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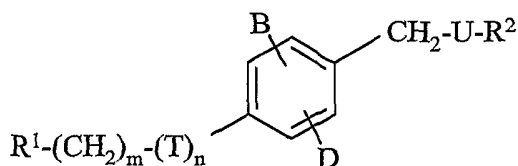
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(54) Title: INSECTICIDAL HETEROCYCLIC 1,4-DISUBSTITUTED BENZENE N-OXIDES



(I)

(57) Abstract: Certain novel heterocyclic 1,4-disubstituted benzene N-oxide derivatives have provided unexpected insecticidal and acaricidal activity. These compounds are represented by formula (I) wherein R^1 , R^2 , B, D, T, U, m, and n are fully described herein. In addition, compositions comprising an insecticidally effective amount of at least one compound of formula I, and optionally, an effective amount of at least one of a second compound,

with at least one insecticidally compatible carrier are also disclosed; along with methods of controlling insects comprising applying said compositions to a locus where insects are present or are expected to be present.



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INSECTICIDAL HETEROCYCLIC 1,4-DISUBSTITUTED BENZENE N- OXIDES

5 This application claims the benefit of U.S. Provisional Application No. 60/644,761, filed January 18, 2005.

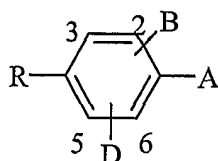
FIELD OF THE INVENTION

10 The present invention generally relates to pesticidal compounds and their use in controlling insects and acarids. In particular, it pertains to compositions of pesticidal heterocyclic 1,4-disubstituted benzene N-oxide derivatives and agriculturally acceptable salts thereof, and methods for their use in controlling insects and acarids.

BACKGROUND OF THE INVENTION

15 It is well known that insects in general can cause significant damage, not only to crops grown in agriculture, but also, for example, to structures and turf where the damage is caused by soil-borne insects, such as termites and white grubs. Such damage may result in the loss of millions of dollars of value associated with a given crop, turf or structure. Thus, there is a continuing demand for new insecticides that are safer, more effective, and less costly. Insecticides are useful for
20 controlling insects which may otherwise cause significant damage to crops such as wheat, corn, soybeans, potatoes, and cotton to name a few. For crop protection, insecticides are desired which can control the insects without damaging the crops, and which have no deleterious effects to mammals and other living organisms.
25

 Certain 1,4-disubstituted benzene derivatives are known in the art. For example, U.S. Patent 6,753,429 discloses certain 1,4-disubstituted benzenes as insecticides. These 1,4-disubstituted benzenes are represented by the following formula :



in which:

A is hydrogen; aryl; alkylheterocyclyl; alkenylaminopolycyclyl; alkenylaminoheterocyclyl; alkylaminopolycyclyl; carbonylaminopolycyclyl; and Formula III, where Formula III is

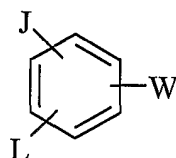


where

n is 0 or 1;

U is $-CH_2-$, $-O-CH_2-$, oxygen, sulfur, sulfonyl, alkyl, oxyalkyloxy, alkenylamino, cabonylamino and $-NR^5$, where R^5 is hydrogen, hydroxy, alkyl, haloalkyl, sulfonylalkyl, cabonylamino, and carbonylalkyl;

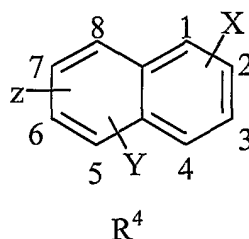
R^2 is aryl; alkylpolycyclyl; heterocyclyl; polycyclyl; $1-R^3$; $1-R^4$; and $2-R^4$, where: R^3 is



15 R^3

where J, L, and W are independently hydrogen, halogen, cyano, nitro, amino, carboxyl, alkyl, haloalkyl, alkenyl, alkoxy, haloalkoxy, aminoalkoxy, nitrilyl, carbonyl, alkylcarbonyl, haloalkylcarbonyl, alkoxy carbonyl, haloalkoxy carbonyl, aryl, aryloxy, and heterocyclyl;

20 R^4 is



where X, Y, and Z are independently hydrogen, halogen, cyano, nitro, amino, azido, carboxyl, alkyl, alkynyl, haloalkyl, haloalkylthio, nitrilyl, alkenyl, alkoxy, haloalkoxy, carbonyl, alkylcarbonyl, haloalkylcarbonyl, alkoxy carbonyl, haloalkoxy carbonyl, phenyl, aryl, aryloxy, and heterocyclyl;

B and D are independently hydrogen, halogen, alkyl, haloalkyl, alkoxy, haloalkoxy, alkoxyaminoalkyl, 2-(Formula III), 3-(Formula III), 5-(Formula III), and 6-(Formula

III), where Formula III, n, U, R², R³, R⁴, R⁵, J, L, W, X, Y, and Z are as defined above;

R is -T-(CH₂)_m-R¹, -N(R⁶)(R⁷) or heterocyclyl;

T is -CH₂-, carbonyl, oxygen, nitrogen, and sulfur;

5 m is 0, 1, 2, 3, or 4;

R¹ is -N(R⁸)(R⁹); alkyl; aryl; -C(O)N(R¹²)(R¹³); oxyalkyl; haloalkyl; heterocyclyl; cycloalkyl; -N(O)(R¹⁴)(R¹⁵); -P(O)(R¹⁴)(R¹⁵); -P(S)(R¹⁴)(R¹⁵); alkylamino, where the cyclohexyl, aryl and heterocyclyl moieties may be optionally substituted with halogen, hydroxy, alkyl, haloalkyl, alkoxy, haloalkoxy, alkoxycarbonyl, aryl, arylcarbonyl, alkylamino; where

R⁶, R⁷, R⁸, R⁹, R¹², R¹³, R¹⁴ and R¹⁵ are independently hydrogen, alkyl, alkoxy, alkylthio, acetyl, alkoxycarbonyl, alkoxyalkyl, aminoalkyl, carbonylamino, and - (CH₂)_p-N(R¹⁶)(R¹⁷), where

p is 1 or 2; and

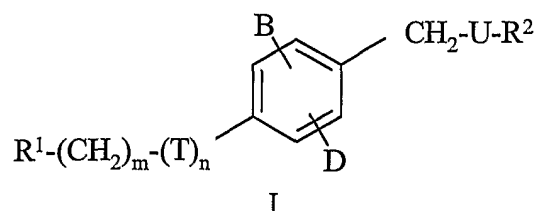
15 R¹⁶ and R¹⁷ are independently hydrogen, alkyl, alkoxy, alkoxyalkyl, and aminoalkyl.

There is no disclosure or suggestion in the above-referenced patent of the structures and insecticidal and acaricidal activity of the compounds of the present invention.

20

SUMMARY OF THE INVENTION

In accordance with the present invention, it has now been found that the N-oxide derivatives of certain novel heterocyclic 1,4-disubstituted benzenes are surprisingly active in the control of insects and acarids when used in the insecticidal and acaricidal compositions and methods of this invention. The compounds of formula I are represented by the following general formula:



30 wherein

R^1 is a non-aromatic heterocyclic N-oxide, where the heterocyclic N-oxide moiety is comprised of one or more nitrogen atoms, where at least one of the nitrogen atoms is oxidized, and where the heterocyclic N-oxide is optionally substituted with a halogen, hydroxyl, alkyl, haloalkyl, alkoxy, haloalkoxy, alkylthio, alkylsulfonyl, alkoxycarbonyl, aryl, aryloxy, arylcarbonyl, benzyl, alkenyl, alkynyl or alkylamino;

m is an integer selected from 0, 1, or 2;

n is an integer selected from 0 or 1,

and when n is 1;

10 T is selected from oxygen or sulfur;

U is selected from $-CH_2-$, $-OCH_2-$, oxygen, sulfur, sulfonyl, oxyalkyloxy, alkenylamino, carbonylamino, or NR^5 where R^5 is selected from hydrogen, hydroxyl, alkyl, haloalkyl, sulfonylalkyl, carbonylamino, and carbonylalkyl;

R^2 is an optionally substituted aryl, an optionally substituted alkylpolycyclyl or an optionally substituted heterocyclyl, where the optional substituents are independently selected from the group consisting of hydrogen, halogen, cyano, nitro, amino, carboxyl, alkyl, haloalkyl, alkylthio, haloalkylthio, alkenyl, alkoxy, haloalkoxy, aminoalkoxy, carbonyl, alkylcarbonyl, haloalkylcarbonyl, alkoxycarbonyl, haloalkoxycarbonyl, aryl, aryloxy, and heterocyclyl; where the aryl and heterocyclyl moieties are optionally substituted with one or more substituents selected from the group consisting of halogen, haloalkyl, alkoxy, and haloalkoxy;

B and D are independently selected from hydrogen, halogen, alkyl, haloalkyl, alkoxy, and haloalkoxy;

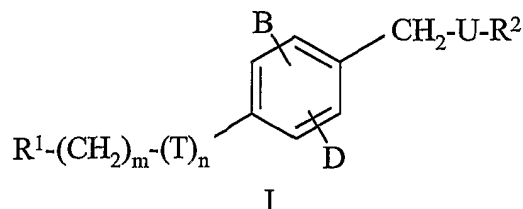
and the corresponding agriculturally acceptably salts thereof.

25 The present invention is also directed to compositions containing an insecticidally effective amount of at least one of a compound of formula I, and optionally, an effective amount of at least one of a second compound, with at least one insecticidally compatible carrier.

30 The present invention is also directed to methods of controlling insects, where control is desired, which comprise applying an insecticidally effective amount of the above composition to the locus of crops, or other areas where insects are present or are expected to be present.

DETAILED DESCRIPTION OF THE INVENTION

The present invention generally relates to certain new and useful compounds, namely novel heterocyclic 1,4-disubstituted benzene N-oxide derivatives (hereinafter termed "compounds of formula I") as depicted in formula I:



wherein:

- 10 R^1 is a non-aromatic heterocyclic N-oxide, where the heterocyclic N-oxide moiety is comprised of one or more nitrogen atoms, where at least one of the nitrogen atoms is oxidized, and where the heterocyclic N-oxide is optionally substituted with a halogen, hydroxyl, alkyl, haloalkyl, alkoxy, haloalkoxy, alkylthio, alkylsulfonyl, alkoxycarbonyl, aryl, aryloxy, arylcarbonyl, benzyl, alkenyl, alkynyl
- 15 or alkylamino;

m is an integer selected from 0, 1, or 2;

n is an integer selected from 0 or 1,

and when n is 1;

T is selected from oxygen or sulfur;

- 20 U is selected from $-\text{CH}_2-$, $-\text{OCH}_2-$, oxygen, sulfur, sulfonyl, oxyalkyloxy, alkenylamino, carbonylamino, or NR^5 where R^5 is selected from hydrogen, hydroxyl, alkyl, haloalkyl, sulfonylalkyl, carbonylamino, and carbonylalkyl;

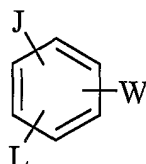
- R^2 is an optionally substituted aryl, an optionally substituted alkylpolycyclyl or an optionally substituted heterocyclyl, where the optional substituents are
- 25 independently selected from the group consisting of hydrogen, halogen, cyano, nitro, amino, carboxyl, alkyl, haloalkyl, alkylthio, haloalkylthio, alkenyl, alkoxy, haloalkoxy, aminoalkoxy, carbonyl, alkylcarbonyl, haloalkylcarbonyl, alkoxycarbonyl, haloalkoxycarbonyl, aryl, aryloxy, and heterocyclyl; where the aryl and heterocyclyl moieties are optionally substituted with one or more substituents
- 30 selected from the group consisting of halogen, haloalkyl, alkoxy, and haloalkoxy;

B and D are independently selected from hydrogen, halogen, alkyl, haloalkyl, alkoxy, and haloalkoxy;

and the corresponding agriculturally acceptably salts thereof.

