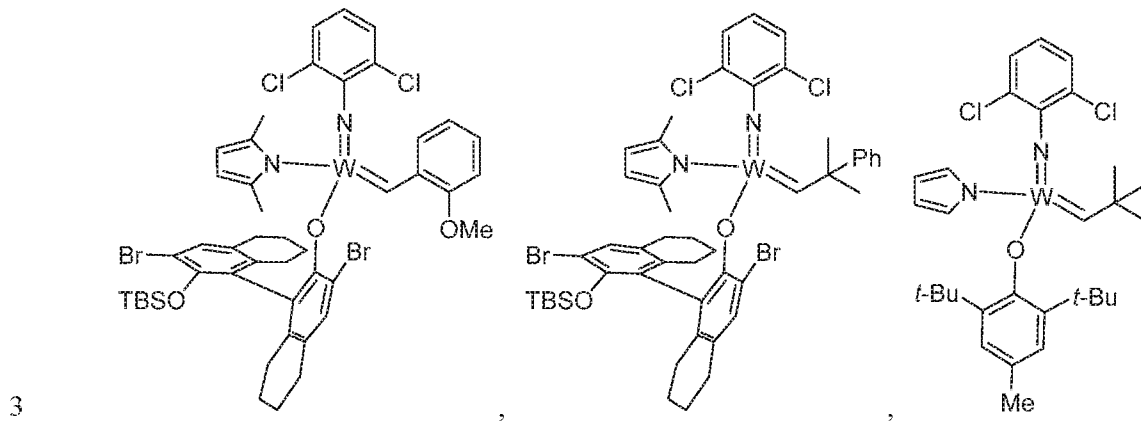
1                   23.     The method of claim 20 or claim 22, wherein R<sup>8a</sup> is



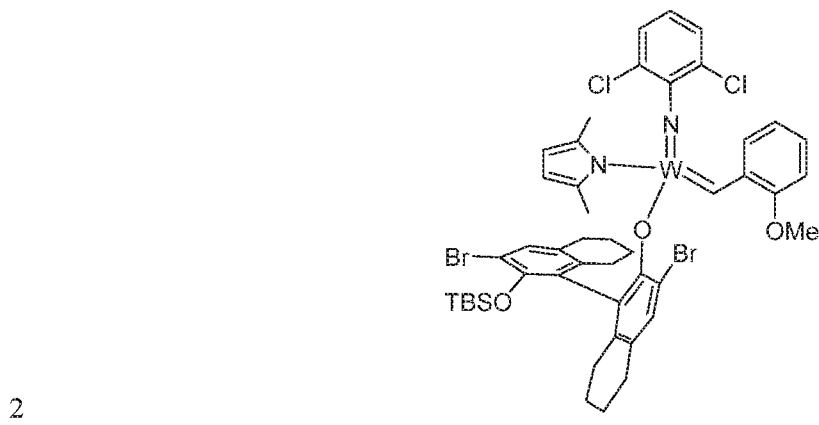


1                    24.    The method of claim 20, wherein R<sup>4b</sup> is methoxy, R<sup>4c</sup> is hydrogen, and  
 2    R<sup>4d</sup> is hydrogen.

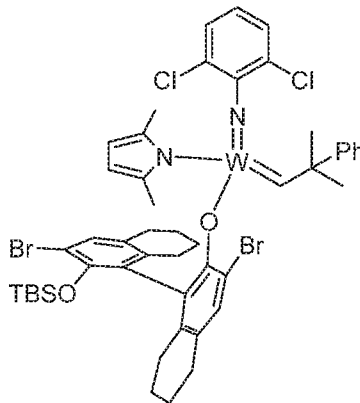
1                    25.    The method of claim 15, wherein the metathesis catalyst is selected  
 2    from the group consisting of



1                    26.    The method of claim 25, wherein the metathesis catalyst is



1                    27.     The method of claim 25, wherein the metathesis catalyst is



1                    28.     The method of claim 15, wherein the catalyst is present in an amount  
2 less than 0.01 mol% with respect to the olefin or to the metathesis reaction partner.

1                    29.     The method of claim 1, wherein the metathesis product comprises an *E*  
2 olefin.

1                    30.     The method of claim 29, wherein greater than about 85% of the olefin  
2 is an *E* olefin.