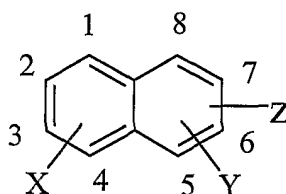
Preferred species of the present invention are those compounds of formula I
 5 where R^2 is 1- R^3 , 1- R^4 , or 2- R^4 ; where:

R^3 is



where J, L, and W are independently selected from hydrogen, halogen, cyano, nitro, amino, carboxyl, alkyl, haloalkyl, alkenyl, alkoxy, haloalkoxy,
 10 aminoalkoxy, carbonyl, alkylcarbonyl, haloalkylcarbonyl, alkoxy carbonyl, haloalkoxy carbonyl, aryl, aryloxy, and heterocyclyl;

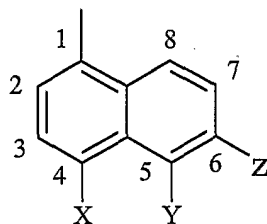
R^4 is



where X, Y, and Z are independently selected from hydrogen, halogen,
 15 cyano, nitro, amino, alkyl, haloalkyl, alkylthio, haloalkylthio, alkenyl, alkoxy, haloalkoxy, carbonyl, haloalkoxycarbonyl, aryl, aryloxy, and heterocyclyl; where the aryl and heterocyclyl moieties are optionally substituted with one or more substituents selected from the group consisting of halogen, haloalkyl, alkoxy, and haloalkoxy.

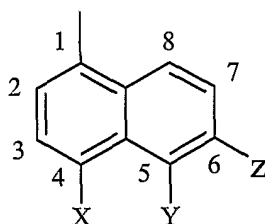
20 More preferred species of the present invention are those compounds of formula I where R^1 is a non-aromatic heterocyclic N-oxide, comprised of five or six members, wherein the heterocyclic N-oxide is optionally substituted with halogen, alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, alkoxy carbonyl, aryl, or aryloxy; n is 1, T is oxygen; U is oxygen; R^2 is 1- R^4 ; and B and D are hydrogen;

25 Even more preferred species of the present invention are those compounds of formula I where R^1 is a non-aromatic heterocyclic N-oxide, optionally substituted with an alkyl and R^2 is 1- R^4 ; where R^4 is



where X, Y, and Z are independently selected from hydrogen, halogen, alkyl, haloalkyl, alkoxy, and haloalkoxy. More particularly, the present invention is those compounds of formula I wherein m is 2 and R¹ is a non-aromatic heterocyclic N-oxide selected from pyrrolid-1-yl 1-oxide or piperidin-1-yl 1-oxide.

Other preferred species of the present invention are those compounds of formula I where R¹ is a non-aromatic heterocyclic N-oxide comprised of six members, where the heterocyclic N-oxide is optionally substituted with a halogen, alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, alkoxycarbonyl, aryl, or aryloxy; m is 0; n is 0; U is oxygen and R² is 1- R⁴. More preferred, those compounds of formula I where R¹ is a non-aromatic heterocyclic N-oxide, optionally substituted with an alkyl and R² is 1- R⁴; where R⁴ is



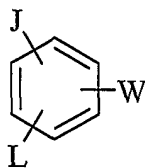
where X, Y, and Z are independently selected from hydrogen, halogen, alkyl, haloalkyl, alkoxy, and haloalkoxy. Even more preferred, those compounds of formula I where R¹ is said non-aromatic heterocyclic N-oxide selected from 1-ethylpiperazin-4-yl 1-oxide, 1-ethylpiperazin-4-yl 4-oxide, or 1-ethylpiperazin-4-yl 1,4-dioxide.

Yet other preferred species of the present invention are those compounds of formula I where R¹ is a non-aromatic heterocyclic N-oxide, where the heterocyclic N-oxide moiety is comprised of one or more nitrogen atoms, where at least one of the nitrogen atoms is oxidized, and where the heterocyclic N-oxide is optionally substituted with a halogen, alkyl, haloalkyl, haloalkoxy, alkylthio, alkylsulfonyl, alkoxycarbonyl, aryl, aryloxy, arylcarbonyl, benzyl, alkenyl or alkynyl;

R⁵ is selected from hydrogen, alkyl, haloalkyl and carbonylamino;

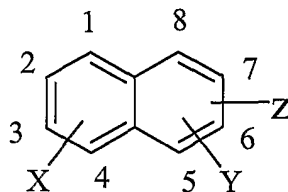
R^2 is 1- R^3 , 1- R^4 , or 2- R^4 ; where:

R^3 is



5 where J, L, and W are independently selected from hydrogen, halogen, cyano, nitro, carboxyl, alkyl, haloalkyl, haloalkoxy, alkylcarbonyl, alkoxy, aryl, aryloxy, and heterocyclyl;

R^4 is



10

where X, Y, and Z are independently selected from hydrogen, halogen, cyano, nitro, alkyl, haloalkyl, alkylthio, haloalkylthio, alkoxy, haloalkoxy, aryl and aryloxy; where the aryl moiety is optionally substituted with one or more substituents selected from the group consisting of halogen and haloalkyl; and

15 B and D are independently selected from hydrogen, halogen, alkyl, haloalkyl and alkoxy.

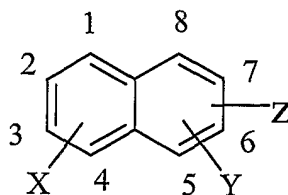
More preferred species of the present invention are those compounds of formula I where R^1 is a non-aromatic heterocyclic N-oxide, where the heterocyclic N-oxide moiety is comprised of one or more nitrogen atoms, where at least one of the nitrogen atoms is oxidized, and where the heterocyclic N-oxide is optionally substituted with an alkyl or alkoxy; and

T is oxygen;

U is oxygen;

R^2 is 1- R^4 where

25 R^4 is



where X, Y, and Z are independently selected from hydrogen, halogen, cyano, nitro, alkyl, haloalkyl, alkylthio, haloalkylthio, alkoxy, haloalkoxy, aryl and
5 aryloxy; where the aryl moiety is optionally substituted with one or more substituents selected from the group consisting of halogen and haloalkyl; and

B and D are independently selected from hydrogen and alkoxy.

In addition, in certain cases the compounds of the present invention may
10 possess asymmetric centers, which can give rise to optical enantiomorphs and diastereomers. The compounds may exist in two or more forms, i.e., polymorphs, which are significantly different in physical and chemical properties. The compounds of the present invention may also exist as tautomers, in which migration of a hydrogen atom within the molecule results in two or more structures, which are
15 in equilibrium. The compounds of the present invention may also possess acidic or basic moieties, which may allow for the formation of agriculturally acceptable salts or agriculturally acceptable metal complexes.

This invention includes the use of such enantiomorphs, polymorphs, tautomers, salts and metal complexes. Agriculturally acceptable salts and metal
20 complexes include, without limitation, for example, ammonium salts, the salts of organic and inorganic acids, such as hydrochloric acid, sulfonic acid, ethanesulfonic acid, trifluoroacetic acid, methylbenzenesulfonic acid, phosphoric acid, gluconic acid, pamoic acid, cinnamic acid, and other acid salts, and the alkali metal and alkaline earth metal complexes with, for example, sodium, potassium, lithium,
25 magnesium, calcium, and other metals.

The methods of the present invention are predicated on causing an insecticidally effective amount of a compound of formula I to be present within insects in order to kill or control the insects. Preferred insecticidally effective amounts are those that are sufficient to kill the insect. It is within the scope of the
30 present invention to cause a compound of formula I to be present within insects by

contacting the insects with a derivative of that compound, which derivative is converted within the insect to a compound of formula I. This invention includes the use of such compounds, which can be referred to as pro-insecticides.

Another aspect of the present invention relates to compositions containing an insecticidally effective amount of at least one compound of formula I with at least one insecticidally compatible carrier therefor.

Another aspect of the present invention relates to compositions containing an insecticidally effective amount of at least one compound of formula I, and an effective amount of at least one second compound, with at least one insecticidally compatible carrier therefor.

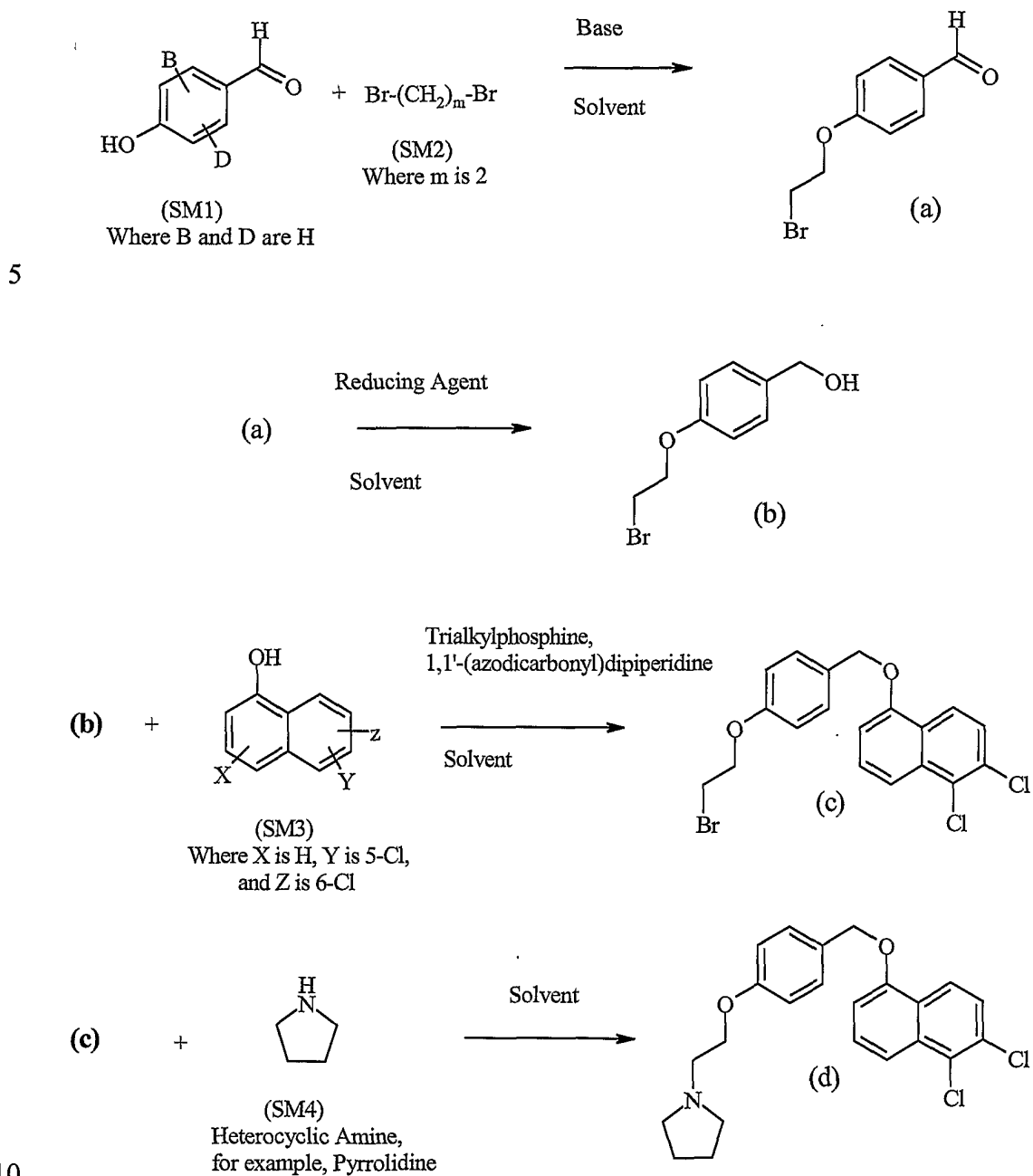
Another aspect of the present invention relates to methods of controlling insects by applying an insecticidally effective amount of a composition set forth above to a locus of crops such as, without limitation, cereals, cotton, vegetables, and fruits, or other areas where insects are present or are expected to be present.

The present invention also includes the use of the compounds and compositions set forth herein for control of non-agricultural insect species, for example, dry wood termites and subterranean termites; as well as for use as pharmaceutical agents and compositions thereof. In the field of veterinary medicine, the compounds of the present invention are expected to be effective against certain *endo*- and *ecto*-parasites, such as insects and worms, which prey on animals. Examples of such animal parasites include, without limitation, *Gastrophilus* spp., *Stomoxys* spp., *Trichodectes* spp., *Rhodnius* spp., *Ctenocephalides canis*, and other species.

As used in this specification and unless otherwise indicated the substituent terms "alkyl" and "alkoxy", used alone or as part of a larger moiety, includes straight or branched chains of at least one or two carbon atoms, as appropriate to the substituent, and preferably up to 12 carbon atoms, more preferably up to ten carbon atoms, most preferably up to seven carbon atoms. The terms "haloalkyl" and "haloalkoxy", alone or as part of a larger moiety, include straight or branched chain alkyls of 1 to 14 carbon atoms, preferably lower straight or branched chain alkyls of 1 to 6 carbon atoms, wherein one or more hydrogen atoms have been replaced with halogen atoms, as, for example, trifluoromethyl or 2,2,2-trifluoroethoxy, respectively. The term "alkenyl" and "alkynyl" used alone or as part of a larger

moiety, includes straight or branched chains of at least two carbon atoms containing at least one carbon-carbon double bond or triple bond, and preferably up to 12 carbon atoms, more preferably up to ten carbon atoms, most preferably up to seven carbon atoms. The term "heterocyclic" refers to a non-aromatic ring structure of
5 four to eight atoms consisting of carbon and nitrogen, and may include oxygen or sulfur. Five member rings include, without limitation, for example, pyrrolidine. Six member rings include, without limitation, for example, piperazine, piperidine, morpholine and thiomorpholine. The term "aryl" refers to an aromatic ring structure, including fused rings, having four to ten carbon atoms, for example,
10 phenyl or naphthyl. The terms "heteroaryl" and "heterocyclyl" refer to an aromatic ring structure, including fused rings, in which at least one of the atoms is other than carbon, for example, without limitation, sulfur, oxygen, or nitrogen. The term "polycyclyl" refers to a non-aromatic fused ring structure. "Amino" refers to compounds of nitrogen that may be considered derived from ammonia and includes
15 primary, secondary and tertiary amines wherein one or more of the hydrogen atoms is replaced with alkyl groups. The term "GC analysis" refers to gas chromatographic analysis of, for example, a chemical reaction mixture. The term "DMF" refers to N,N-dimethylformamide. The term "THF" refers to tetrahydrofuran. The term "TEA" refers to triethylamine. The term "halogen" or
20 "halo" refers to fluorine, bromine, iodine, or chlorine. The term "ambient temperature" or "room temperature" often abbreviated as "RT", for example, in reference to a chemical reaction mixture temperature, refers to a temperature in the range of 20 °C to 30 °C. The term "insecticidal" or "acaricidal", "insecticide" or "acaricide" refers to a compound of the present invention, either alone or in
25 admixture with at least one of a second compound, or with at least one compatible carrier, which causes the destruction or the inhibition of action of insects or acarids.

The compounds of the present invention were prepared by methods generally known to those skilled in the art. A number of intermediate heterocyclic 1,4-disubstituted benzene compounds for use in preparing compounds of formula I were
30 prepared in the manner shown in Scheme 1.

Scheme 1

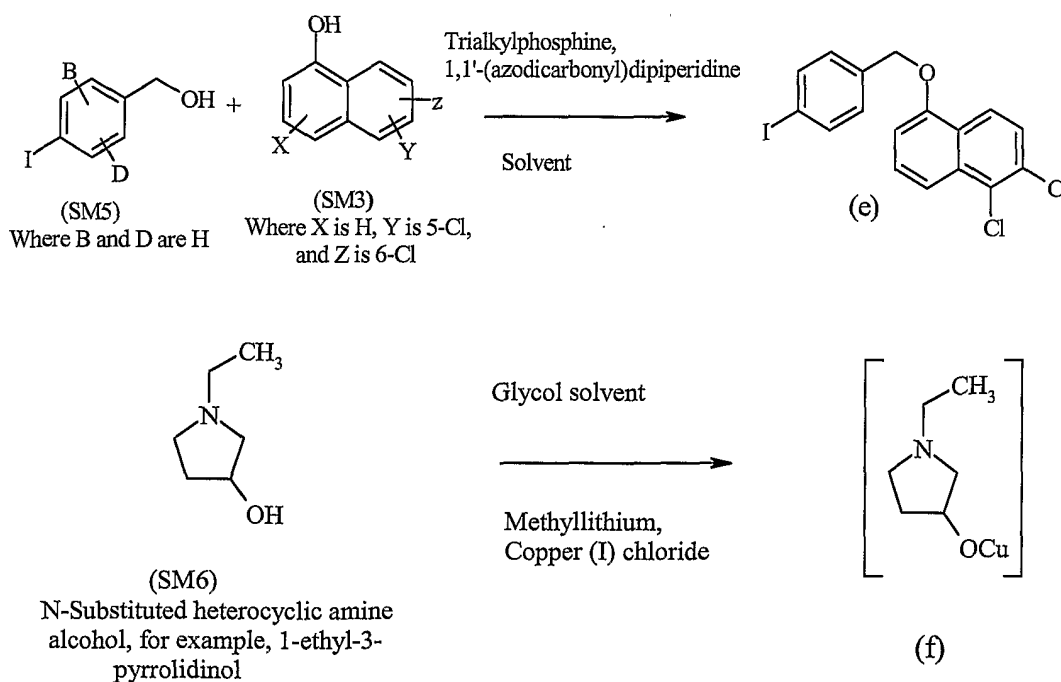
As depicted in Scheme 1, the reaction of an appropriately substituted 4-hydroxybenzaldehyde (SM1) with an alkyl dibromide (SM2), in an appropriate solvent, under mildly basic conditions, yielded the appropriately substituted

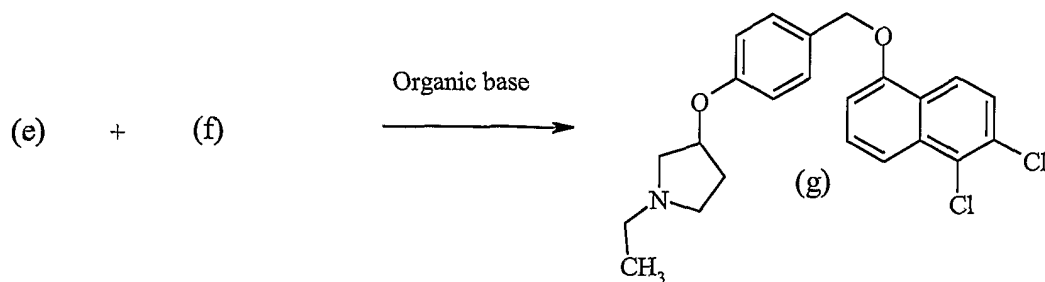
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haloalkoxy benzaldehyde (a), for example, 4-(2-bromoethoxy)benzaldehyde. Benzaldehyde (a) was treated with a reducing agent, in an alcoholic solvent to yield an appropriately substituted haloalkoxy phenol (b), for example, 4-(2-bromoethoxy)phenol. Haloalkoxy phenol (b) was then reacted with a substituted naphthol (SM3), in the presence of a trialkylphosphine and 1,1'-(azodicarbonyl)dipiperidine, in an appropriate solvent, to yield the corresponding halo-(((substituted-naphthyloxy)methyl)phenoxy)alkane (c), for example, 2-bromo-1-(4-((5,6-dichloronaphthyloxy)methyl)phenoxy)ethane. Alkane (c) was then reacted with a heterocyclic amine (SM4) to yield the appropriately substituted 1-(2-(pyrrolidinyl)ethoxy)-4-((substituted-naphthyloxy)methyl)benzene (d), for example 1-(2-(pyrrolidinyl)ethoxy)-4-((5,6-dichloronaphthyloxy)methyl)benzene, an intermediate heterocyclic 1,4-disubstituted benzene compound described in detail in Example 1 set forth below.

Scheme 2 provides an alternative preparation of intermediate heterocyclic 1,4-disubstituted benzenes for use in preparing compounds of formula I

Scheme 2

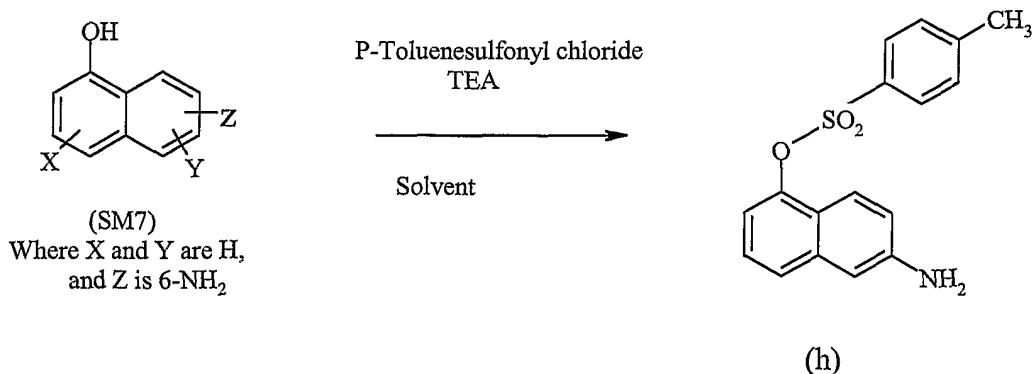


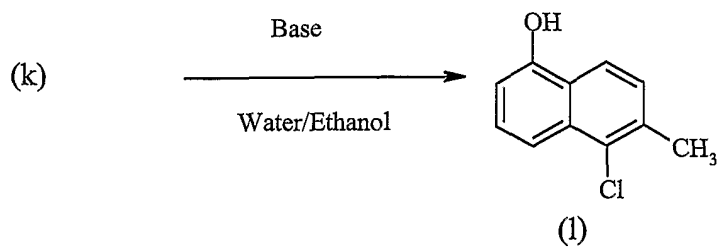
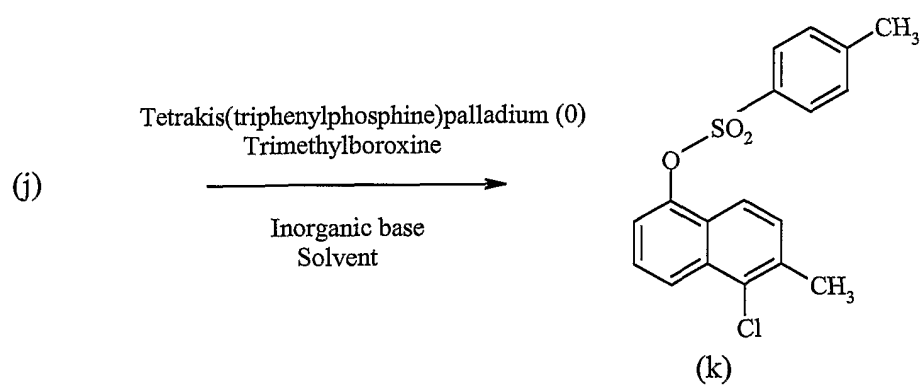
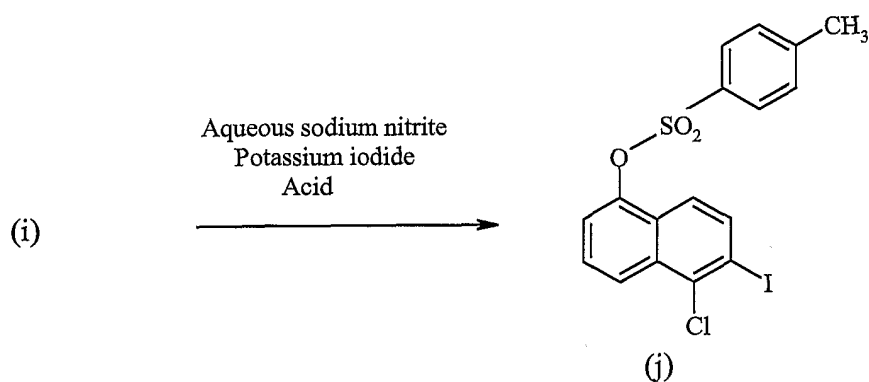
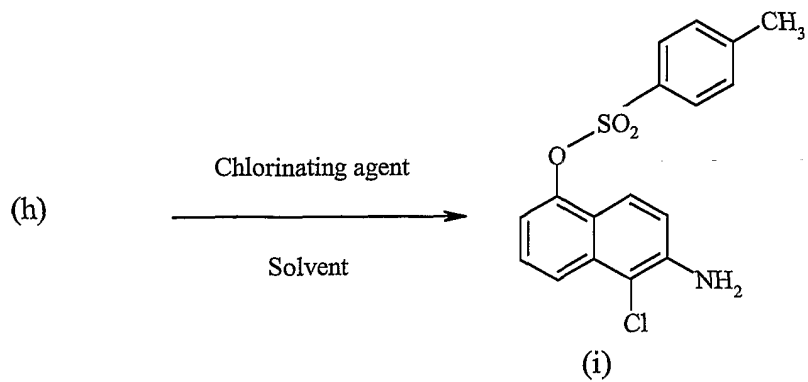