1                    31.     The method of claim 29, wherein at least about 90% of the olefin is an  
2 *E* olefin.

1                    32.     The method of claim 29, wherein the metathesis catalyst is an *E*-  
2 selective ruthenium catalyst.

1                    33.     The method of claim 1, wherein the molar ratio of the olefin to the  
2 metathesis reaction partner ranges from about 1:1 to about 5:1.

1                    34.     The method of claim 33, wherein the molar ratio of the olefin to the  
2 metathesis reaction partner ranges from about 2:1 to about 3:1

1                    35.     The method of claim 1, wherein the metathesis reaction partner is  
2 derived from a natural oil.

1                    36.     The method of claim 35, wherein the natural oil is selected from the  
2 group consisting of canola oil, rapeseed oil, coconut oil, corn oil, cottonseed oil, olive oil,

3 palm oil, peanut oil, safflower oil, sesame oil, soybean oil, sunflower oil, linseed oil, palm  
4 kernel oil, tung oil, jatropha oil, jojoba oil, mustard oil, pennycress oil, camelina oil, castor  
5 oil, and combinations thereof.

1           37.     The method of claim 35, wherein the metathesis reaction partner  
2 comprises one or more catalyst-poisoning contaminants.

1           38.     The method of claim 37, further comprising treating the metathesis  
2 reaction partner with a metal alkyl compound under conditions sufficient to reduce the  
3 concentration of at least one of the catalyst-poisoning contaminants, wherein the treating is  
4 conducted prior to contacting the olefin with the metathesis reaction partner.

1           39.     The method of claim 1, wherein  
2 the olefin according to Formula I is a linear C<sub>3</sub>-C<sub>12</sub> alpha olefin,  
3 the metathesis reaction partner according to Formula IIb is a Δ<sup>9</sup>-unsaturated  
4 fatty acid alkyl ester,  
5 the metathesis catalyst is a Z-selective metathesis catalyst, and  
6 the metathesis product according to Formula IIIb is a  
7 C<sub>11</sub>-C<sub>20</sub> (Z)-9-unsaturated fatty acid alkyl ester.

1           40.     The method of claim 39, wherein converting the metathesis product to  
2 the fatty olefin derivative comprises contacting the C<sub>11</sub>-C<sub>20</sub> (Z)-9-unsaturated fatty acid alkyl  
3 ester with a reducing agent under conditions sufficient to form a C<sub>11</sub>-C<sub>20</sub> (Z)-9-fatty alcohol.

1           41.     The method of claim 40, wherein the reducing agent is sodium bis(2-  
2 methoxyethoxy)aluminum hydride.

1           42.     The method of claim 40, wherein converting the metathesis product to  
2 the fatty olefin derivative further comprises contacting the C<sub>11</sub>-C<sub>20</sub> (Z)-9-fatty alcohol with an  
3 acylating agent in the presence of a base under conditions sufficient to form an acetate ester  
4 of the C<sub>11</sub>-C<sub>20</sub> (Z)-9-fatty alcohol.

1           43.     The method of claim 42, wherein the acylating agent is acetic  
2 anhydride.

1                   44.     The method of claim 40, wherein converting the metathesis product to  
2 the fatty olefin derivative further comprises oxidizing the C<sub>11</sub>-C<sub>20</sub> (Z)-9-fatty alcohol to form  
3 a C<sub>11</sub>-C<sub>20</sub> (Z)-9-alkenal.

1                   45.     The method of claim 39, wherein converting the metathesis product to  
2 the fatty olefin derivative comprises contacting the C<sub>11</sub>-C<sub>20</sub> (Z)-9-fatty acid alkyl ester with a  
3 reducing agent under conditions sufficient to form a C<sub>11</sub>-C<sub>20</sub> (Z)-9-alkenal.

1                   46.     The method of claim 45, wherein the reducing agent is amine-modified  
2 sodium bis(2-methoxyethoxy)aluminumhydride.