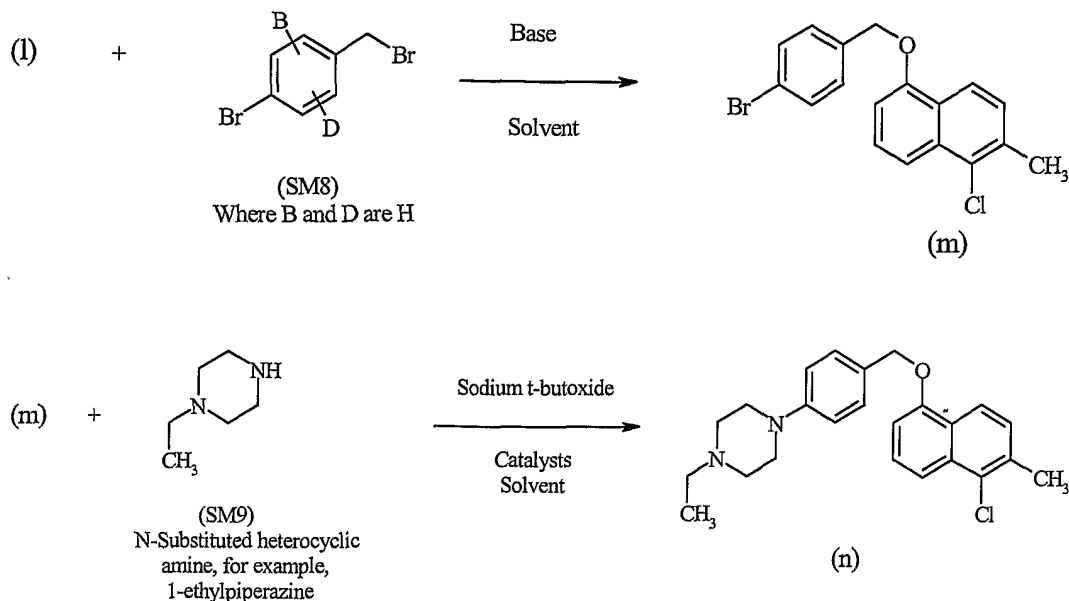
As depicted in Scheme 2, in one reaction, an appropriately substituted
 5 iodobenzyl alcohol (SM5) was reacted with an appropriately substituted naphthol
 (SM3), for example, 5,6-dichloro-1-naphthol, in the presence of a trialkylphosphine
 and 1,1'-(azodicarbonyl)dipiperidine, in an appropriate solvent, yielding the
 appropriately substituted (iodophenyl)methoxynaphthalene (e), for example, 5-((4-
 iodophenyl)methoxy)1,2-dichloronaphthalene. In a second reaction, a N-substituted
 10 heterocyclic amine alcohol (SM6) was reacted with methyllithium and copper (I)
 chloride in a glycol solvent, affording copper (I) intermediate (f). The copper (I)
 intermediate (f) was then reacted with naphthalene (e) in the presence of an organic
 base, producing the appropriately substituted ((alkylamine)oxy)-
 ((naphthyloxy)methyl)benzene (g), for example, 1-((1-ethylpyrrolidin-3-yl)oxy)-4-
 15 ((5,6-dichloronaphthyloxy)methyl)benzene, an intermediate heterocyclic 1,4-
 disubstituted benzene compound described in detail in Example 2 set forth below.

Another method for the preparation of heterocyclic 1,4-disubstituted benzene
 intermediates for use in preparing compounds of formula I is provided in Scheme 3.

Scheme 3







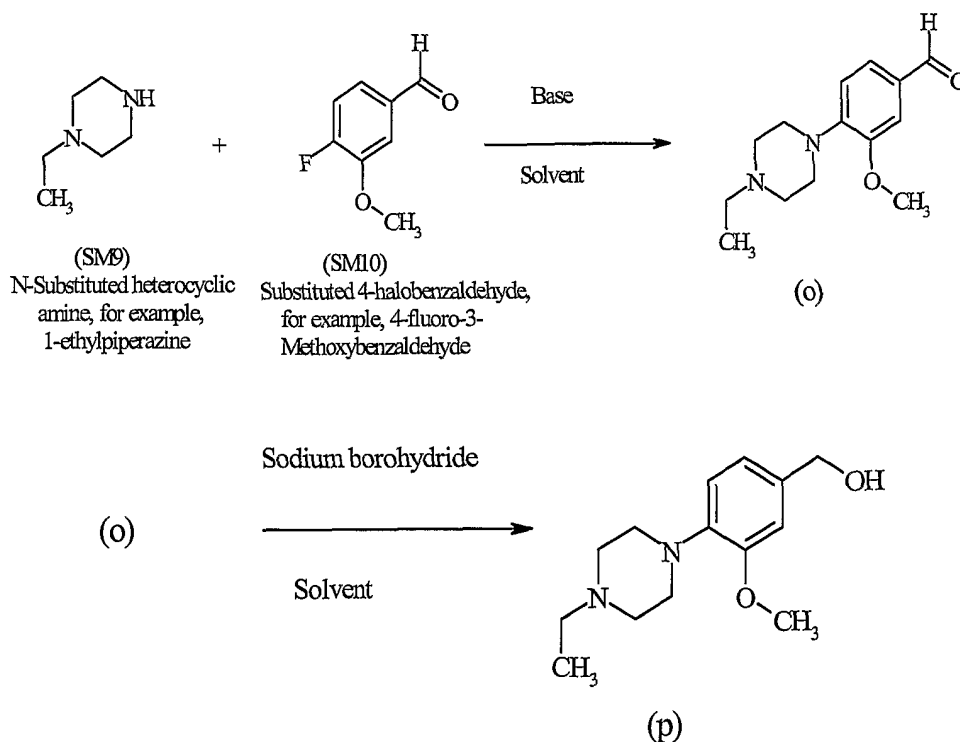
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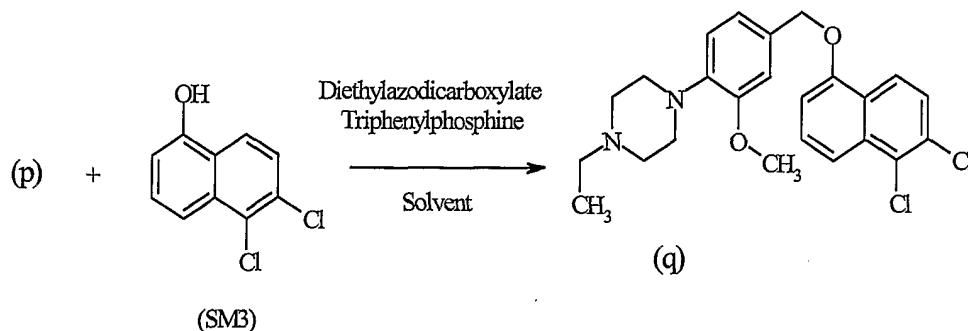
As depicted in Scheme 3, an appropriately substituted amino-naphthol (SM7) was reacted with p-toluenesulfonyl chloride and an organic base in an appropriate solvent producing the corresponding (aminonaphthyl)-4-methylbenzenesulfonate (h), for example, (6-aminonaphthyl)-4-methylbenzenesulfonate. The (aminonaphthyl)sulfonate (h) was chlorinated in an appropriate solvent, yielding the chlorinated (aminonaphthyl)sulfonate (i), for example, (6-amino-5-chloronaphthyl)-4-methylbenzenesulfonate. The chlorinated (aminonaphthyl)sulfonate (i) was then treated with hydrochloric acid, an aqueous solution of sodium nitrite, and potassium iodide producing the (chloro-iodonaphthyl)sulfonate (j), for example, (5-chloro-6-iodonaphthyl)-4-methylbenzenesulfonate. The iodide was in turn converted to a methyl group by the reaction of (chloro-iodonaphthyl)sulfonate (j) with trimethylboroxine in the presence of a catalytic amount of tetrakis(triphenylphosphine)palladium(0), under mildly basic conditions yielding the (chloro-methylnaphthyl)-4-methylbenzenesulfonate (k), for example, (5-chloro-6-methylnaphthyl)-4-methylbenzenesulfonate. The sulfonate-protecting group was then removed by treatment of the (naphthyl)sulfonate (k) with an aqueous alcohol solution of an inorganic base yielding the chloro-methylnaphthol (l), for example, 5-chloro-6-methyl-1-naphthol. Naphthol (l) was reacted with a bromobenzyl bromide (SM8) under basic conditions, yielding the ((bromophenyl)methoxy)naphthalene

(m), for example, 5-((4-bromophenyl)methoxy)-1-chloro-2-methylnaphthylene. The ((bromophenyl)methoxy)-naphthalene (m) was in turn reacted with an appropriately substituted heterocyclic amine (SM9) in the presence of catalytic amounts of tris(dibenzylideneacetone) and 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl, yielding the appropriately substituted (((heterocyclic amine)phenyl)methoxy)naphthalene (n), for example, 1-chloro-5-((4-(4-ethylpiperazinyl)phenyl)methoxy)-2-methylnaphthalene, an intermediate heterocyclic 1,4-disubstituted benzene compound described in detail in Example 5 set forth below.

10 Scheme 4 below sets forth a method for the preparation of heterocyclic-1,4-disubstituted benzene intermediates for use in preparing compounds of formula I in which a "B" substituent is present.

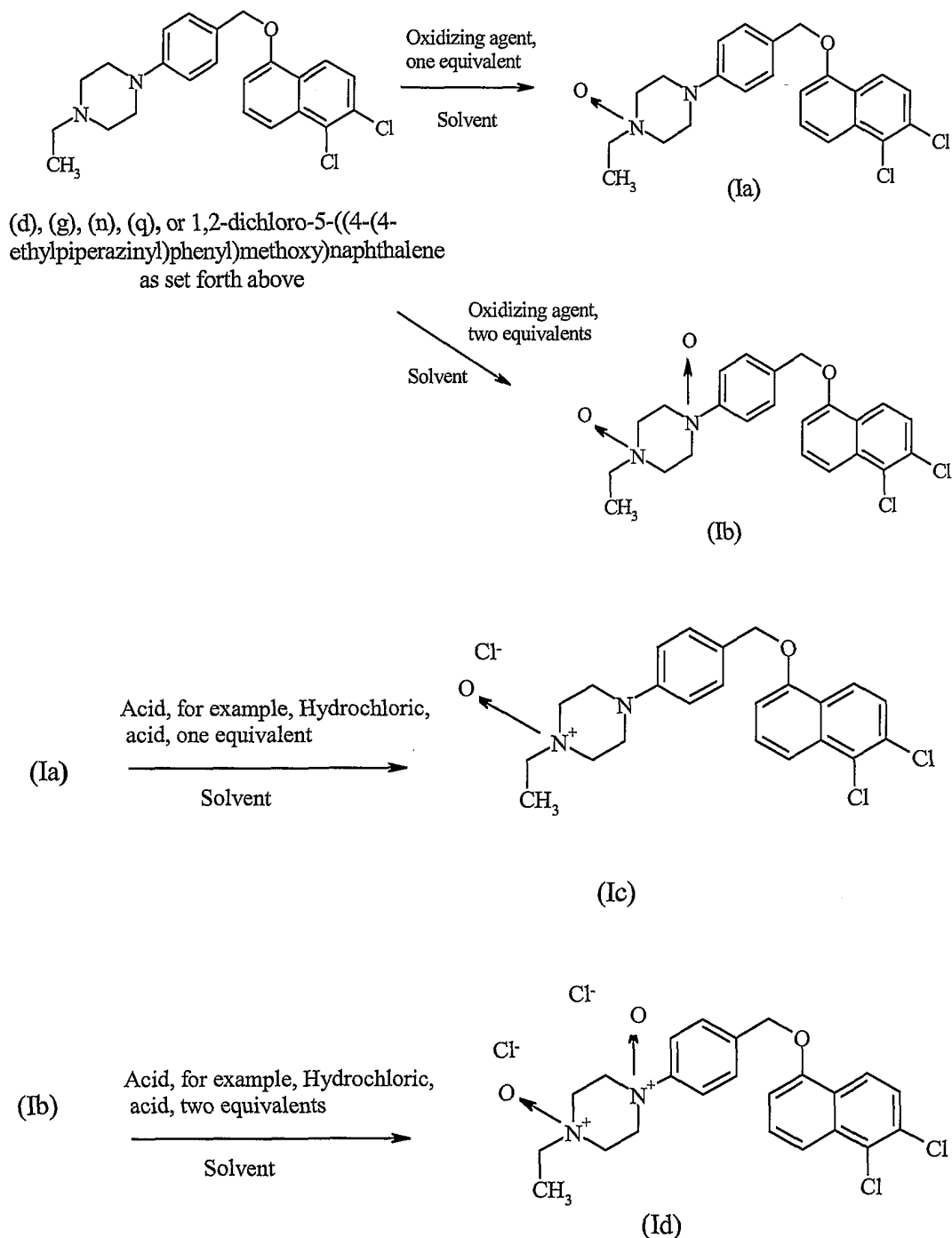
Scheme 4





As depicted in Scheme 4, a N-substituted heterocyclic amine (SM9) was reacted with an appropriately substituted 4-halobenzaldehyde (SM10) under basic conditions in an appropriate solvent yielding the correspondingly substituted (heterocyclic amine)benzaldehyde (o), for example, 4-(4-ethylpiperazinyl)-3-methoxybenzaldehyde. Benzaldehyde (o) was reduced to the corresponding benzyl alcohol (p), for example, 4-(4-ethylpiperazinyl)-3-methylbenzyl alcohol, by treatment of (o) with sodium borohydride in an alcoholic solvent. Benzyl alcohol (p) was then reacted with an appropriately substituted naphthol (SM3), in the presence of diethylazodicarboxylate and triphenylphosphine, providing the correspondingly substituted (((heterocyclicamine) phenyl)methoxy)naphthalene (q), for example, 1,2-dichloro-5-(((4-(4-ethylpiperazinyl)-3-methoxyphenyl)methoxy)naphthalene. Example 6 set forth below provides in detail the preparation of this heterocyclic 1,4-disubstituted benzene intermediate.

Scheme 5 below illustrates a general procedure for synthesizing Heterocyclic 1,4disubstituted benzene N-oxide derivatives of formula I, *inter alia*,

Scheme 5

As depicted in Scheme 5, compounds of formula I were prepared from
 10 heterocyclic 1,4-disubstituted benzene intermediates (d), (g), (n), or (q) described
 above or from the intermediate 1,2-dichloro-5-((4-(4-

ethylpiperazinyl)phenyl)methoxy)naphthalene (a known compound, U.S. Patent 6,753,429), by oxidation of the afore mentioned heterocyclic benzene intermediates with at least one equivalent of an oxidizing agent in an appropriate solvent, yielding the appropriately substituted heterocyclic-1-oxide (Ia), for example 4-(4-((5,6-
5 dichloronaphthyloxy)methyl)phenyl)-1-ethylpiperazine-1-oxide. Examples 1, 2, 3, 5, and 6 set forth below provide in detail the preparation of compounds of formula Ia.

In a case where the heterocyclic portion of the molecule contains more than one nitrogen, for example, where the heterocyclic moiety is a piperazinyl group, the
10 dioxide may be produced by treatment of the piperazinyl benzene intermediate with at least two equivalents of an oxidizing agent, yielding the appropriately substituted heterocyclic dioxide (Ib), for example, 4-(4-((5,6-dichloronaphthyloxy)methyl)phenyl)-1-ethylpiperazine-1,4-dioxide. Examples 6 and 7 set forth below provide in detail the preparation of compounds of formula Ib.

15 Agriculturally acceptable salts of heterocyclic oxides (Ia) and (Ib) were prepared by treatment of the oxide with the desired salt's acid, for example, hydrochloric acid, in an appropriate solvent, to produce the hydrochloride salt (Ic), for example, 4-(4-((5,6-dichloronaphthyloxy)methyl)phenyl)-1-ethylpiperazine-1-oxide hydrochloride, or the di-hydrochloride salt (Id), for example, 4-(4-((5,6-
20 dichloronaphthyloxy)methyl)phenyl)-1-ethylpiperazine-1,4-dioxide dihydrochloride. Example 4 set forth below provides in detail the preparation of compounds of formula (Ic). Example 7 set forth below provides in detail the preparation of compounds of formula (Id).

One skilled in the art will, of course, recognize that the formulation and
25 mode of application of a toxicant may affect the activity of the material in a given application. Thus, for agricultural use the present insecticidal compounds may be formulated as a granular of relatively large particle size (for example, 8/16 or 4/8 US Mesh), as water-soluble or water-dispersible granules, as powdery dusts, as wettable powders, as emulsifiable concentrates, as aqueous emulsions, as solutions, or as any
30 of other known types of agriculturally-useful formulations, depending on the desired mode of application. It is to be understood that the amounts specified in this

specification are intended to be approximate only, as if the word "about" were placed in front of the amounts specified.

These insecticidal compositions may be applied either as water-diluted sprays, or dusts, or granules to the areas in which suppression of insects is desired.

5 These formulations may contain as little as 0.1%, 0.2% or 0.5% to as much as 95% or more by weight of active ingredient.

Dusts are free flowing admixtures of the active ingredient with finely divided solids such as talc, natural clays, kieselguhr, flours such as walnut shell and cottonseed flours, and other organic and inorganic solids which act as dispersants and carriers for the toxicant; these finely divided solids have an average particle size

10 of less than about 50 microns. A typical dust formulation useful herein is one containing 1.0 part or less of the insecticidal compound and 99.0 parts of talc.

Wettable powders, also useful formulations for insecticides, are in the form of finely divided particles that disperse readily in water or other dispersant. The

15 wettable powder is ultimately applied to the locus where insect control is needed either as a dry dust or as an emulsion in water or other liquid. Typical carriers for wettable powders include Fuller's earth, kaolin clays, silicas, and other highly absorbent, readily wet inorganic diluents. Wettable powders normally are prepared to contain about 5-80% of active ingredient, depending on the absorbency of the

20 carrier, and usually also contain a small amount of a wetting, dispersing or emulsifying agent to facilitate dispersion. For example, a useful wettable powder formulation contains 80.0 parts of the insecticidal compound, 17.9 parts of Palmetto clay, and 1.0 part of sodium lignosulfonate and 0.3 part of sulfonated aliphatic polyester as wetting agents. Additional wetting agent and/or oil will frequently be

25 added to a tank mix to facilitate dispersion on the foliage of the plant.

Other useful formulations for insecticidal applications are emulsifiable concentrates (ECs) which are homogeneous liquid compositions dispersible in water or other dispersant, and may consist entirely of the insecticidal compound and a liquid or solid emulsifying agent, or may also contain a liquid carrier, such as

30 xylene, heavy aromatic naphthas, isphorone, or other non-volatile organic solvents. For insecticidal application these concentrates are dispersed in water or other liquid carrier and normally applied as a spray to the area to be treated. The percentage by weight of the essential active ingredient may vary according to the manner in which

the composition is to be applied, but in general comprises 0.5 to 95% of active ingredient by weight of the insecticidal composition.

Flowable formulations are similar to ECs, except that the active ingredient is suspended in a liquid carrier, generally water. Flowables, like ECs, may include a small amount of a surfactant, and will typically contain active ingredients in the range of 0.5 to 95%, frequently from 10 to 50%, by weight of the composition. For application, flowables may be diluted in water or other liquid vehicle, and are normally applied as a spray to the area to be treated.

Typical wetting, dispersing or emulsifying agents used in agricultural formulations include, but are not limited to, the alkyl and alkylaryl sulfonates and sulfates and their sodium salts; alkylaryl polyether alcohols; sulfated higher alcohols; polyethylene oxides; sulfonated animal and vegetable oils; sulfonated petroleum oils; fatty acid esters of polyhydric alcohols and the ethylene oxide addition products of such esters; and the addition product of long-chain mercaptans and ethylene oxide. Many other types of useful surface-active agents are available in commerce. Surface-active agents, when used, normally comprise 1 to 15% by weight of the composition.

Other useful formulations include suspensions of the active ingredient in a relatively non-volatile solvent such as water, corn oil, kerosene, propylene glycol, or other suitable solvents.

Still other useful formulations for insecticidal applications include simple solutions of the active ingredient in a solvent in which it is completely soluble at the desired concentration, such as acetone, alkylated naphthalenes, xylene, or other organic solvents. Granular formulations, wherein the toxicant is carried on relative coarse particles, are of particular utility for aerial distribution or for penetration of cover crop canopy. Pressurized sprays, typically aerosols wherein the active ingredient is dispersed in finely divided form as a result of vaporization of a low-boiling dispersant solvent carrier may also be used. Water-soluble or water-dispersible granules are free flowing, non-dusty, and readily water-soluble or water-miscible. In use by the farmer on the field, the granular formulations, emulsifiable concentrates, flowable concentrates, aqueous emulsions, solutions, etc., may be diluted with water to give a concentration of active ingredient in the range of say 0.1% or 0.2% to 1.5% or 2%.

The active insecticidal and acaricidal compounds of this invention may be formulated and/or applied with one or more second compounds. Such combinations may provide certain advantages, such as, without limitation, exhibiting synergistic effects for greater control of insect pests, reducing rates of application of insecticide
5 thereby minimizing any impact to the environment and to worker safety, controlling a broader spectrum of insect pests, safening of crop plants to phytotoxicity, and improving tolerance by non-pest species, such as mammals and fish.

Second compounds include, without limitation, other pesticides, plant growth regulators, fertilizers, soil conditioners, or other agricultural chemicals. In
10 applying an active compound of this invention, whether formulated alone or with other agricultural chemicals, an effective amount and concentration of the active compound is of course employed; the amount may vary in the range of, e.g. about 0.001 to about 3 kg/ha, preferably about 0.03 to about 1 kg/ha. For field use, where there are losses of insecticide, higher application rates (e.g., four times the rates
15 mentioned above) may be employed.

When the active insecticidal compounds of the present invention are used in combination with one or more of second compounds, e.g., with other pesticides such as herbicides, the herbicides include, without limitation, for example: N-(phosphonomethyl)glycine ("glyphosate"); aryloxyalkanoic acids such as (2,4-
20 dichlorophenoxy)acetic acid ("2,4-D"), (4-chloro-2-methylphenoxy)acetic acid ("MCPA"), (+/-)-2-(4chloro-2-methylphenoxy)propanoic acid ("MCPP"); ureas such as N,N-dimethyl-N'-[4-(1-methylethyl)phenyl]urea ("isoproturon"); imidazolinones such as 2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1H-imidazol-2-yl]-3-pyridinecarboxylic acid ("imazapyr"), a reaction product
25 comprising (+/-)-2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1H-imidazol-2-yl]-4-methylbenzoic acid and (+/-)-2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1H-imidazol-2-yl]-5-methylbenzoic acid ("imazamethabenz"), (+/-)-2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1H-imidazol-2-yl]-5-ethyl-3-pyridinecarboxylic acid ("imazethapyr"), and (+/-)-2-[4,5-dihydro-4-methyl-4-(1-
30 methylethyl)-5-oxo-1H-imidazol-2-yl]-3-quinolinecarboxylic acid ("imazaquin"); diphenyl ethers such as 5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitrobenzoic acid ("acifluorfen"), methyl 5-(2,4-dichlorophenoxy)-2-nitrobenzoate ("bifenox"), and 5-[2-chloro-4-(trifluoromethyl)phenoxy]-N-(methylsulfonyl)-2-nitrobenzamide