1                   47.     The method of claim 1, wherein:  
2 the fatty acid derivative is (Z)-tetradec-9-en-1-yl acetate;  
3 the olefin according to Formula I is hex-1-ene,  
4 the metathesis reaction partner according to Formula IIb is a  $\Delta^9$ -unsaturated  
5 fatty acid alkyl ester,  
6 the metathesis catalyst is a Z-selective metathesis catalyst, and  
7 the metathesis product according to Formula IIIb is an alkyl ester of (Z)-9-  
8 tetradec-9-enoate; and  
9 wherein converting the metathesis product to the fatty olefin derivative  
10 comprises:  
11 contacting the alkyl ester of (Z)-9-tetradec-9-enoate with a reducing agent  
12 under conditions sufficient to form (Z)-tetradec-9-en-1-ol, and  
13 acylating the (Z)-tetradec-9-en-1-ol to form the (Z)-tetradec-9-en-1-yl acetate.

1                   48.     The method of claim 47, wherein the metathesis reaction partner  
2 according to Formula IIb is methyl 9-decenoate and the metathesis product is methyl (Z)-  
3 tetradec-9-enoate.

1                   49.     The method of claim 47, wherein the reducing agent is sodium bis(2-  
2 methoxyethoxy)aluminumhydride.

1                   50.     The method of claim 47, wherein acylating the (Z)-tetradec-9-en-1-ol  
2 comprises contacting the (Z)-tetradec-9-en-1-ol with an acylating agent in the presence of a  
3 base under conditions sufficient to form (Z)-tetradec-9-en-1-yl acetate.

1                   51.     The method of claim 50, wherein the acylating agent is acetic  
2 anhydride.

1                   52.     The method of claim 47, wherein the metathesis reaction partner  
2 according to Formula IIb is methyl 9-decenoate and the metathesis product is methyl (Z)-  
3 tetradec-9-enoate.

1                   53.     The method of claim 1, wherein:  
2                   the fatty acid derivative is (Z)-tetradec-9-enal,  
3                   the olefin according to Formula I is hex-1-ene,  
4                   the metathesis reaction partner according to Formula IIb is a  $\Delta^9$ -unsaturated  
5 fatty acid alkyl ester,  
6                   the metathesis catalyst is a Z-selective metathesis catalyst, and  
7                   the metathesis product according to Formula IIIb is an alkyl ester of (Z)-9-  
8 tetradec-9-enoate; and  
9                   wherein converting the metathesis product to the fatty olefin derivative  
10 comprises contacting the alkyl ester of (Z)-9-tetradec-9-enoate with a reducing agent under  
11 conditions sufficient to form the (Z)-tetradec-9-enal.

1                   54.     The method of claim 53, wherein the reducing agent is amine-modified  
2 sodium bis(2-methoxyethoxy) aluminumhydride.

1                   55.     The method of claim 53, wherein the  $\Delta^9$ -unsaturated fatty acid alkyl  
2 ester according to Formula IIg is methyl 9-decenoate and the metathesis product is methyl  
3 (Z)-tetradec-9-enoate.

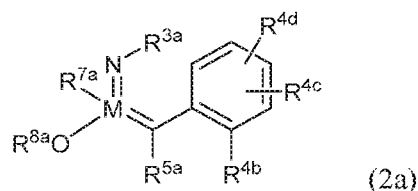
1                   56.     The method of claim 1, wherein:  
2                   the fatty acid derivative is (Z)-tetradec-9-enal,  
3                   the olefin according to Formula I is hex-1-ene,  
4                   the metathesis reaction partner according to Formula IIb is a  $\Delta^9$ -unsaturated  
5 fatty acid alkyl ester,  
6                   the metathesis catalyst is a Z-selective metathesis catalyst, and  
7                   the metathesis product according to Formula IIIb is an alkyl ester of (Z)-9-  
8 tetradec-9-enoate; and

9 wherein converting the metathesis product to the fatty olefin derivative  
 10 comprises  
 11 contacting the alkyl ester of (Z)-9-tetradec-9-enoate with a reducing agent  
 12 under conditions sufficient to form (Z)-tetradec-9-en-1-ol, and  
 13 oxidizing the (Z)-tetradec-9-en-1-ol to form the (Z)-tetradec-9-enal.

1 57. The method of claim 56, wherein the reducing agent is sodium bis(2-  
 2 methoxyethoxy)aluminumhydride.

1 58. The method of claim 56, wherein the  $\Delta^9$ -unsaturated fatty acid alkyl  
 2 ester according to Formula IIg is methyl 9-decenoate and the metathesis product is methyl  
 3 (Z)-tetradec-9-enoate.