("fomasafen"); hydroxybenzonitriles such as 4-hydroxy-3,5-diiodobenzonitrile ("ioxynil") and 3,5-dibromo-4-hydroxybenzonitrile ("bromoxynil"); sulfonylureas such as 2-[[[(4-chloro-6-methoxy-2-pyrimidinyl)amino]carbonyl]amino]sulfonyl]benzoic acid ("chlorimuron"), 2-chloro-N-[[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl]benzenesulfonamide (achlorsulfuron"), 2-[[[[[(4,6-dimethoxy-2-pyrimidinyl)amino]carbonyl]amino]sulfonyl]methyl]benzoic acid ("bensulfuron"), 2-[[[[[(4,6-dimethoxy-2-pyrimidinyl)amino]carbonyl]amino]sulfonyl]-1-methyl-1H-pyrazol-4-carboxylic acid ("pyrazosulfuron"), 3-[[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl]amino]sulfonyl]-2-thiophenecarboxylic acid ("thifensulfuron"), and 2-(2-chloroethoxy)-N[[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl]benzenesulfonamide ("triasulfuron"); 2-(4-aryloxyphenoxy)alkanoic acids such as (+/-)-2-[4-[(6-chloro-2-benzoxazolyl)oxy]phenoxy]propanoic acid (fenoxaprop"), (+/-)-2-[4-[[5-(trifluoromethyl)-2-pyridinyl]oxy]phenoxy]propanoic acid ("fluazifop"), (+/-)-2-[4-(6-chloro-2-quinoxalinyloxy)phenoxy]propanoic acid ("quizalofop"), and (+/-)-2-[(2,4-dichlorophenoxy)phenoxy]propanoic acid ("diclofop"); benzothiadiazinones such as 3-(1-methylethyl)-1H-1,2,3-benzothiadiazin-4(3H)-one-2,2-dioxide ("bentazone"); 2-chloroacetanilides such as N-(butoxymethyl)-2-chloro-N-(2,6-diethylphenyl)acetamide ("butachlor"), 2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl)acetamide ("metolachlor"), 2-chloro-N-(ethoxymethyl)-N-(2-ethyl-6-methylphenyl)acetamide ("acetochlor"), and (RS)-2-chloro-N-(2,4-dimethyl-3-thienyl)-N-(2-methoxy-1-methylethyl)acetamide ("dimethenamide"); arenecarboxylic acids such as 3,6-dichloro-2-methoxybenzoic acid ("dicamba"); pyridyloxyacetic acids such as [(4-amino-3,5-dichloro-6-fluoro-2-pyridinyl)oxy]acetic acid ("fluroxypyr"), and other herbicides.

When the active insecticidal compounds of the present invention are used in combination with one or more of second compounds, e.g., with other pesticides such as other insecticides, the other insecticides include, for example: organophosphate insecticides, such as chlorpyrifos, diazinon, dimethoate, malathion, parathion-methyl, and terbufos; pyrethroid insecticides, such as fenvalerate, deltamethrin, fenpropathrin, cyfluthrin, flucythrinate, *alpha*-cypermethrin, bifenthrin, cypermethrin, resolved cyhalothrin, etofenprox, esfenvalerate, tralomethrin,

tefluthrin, cycloprothrin, betacyfluthrin, and acrinathrin; carbamate insecticides, such as aldecarb, carbaryl, carbofuran, and methomyl; organochlorine insecticides, such as endosulfan, endrin, heptachlor, and lindane; benzoylurea insecticides, such as diflubenuron, triflumuron, teflubenzuron, chlorfluazuron, flucycloxuron, 5 hexaflumuron, flufenoxuron, and lufenuron; and other insecticides, such as amitraz, clofentezine, fenpyroximate, hexythiazox, spinosad, and imidacloprid.

When the active insecticidal compounds of the present invention are used in combination with one or more of second compounds, e.g., with other pesticides such as fungicides, the fungicides include, for example: benzimidazole fungicides, such as benomyl, carbendazim, thiabendazole, and thiophanate-methyl; 1,2,4-triazole 10 fungicides, such as epoxyconazole, cyproconazole, flusilazole, flutriafol, propiconazole, tebuconazole, triadimefon, and triadimenol; substituted anilide fungicides, such as metalaxyl, oxadixyl, procymidone, and vinclozolin; organophosphorus fungicides, such as fosetyl, iprobenfos, pyrazophos, edifenphos, 15 and tolclofos-methyl; morpholine fungicides, such as fenpropimorph, tridemorph, and dodemorph; other systemic fungicides, such as fenarimol, imazalil, prochloraz, tricyclazole, and triforine; dithiocarbamate fungicides, such as mancozeb, maneb, propineb, zineb, and ziram; non-systemic fungicides, such as chlorothalonil, dichlofluanid, dithianon, and iprodione, captan, dinocap, dodine, fluazinam, 20 gluazatine, PCNB, penycuron, quintozene, tricylamide, and validamycin; inorganic fungicides, such as copper and sulphur products, and other fungicides.

When the active insecticidal compounds of the present invention are used in combination with one or more of second compounds, e.g., with other pesticides such as nematicides, the nematicides include, for example: carbofuran, carbosulfan, 25 terbufos, aldecarb, ethoprop, fenamphos, oxamyl, isazofos, cadusafos, and other nematicides.

When the active insecticidal compounds of the present invention are used in combination with one or more of second compounds, e.g., with other materials such as plant growth regulators, the plant growth regulators include, for example: maleic 30 hydrazide, chlormequat, ethephon, gibberellin, mepiquat, thidiazon, inabenfide, triaphenthenol, paclobutrazol, uniconazole, DCPA, prohexadione, trinexapac-ethyl, and other plant growth regulators.

Soil conditioners are materials which, when added to the soil, promote a variety of benefits for the efficacious growth of plants. Soil conditioners are used to reduce soil compaction, promote and increase effectiveness of drainage, improve soil permeability, promote optimum plant nutrient content in the soil, and promote better pesticide and fertilizer incorporation. When the active insecticidal compounds of the present invention are used in combination with one or more of second compounds, e.g., with other materials such as soil conditioners, the soil conditioners include organic matter, such as humus, which promotes retention of cation plant nutrients in the soil; mixtures of cation nutrients, such as calcium, magnesium, potash, sodium, and hydrogen complexes; or microorganism compositions which promote conditions in the soil favorable to plant growth. Such microorganism compositions include, for example, *bacillus*, *pseudomonas*, *azotobacter*, *azospirillum*, *rhizobium*, and soil-borne *cyanobacteria*.

Fertilizers are plant food supplements, which commonly contain nitrogen, phosphorus, and potassium. When the active insecticidal compounds of the present invention are used in combination with one or more of second compounds, e.g., with other materials such as fertilizers, the fertilizers include nitrogen fertilizers, such as ammonium sulfate, ammonium nitrate, and bone meal; phosphate fertilizers, such as superphosphate, triple superphosphate, ammonium sulfate, and diammonium sulfate; and potassium fertilizers, such as muriate of potash, potassium sulfate, and potassium nitrate, and other fertilizers.

The following examples further illustrate the present invention, but, of course, should not be construed as in any way limiting its scope. The examples are organized to present protocols for the synthesis of the compounds of formula I of the present invention, set forth a list of such synthesized species, and set forth certain biological data indicating the efficacy of such compounds.

EXAMPLE 1

This example illustrates one protocol for the preparation of 1-(2-(4-((5,6-dichloronaphthyloxy)methyl)phenoxy)ethyl)pyrrolidine-1-oxide

(Compound 1)

Step A Synthesis of 4-(2-bromoethoxy)benzaldehyde as an intermediate

A mixture of 12.21 grams (0.10 mole) of 4-hydroxybenzaldehyde, 9.14 grams (0.50 mole) of 1,2-dibromoethane, and 13.8 grams (0.1 mole) of potassium carbonate in 200 mL of DMF was stirred at 80°C for 18 hours. The resulting mixture was allowed to cool, and then it was poured into water. The aqueous mixture was extracted with diethyl ether and the organic phase was dried with anhydrous magnesium sulfate, and the mixture was filtered. The filtrate was concentrated under reduced pressure, yielding 14.53 grams of the title compound as a solid.

10 Step B Synthesis of 4-(2-bromoethoxy)phenol as an intermediate

A stirred solution of 14.0 grams (0.061 mole) of 4-(2-bromoethoxy)benzaldehyde dissolved in 80 mL of methanol was cooled to 10°C. Sodium borohydride (5.55 grams, 0.15 mole) was then added slowly to the cold solution. After completion of addition, the mixture was allowed to warm to ambient temperature where it stirred for two hours. After this time, the reaction mixture was poured into water forming a white precipitate. The precipitate was collected by vacuum filtration, yielding 11.35 grams of the title compound.

20 Step C Synthesis of 2-bromo-1-(4-((5,6-dichloronaphthyl)oxy)methyl)-phenoxy)ethane as an intermediate

Under a dry nitrogen atmosphere, a stirred solution of 2.8 grams (0.012 mole) of 4-(2-bromoethoxy)phenol, 3.35 grams (0.016 mole) of 5,6-dichloronaphthol (U.S. Patent 6,753,429), and 4.3 mL (0.017 mole) of tributylphosphine in 150 mL of THF was cooled in an ice bath and 4.35 grams (0.017 mole) of 1-1'-(azodicarbonyl)dipiperidine was added portion-wise. Upon completion of addition, the reaction mixture was allowed to warm to ambient temperature where it was stirred for about 18 hours. The reaction mixture was then diluted with hexanes, forming a precipitate. The precipitate was removed by filtration and the filtrate was concentrated under reduced pressure to a residue. The residue was purified by column chromatography on silica gel, eluting with mixtures of 10% to 30% ethyl acetate in hexane. The appropriate fractions were combined

and concentrated under reduced pressure, yielding 3.89 grams of the title compound. The NMR spectrum was consistent with the proposed structure.

5 Step D Synthesis of 1-(2-(pyrrolidinyl)ethoxy)-4-((5,6-dichloronaphthyloxy)methyl)benzene as an intermediate

Under a dry nitrogen atmosphere, a stirred solution of 0.43 gram (0.001 mole) of 2-bromo-1-(4-((5,6-dichloronaphthyloxy)methyl)phenoxy)ethane, 20 mL of acetonitrile, and 0.63 mL (0.0075 mole) of pyrrolidine was heated between 85°C and 90°C for about 18 hours. The reaction mixture was then allowed to cool and was poured into a saturated aqueous sodium bicarbonate solution. The aqueous mixture was extracted with ethyl acetate, and the extract was washed with an aqueous saturated sodium chloride solution, dried with anhydrous magnesium sulfate and filtered. The filtrate was concentrated under reduced pressure to a residue. The residue was purified by column chromatography on silica gel, eluting with a solution of 10% methanol in methylene chloride. The appropriate fractions were combined and concentrated under reduced pressure, yielding 0.40 gram of the title compound.

20 Step E Synthesis of 1-(2-(4-((5,6-dichloronaphthyloxy)methyl)-phenoxy)ethyl)pyrrolidine-1-oxide
(Compound 1)

A solution of 0.26 gram (0.00114 mole) of 3-chloroperoxybenzoic acid (77%) in 10 mL of chloroform was added drop wise to a stirred, cold (0°C) solution of 0.395 gram of 1-(2-(pyrrolidinyl)ethoxy)-4-((5,6-dichloronaphthyloxy)methyl)benzene in 10 mL of chloroform. The reaction mixture was then stirred at 0°C for two hours, then it was allowed to warm to ambient temperature where it stirred for two hours. The reaction mixture was concentrated under reduced pressure to a residue. The residue was purified by column chromatography on silica gel, eluting with mixtures of 20% to 40% methanol in methylene chloride. The appropriate fractions were combined and concentrated

under reduced pressure, yielding 0.40 gram of Compound 1 as a solid, mp 157°C-159°C. The NMR spectrum was consistent with the proposed structure.

EXAMPLE 2

5 This example illustrates one protocol for the preparation of 3-(4-((5,6-dichloronaphthyloxy)methyl)phenyl)-1-ethylpyrrolidine-1-oxide
(Compound 5)

10 Step A Synthesis of 5-((4-iodophenyl)methoxy)-1,2-dichloronaphthalene as an intermediate

Under a dry nitrogen atmosphere, a stirred mixture of 4.39 grams (0.0187 mole) of 4-iodobenzyl alcohol, 4.2 grams (0.0197 mole) of 5,6-dichloronaphthol, and 5.61 mL (0.0225 mole) of tributylphosphine in 188 mL of THF was cooled to
15 0°C and 5.68 grams (0.0225 mole) of 1,1'-(azodicarbonyl)dipiperidine was added portion wise. The reaction mixture was then allowed to warm to ambient temperature where it stirred for about 18 hours. The reaction mixture was diluted with hexanes, and the resulting precipitate was removed by vacuum filtration. The filtrate was concentrated under reduced pressure to a residue. This residue was
20 purified by column chromatography on silica gel, eluted with mixtures of 10% to 25% ethyl acetate in hexanes. The appropriate fractions were combined and concentrated under reduced pressure, yielding 2.7 grams of the title compound.

25 Step B Synthesis of 1-((1-ethylpyrrolidin-3-yl)oxy)-4-((5,6-dichloronaphthyloxy)methyl)benzene as an intermediate

Under a dry nitrogen atmosphere, a stirred mixture of 0.24 mL (0.002 mole) of 1-ethyl-3-pyrrolidinol in 5 mL of ethylene glycol dimethyl ether was cooled to 0°C and 1.38 mL of methyllithium (1.6 molar solution in diethyl ether, 0.0022 mole)
30 was added. Upon completion of addition, the resultant mixture was stirred for ten minutes.

A second reaction vessel was flushed with dry nitrogen and 0.2 gram of copper(I) chloride (0.002 mole) was added to it. The reaction mixture prepared

above was then added to the copper(I) chloride and the mixture was stirred at ambient temperature for about 30 minutes. While maintaining a dry nitrogen atmosphere, 0.94 gram (0.0022 mole) of 5-((4-iodophenyl)methoxy)-1,2-dichloronaphthalene and 20 mL of pyridine were then added. Upon completion of addition, the reaction mixture was heated to reflux where it stirred for 48 hours. The mixture was then cooled and concentrated under reduced pressure to a residue. The residue was slurried in a mixture of ethyl acetate and water and the mixture was filtered through a pad of silicon dioxide filter agent. An organic phase was separated and was washed first with an aqueous copper(II) sulfate solution, then with a saturated aqueous sodium chloride solution. The organic phase was dried with anhydrous magnesium sulfate, filtered and the filtrate concentrated under reduced pressure to a residue. The residue was purified by column chromatography on silica gel, eluted with mixtures of 6% to 10% methanol in methylene chloride. The appropriate fractions were combined and concentrated under reduced pressure, yielding 0.13 gram of the title compound. The NMR spectrum was consistent with the proposed structure.

Step C Synthesis of 3-(4-((5,6-dichloronaphthyloxy)methyl)phenyl)-1-ethylpyrrolidine-1-oxide

(Compound 5)

This compound was prepared in the manner of Example 1, Step E using 0.125 gram (0.0003 mole) of 1-((1-ethylpyrrolidin-3-yl)oxy)-4-((5,6-dichloronaphthyloxy)-methyl)benzene, and 0.074 gram (0.00033 mole) of 3-chloroperoxybenzoic acid (77%) in 6 mL of chloroform, yielding 0.078 gram of Compound 5 as a solid, MP 145.5 to 148°C. The NMR spectrum was consistent with the proposed structure.

EXAMPLE 3

This example illustrates one protocol for the preparation of 4-(4-((5,6-dichloronaphthyloxy)methyl)phenyl)-1-ethylpiperazine-1-oxide (Compound 9)

A solution of 0.07 gram (0.00017 mole) of 1,2-dichloro-5-((4-(4-ethylpiperazinyl)phenyl)methoxy)naphthalene (US Patent 6,753,429) in 15 mL of chloroform was stirred and 0.05 gram (0.0002 mole) of 3-chloroperoxybenzoic acid (77%) was added. The reaction mixture was stirred at ambient temperature for about 36 hours. The reaction mixture was transferred to a column of basic alumina (deactivated with water, 6% w/w) and purified by chromatography, eluting with mixtures of 3% to 5% methanol in methylene chloride. The appropriate fractions were combined and concentrated under reduced pressure, yielding 0.039 gram of Compound 9 as a solid. The NMR spectrum was consistent with the proposed structure.

EXAMPLE 4

This example illustrates one protocol for the preparation of 4-(4-((5,6-dichloronaphthyloxy)methyl)phenyl)-1-ethylpiperazine-1-oxide hydrochloride (Compound 11)

To a stirred solution of 0.07 gram (0.00016 mole) of 4-(4-((5,6-dichloronaphthyloxy)methyl)phenyl)-1-ethylpiperazinyl-1-oxide (Compound 9, prepared as in Example 3) and two drops of ethanol in 25 mL of methylene chloride was added 1 mL of a 1.0 Molar solution of hydrochloric acid in diethyl ether. The reaction mixture was stirred at ambient temperature for about 18 hours after which time it was concentrated to near dryness. Diethyl ether was added to the concentrate forming a white precipitate. The precipitate was collected by filtration and was dried under reduced pressure, yielding 0.065 gram of Compound 11. The NMR spectrum was consistent with the proposed structure.

EXAMPLE 5

This example illustrates one protocol for the preparation of 4-(4-((5-chloro-6-methylnaphthyloxy)methyl)phenyl)-1-ethylpiperazine-1-oxide (Compound 16)

Step A Synthesis of (6-aminonaphthyl)-4-methylbenzenesulfonate as an intermediate

5 A stirred solution of 8.58 grams (0.054 mole) of 6-amino-1-naphthol and 10.8 grams (0.057 mole) of p-toluenesulfonyl chloride in 150 mL of methylene chloride was cooled in an ice bath, and a solution of 6.56 grams (0.065 mole) of triethylamine in 50 mL of methylene chloride was added drop-wise. The reaction mixture was then allowed to warm to ambient temperature where it stirred for about 18 hours. The reaction mixture was washed with 200 mL of water, and the aqueous wash was extracted with two 200 mL portions of methylene chloride. The combined extracts were dried with sodium sulfate and filtered. The filtrate was concentrated under reduced pressure, yielding 16.89 grams of the title compound. The NMR spectrum was consistent with the proposed structure.

15 Step B Synthesis of (6-amino-5-chloronaphthyl)-4-methylbenzenesulfonate as an intermediate

20 A solution of 3.47 grams (0.026) of N-chlorosuccinimide in 25 mL of DMF was added drop-wise to a stirred solution of 8.0 grams (0.026 mole) of (6-aminonaphthyl)-4-methylbenzenesulfonate. Upon completion of addition the reaction mixture was stirred for 90 minutes, then it was diluted with water and extracted with two portions of diethyl ether. The extracts were combined, dried with anhydrous magnesium sulfate and filtered. The filtrate was concentrated under reduced pressure to a residue. The residue was purified by column chromatography on silica gel, eluting with mixtures of 50% to 75% methylene chloride in petroleum ether. The appropriate fractions were combined and concentrated under reduced pressure, yielding 2.97 grams of the title compound. The NMR was consistent with the proposed structure.

30 Step C Synthesis of (5-chloro-6-iodonaphthyl)-4-methylbenzenesulfonate as an intermediate

A stirred mixture of 2.95 grams (0.0085 mole) of (6-amino-5-chloronaphthyl)-4-methylbenzenesulfonate and 30 mL of 6N hydrochloric acid was heated at 35°C for 30 minutes. The reaction mixture was cooled to 0°C and an aqueous solution of 0.65 gram (0.0094 mole) of sodium nitrite was added drop wise, during a ten-minute period. This mixture was stirred for an additional 30 minutes, then a solution of 2.12 grams (0.013 mole) of potassium iodide in 15 mL of water was added. The reaction mixture was stirred for 1.5 hours during which time the reaction mixture came to ambient temperature. The reaction mixture was then extracted with three 200 mL portions of diethyl ether. The combined extracts were dried with anhydrous magnesium sulfate, filtered, and the filtrate concentrated under reduced pressure to a residue. The residue was triturated with a mixture of methylene chloride and petroleum ether producing a solid that was collected by filtration. The solid was dried, yielding 0.51 gram of the title compound. The NMR spectrum was consistent with the proposed structure. Additional quantities of the title compound contained in the filtrate was purified by adsorption of the filtrate onto silica gel followed by column chromatography of the mixture on silica gel, eluting with mixtures of 25% to 40% diethyl ether in petroleum ether. The appropriate fractions were combined and concentrated under reduced pressure, yielding 1.6 grams of a solid. This solid was triturated with a diethyl ether and petroleum ether mixture and the resulting solid was collected by filtration. The solid was dried, yielding 1.1 grams of the title compound. The NMR spectrum was consistent with the proposed structure. The purified materials were combined, yielding a total of 1.61 grams of the title compound.

25 Step D Synthesis of (5-chloro-6-methylnaphthyl)-4-methylbenzenesulfonate
 as an intermediate

Tetrakis(triphenylphosphine)palladium(0) (0.37 gram, 0.00032 mole) was added to a stirred mixture of 1.45 grams (0.0032 mole) of (5-chloro-6-iodonaphthyl)-4-methylbenzenesulfonate, 0.7 gram (0.0056 mole) of trimethylboroxine, and 1.55 grams (0.0112 mole) of potassium carbonate in 50 mL of 1,4-dioxane. The reaction mixture was degassed by three repetitions of purging the atmosphere in the reaction vessel under vacuum and replacing the atmosphere

with dry nitrogen. While maintaining the dry nitrogen atmosphere, the reaction mixture was heated to 100°C where it stirred for about 24 hours. The reaction mixture was then cooled, diluted with water, and extracted with two portions of diethyl ether. The combined extracts were dried with anhydrous magnesium sulfate, and filtered. The filtrate was concentrated under reduced pressure to a residue. The residue was purified by column chromatography on silica gel, eluting with mixtures of 25% to 35% methylene chloride in petroleum ether. The appropriate fractions were combined and concentrated under reduced pressure, yielding 0.88 gram of the title compound. The NMR spectrum conformed to the proposed structure.

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Step E Synthesis of 5-chloro-6-methyl-1-naphthol as an intermediate

A solution of 0.37 gram (0.0059 mole) of potassium hydroxide (85%) in 10 mL of water was added to a stirred mixture of 0.87 gram (0.0025 mole) of (5-chloro-6-methylnaphthyl)-4-methylbenzenesulfonate in 75 mL of ethanol. The reaction mixture was then heated at reflux for 2.5 hours, after which time the mixture was allowed to cool to ambient temperature. The reaction mixture was diluted with 100 mL of water and then extracted with two 100 mL portions of diethyl ether. The extracts were combined, washed with 100 mL of an aqueous lithium chloride solution and dried with anhydrous magnesium sulfate. The mixture was filtered and the filtrate was concentrated under reduced pressure to a residue. The residue was purified by column chromatography on silica gel, eluted with mixtures of 50% to 99% methylene chloride in petroleum ether. The appropriate fractions were combined and concentrated under reduced pressure, yielding 0.27 gram of the title compound. The NMR spectrum was consistent with the proposed structure.

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Step F Synthesis of 1-chloro-5-((4-bromophenyl)methoxy)-2-methylnaphthalene as an intermediate.

To a stirred solution of 0.26 gram (0.00135 mole) of 5-chloro-6-methyl-1-naphthol in 30 mL of DMF was added 0.065 gram (0.0016 mole) of sodium hydride (60% dispersion in mineral oil). The reaction mixture was stirred for 30 minutes, then a solution of 0.37 gram (0.0015 mole) of 4-bromobenzyl bromide in 5 mL of

30

DMF was added. Upon completion of addition, the reaction mixture was stirred at ambient temperature for about 18 hours after which time the mixture was diluted with 200 mL of water. The aqueous mixture was extracted with two 150 mL portions of methylene chloride. The combined extracts were dried with anhydrous
5 magnesium sulfate, filtered, and the filtrate was concentrated under reduced pressure to a residue. The residue was triturated with a mixture of diethyl ether and petroleum ether to producing a white solid which was collected by filtration. The solid was dried under reduced pressure, yielding 0.38 gram of the title compound. The NMR spectrum was consistent with the proposed structure.

10

Step G Synthesis of 1-chloro-5-((4-(4-ethylpiperazinyl)phenyl)methoxy)-2-methyl naphthalene as an intermediate

A stirred mixture of 0.015 gram (0.0000163 mole) of
15 tris(dibenzylideneacetone) and 0.031 gram (0.00005 mole) of 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl in 40 mL of toluene was degassed by three repetitions of purging the atmosphere in the reaction vessel under vacuum and replacing the atmosphere with dry nitrogen. While maintaining the dry nitrogen atmosphere, 0.35 gram (0.00097 mole) of 1-chloro-5-((4-bromophenyl)methoxy)-2-
20 methylnaphthalene, 0.22 gram (0.00194 mole) of 1-ethylpiperazine, and 0.19 gram (0.00194 mole) of sodium tert-butoxide were added. Upon completion of addition, the reaction mixture was heated between 80°C and 85°C for 16 hours, and then was allowed to cool to ambient temperature. The mixture was filtered through a pad of silicon dioxide filter agent, followed by rinsing the filter pad with toluene. The
25 combined filtrate and rinse was concentrated under reduced pressure to a residue. The residue was purified by column chromatography on neutral alumina (deactivated with water, 6% w/w), eluted with a solution of 25% petroleum ether in methylene chloride. The appropriate fractions were combined and concentrated under reduced pressure, yielding 0.3 gram of the title compound. The NMR
30 spectrum was consistent with the proposed structure.