1 59. The method of claim 39, wherein the metathesis catalyst has a structure  
 2 according to Formula 2a:



3  
 4 wherein:

5 M is Mo or W;

6  $R^{3a}$  is aryl, heteroaryl, alkyl, or cycloalkyl, each of which is optionally  
 7 substituted;

8  $R^{7a}$  is pyrrolyl, imidazolyl, indolyl, pyrazolyl, azaindolyl, or indazolyl, each of  
 9 which is optionally substituted;

10  $R^{8a}$  is optionally substituted aryl;

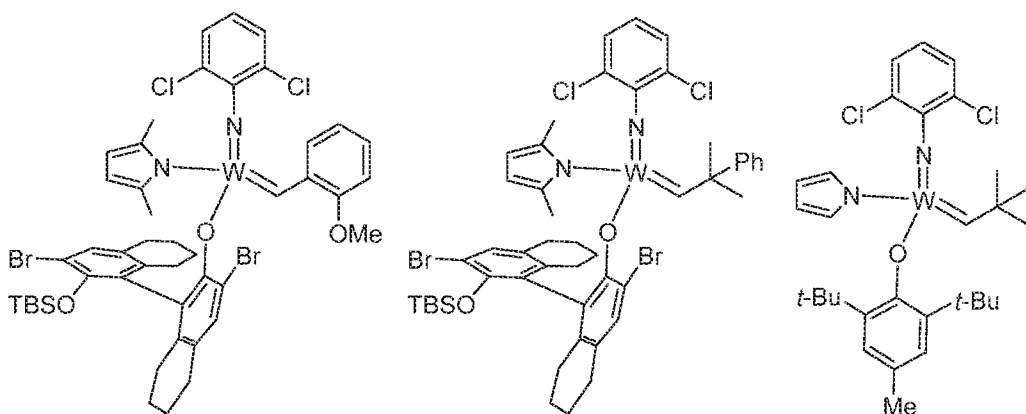
11  $R^{5a}$  is a hydrogen atom, alkyl, or alkoxy;

12  $R^{4b}$  is a hydrogen atom, -O-(C<sub>1-6</sub> alkyl), -CH<sub>2</sub>-O-(C<sub>1-6</sub> alkyl), heteroalkoxy, or  
 13 -N(C<sub>1-6</sub> alkyl)<sub>2</sub>; and

14  $R^{4c}$  and  $R^{4d}$  are independently a hydrogen atom, C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, a  
 15 halogen atom, -NO<sub>2</sub>, an amide, or a sulfonamide.

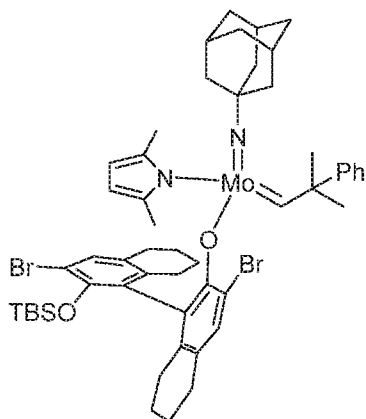
1 60. The method of claim 59, wherein the metathesis catalyst is selected  
 2 from the group consisting of:

3



4

and



1

61. A fatty olefin derivative synthesized according to the method of claim

2 1.

1

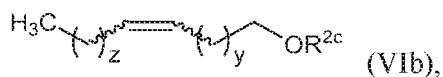
62. The fatty olefin derivative of claim 61, which is an insect pheromone.

1

63. A method for synthesizing a fatty olefin derivative according to

2 Formula VIb:

3



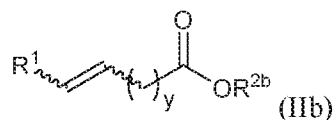
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the method comprising:

5

i) reducing an alkyl ester according to Formula IIb

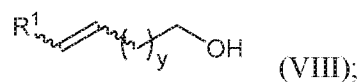
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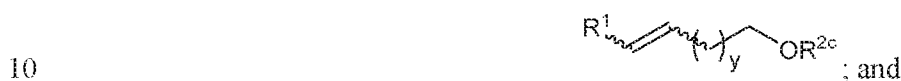
to form an alkenol according to Formula VIII

8



9

ii) acylating the alkenol to form an acylated alkenol according to Formula IX



11 iii) contacting the acylated alkenol with an olefin according to Formula I



13 in the presence of a metathesis catalyst under conditions sufficient to form the  
14 fatty olefin derivative; wherein:

15  $R^1$  is selected from the group consisting of H,  $C_{1-18}$  alkyl, and  $C_{2-18}$  alkenyl;

16  $R^{2b}$  is  $C_{1-8}$  alkyl,

17  $R^{2c}$  is  $C_{1-6}$  acyl,

18 subscript y is an integer ranging from 0 to 17;

19 subscript z is an integer ranging from 0 to 17; and

20 the metathesis catalyst is a tungsten catalyst or a molybdenum catalyst.