Step H Synthesis of 4-(4-((5-chloro-6-methylnaphthyloxy)methyl)phenyl)-1-ethylpiperazine-1-oxide

(Compound 16)

This compound was prepared in the manner of Example 3 using 0.12 gram (0.0003 mole) of 1-chloro-5-((4-(4-ethylpiperazinyl)phenyl)methoxy)-2-methylnaphthalene, 0.075 gram (0.00033 mole) of 3-chloroperoxybenzoic acid (77%) and 15 mL of chloroform, yielding 0.1 gram of Compound 16 as a solid. The NMR spectrum was consistent with the proposed structure.

EXAMPLE 6

This example illustrates one protocol for the preparation of 4-(4-((5,6-dichloronaphthyloxy)methyl)-3-methoxyphenyl)-1-ethylpiperazine-1-oxide (Compound 17) and 4-(4-((5,6-dichloronaphthyloxy)methyl)-3-methoxyphenyl)-1-ethylpiperazine-1,4-dioxide (Compound 18)

Step A Synthesis of (4-(4-ethylpiperazinyl)-3-methoxyphenyl)formaldehyde as an intermediate.

A stirred mixture of 3.0 grams (0.019 mole) of 4-fluoro-3-methoxybenzaldehyde, 2.88 grams (0.025 mole) of N-ethylpiperazine, and 3.48 grams (0.025 mole) of potassium carbonate in 75 mL of N,N-dimethylacetamide was heated at 90°C for four days, and then was allowed to cool to ambient temperature. The reaction mixture was diluted with water and extracted with five 100 mL portions of diethyl ether. The combined extracts were dried with anhydrous magnesium sulfate and filtered. The filtrate was concentrated under reduced pressure to a residue. The residue was purified by column chromatography on neutral alumina, eluted with mixtures of 5% to 10% ethyl acetate in methylene chloride. The appropriate fractions were combined and concentrated under reduced pressure, yielding 3.25 grams of title compound. The NMR spectrum was consistent with the proposed structure.

Step B Synthesis of 4-(4-ethylpiperazinyl)-3-methoxybenzylalcohol as an intermediate.

5 A mixture of 3.25 grams (0.013 mole) of (4-(4-ethylpiperazinyl)-3-methoxyphenyl)formaldehyde and 0.49 gram (0.013 mole) of sodium borohydride in 75 mL of ethanol was stirred at ambient temperature for about 18 hours. The reaction mixture was then diluted with water, and was extracted with two 150 mL portions of diethyl ether. The combined extracts were washed with an aqueous lithium chloride solution, dried with anhydrous magnesium sulfate and filtered. The
10 filtrate was condensed under reduced pressure, yielding 2.09 grams of the title compound as a tan solid. The NMR spectrum was consistent with the proposed structure.

Step C Synthesis of 1,2-dichloro-5-((4-(4-ethylpiperazinyl)-3-methoxyphenyl)methoxy)naphthalene as an intermediate.
15

 A stirred mixture of 0.6 gram (0.0028 mole) of 5,6-dichloronaphthol, 0.54 gram (0.0022 mole) of 4-(4-ethylpiperazinyl)-3-methoxybenzyl alcohol, and 1.4 grams of polymer-supported triphenylphosphine in 50 mL of methylene chloride
20 was cooled in a water and ice bath and a solution of 0.58 gram (0.0033 mole) of diethylazodicarboxylate dissolved in a small amount of methylene chloride was added drop wise. Upon completion of addition, the reaction mixture was allowed to warm slowly to ambient temperature where it stirred for three days. The reaction mixture was filtered through a pad of silicon dioxide filter aid and the filtrate was
25 concentrated under reduced pressure to a residue. The residue was purified by column chromatography on neutral alumina (deactivated with water, 6% w/w) eluted with methylene chloride. The appropriate fractions were combined and concentrated under reduced pressure, yielding 0.06 gram of the title compound. The NMR spectrum was consistent with the proposed structure.

Step D Synthesis of 4-(4-((5,6-dichloronaphthyloxy)methyl)-3-methoxyphenyl)-1-ethylpiperazine-1-oxide
(Compound 17)

5 and 4-(4-((5,6-dichloronaphthyloxy)methyl)-3-methoxyphenyl)-1-ethylpiperazine-1,4-dioxide
(Compound 18)

A mixture of 0.095 gram (0.00021 mole) of 1,2-dichloro-5-((4-(4-ethylpiperazinyl)-3-methoxyphenyl)methoxy)-naphthalene and 0.052 gram (0.00023 mole) 3-chloroperoxybenzoic acid (77%) in 15 mL of chloroform was stirred at ambient temperature for 1.5 hours. The reaction mixture was then transferred to a column of basic alumina (deactivated with water, 6% w/w) for purification. Elution was accomplished with mixtures of 3% to 5% methanol in methylene chloride, which resulted in the isolation of two compounds. Fractions of the first compound to elute were combined and concentrated under reduced pressure, yielding 0.04 gram of Compound 17 as a solid. The NMR spectrum was consistent with the proposed structure. Fractions of the second compound to elute were combined and concentrated under reduced pressure, yielding 0.02 gram of Compound 18 as a solid. The NMR spectrum was consistent with the proposed structure.

EXAMPLE 7

This example illustrates one protocol for the preparation of 4-(4-((5,6-dichloronaphthyloxy)methyl)phenyl)-1-ethylpiperazine-1,4-dioxide dihydrochloride
(Compound 12)

Step A Synthesis of 4-(4-((5,6-dichloronaphthyloxy)methyl)phenyl)-1-ethylpiperazine-1,4-dioxide (Compound 10) as an intermediate.

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To a stirred solution of 0.4 gram (0.0011 mole) of 4-(4-((5,6-dichloronaphthyloxy)methyl)phenyl)-1-ethylpiperazine in 20 mL of chloroform was added 0.61 gram (0.0027 mole) of 3-chloroperbenzoic acid (77%). The mixture was

stirred at room temperature for 1.5 hours. The reaction mixture was transferred to a column of basic alumina (deactivated with water, 6% w/w) for purification, eluted with mixtures of 5% to 7% methanol in methylene chloride. The appropriate fractions were combined and concentrated under reduced pressure, yielding 0.43 gram of Compound 10. The NMR spectrum was consistent with the proposed structure.

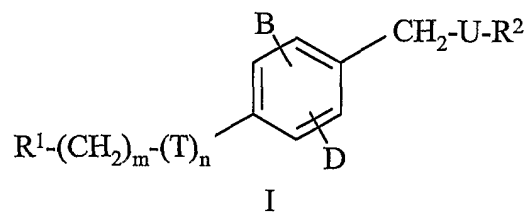
Step B Synthesis of 4-(4-((5,6-dichloronaphthyloxy)methyl)phenyl)-1-ethylpiperazine-1,4-dioxide dihydrochloride
(Compound 12)

A mixture of 0.1 gram (0.00022 mole) of 4-(4-((5,6-dichloronaphthyloxy)methyl)phenyl)-1-ethylpiperazine-1,4-dioxide, 10 mL of chloroform, 2 mL of ethanol, and 1 mL of a 1.0 Molar solution of hydrochloric acid in diethyl ether was stirred at ambient temperature for ten days. The reaction mixture was concentrated to near dryness and the solid residue triturated with diethyl ether, forming a brown solid, which was collected by filtration. The brown solid was added to 20 mL of ethanol and the mixture was stirred and heated at reflux for about 30 minutes. The mixture was allowed to cool to ambient temperature producing a tan solid, which was collected by filtration. The solid was dried under reduced pressure yielding 0.02 gram of Compound 12 as a solid. The NMR spectrum was consistent with the proposed structure.

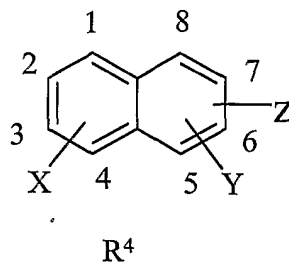
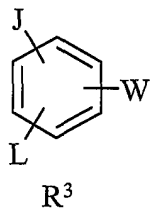
It is well known to one of ordinary skill in the art that compounds like the compounds of formula I of the present invention can contain optically active and racemic forms. It is also well known in the art that compounds like the compounds of formula I may contain stereoisomeric forms, tautomeric forms and/or exhibit polymorphism. It is to be understood that the present invention encompasses any racemic, optically active, polymorphic, tautomeric, or stereoisomeric form, or mixtures thereof. It should be noted that it is well known in the art how to prepare optically active forms, for example by resolution of a racemic mixture, or by synthesis from optically active intermediates.

The following table sets forth some additional examples of compounds of formula I useful in the present invention:

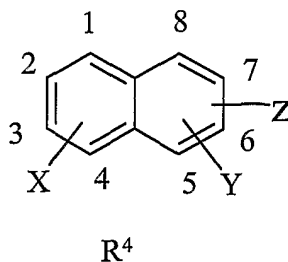
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Insecticidal Heterocyclic 1,4-Disubstituted Benzene N-Oxides



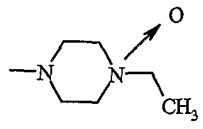
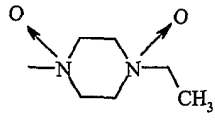
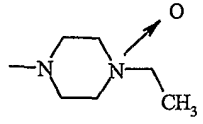
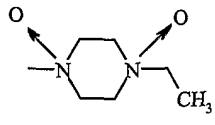
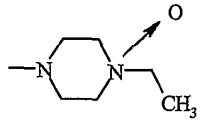
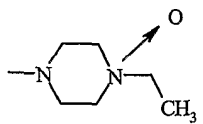
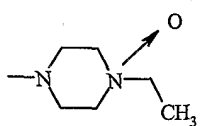
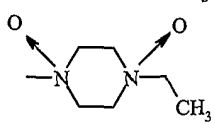
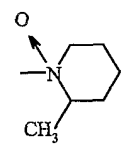
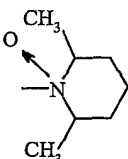
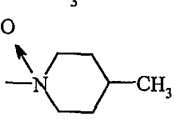
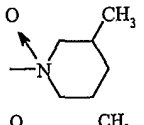
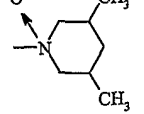
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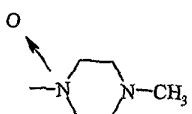
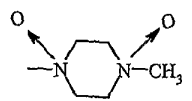
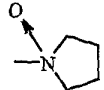
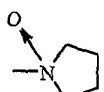
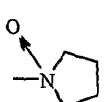
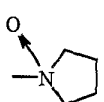
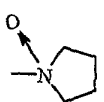
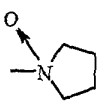
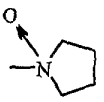
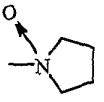
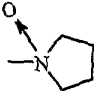
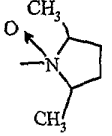
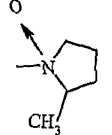
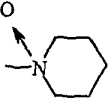


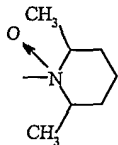
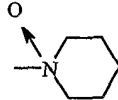
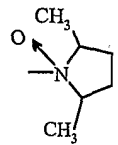
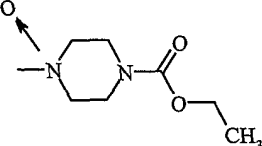
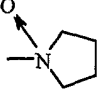
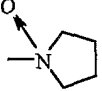
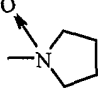
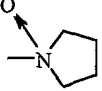
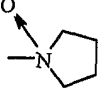
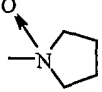
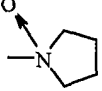
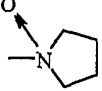