1 64. The method of claim 63, wherein  $R^1$  is H,  $R^{2b}$  is methyl,  $R^{2c}$  is acetyl,  
2 subscript y is 7, and subscript z is 3.

1 65. The method of claim 63, wherein the metathesis product comprises an  
2 E olefin.

1 66. The method of claim 63, wherein the metathesis product comprises a Z  
2 olefin.

1 67. The method of claim 66, wherein the metathesis catalyst is a Z-  
2 selective molybdenum catalyst or a Z-selective tungsten catalyst.

1 68. The method of claim 67, wherein the metathesis catalyst has a structure  
2 according to Formula 2:



4 wherein:

5 M is Mo or W;

6  $R^{3a}$  is selected from the group consisting of aryl, heteroaryl, alkyl, heteroalkyl,  
7 cycloalkyl, and heterocycloalkyl, each of which is optionally substituted;



8  $R^{4a}$  and  $R^{5a}$  are independently selected from the group consisting of hydrogen,  
 9 optionally substituted alkyl, optionally substituted alkenyl, optionally substituted heteroalkyl,  
 10 optionally substituted heteroalkenyl, optionally substituted aryl, and optionally substituted  
 11 heteroaryl;

12  $R^{7a}$  is selected from the group consisting of alkyl, alkoxy, heteroalkyl, aryl,  
 13 aryloxy, heteroaryl, silylalkyl, and silyloxy, each of which is optionally substituted; and

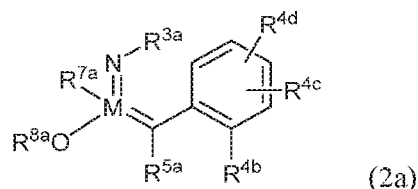
14  $R^{6a}$  is  $R^{8a}$ -X-, wherein

15 X is O or S and  $R^{8a}$  is optionally substituted aryl; or

16 X is O and  $R^{8a}$  is  $SiR^{9a}R^{10a}R^{11a}$  or  $CR^{12a}R^{13a}R^{14a}$ , wherein  $R^{9a}$ ,  $R^{10a}$ ,  $R^{11a}$ ,  $R^{12a}$ ,  
 17  $R^{13a}$ , and  $R^{14a}$  are independently selected from the group consisting of optionally substituted  
 18 alkyl and optionally substituted phenyl; or

19  $R^{6a}$  and  $R^{7a}$  are linked together and are bonded to M via oxygen.

1 69. The method of claim 68, wherein the metathesis catalyst has a structure  
 2 according to Formula 2a:



3

4 wherein:

5  $R^{3a}$  is aryl, heteroaryl, alkyl, or cycloalkyl, each of which is optionally  
 6 substituted;

7  $R^{7a}$  is pyrrolyl, imidazolyl, indolyl, pyrazolyl, azaindolyl, or indazolyl, each of  
 8 which is optionally substituted;

9  $R^{8a}$  is optionally substituted aryl;

10  $R^{5a}$  is a hydrogen atom, alkyl, or alkoxy;

11  $R^{4b}$  is a hydrogen atom,  $-O-(C_{1-6}$  alkyl),  $-CH_2-O-(C_{1-6}$  alkyl), heteroalkoxy, or  
 12  $-N(C_{1-6}$  alkyl)<sub>2</sub>; and

13  $R^{4c}$  and  $R^{4d}$  are independently a hydrogen atom,  $C_{1-6}$  alkyl,  $C_{1-6}$  alkoxy, a  
 14 halogen atom,  $-NO_2$ , an amide, or a sulfonamide.

1                    70.    The method of claim 68, wherein the metathesis catalyst is selected  
 2    from the group consisting of:

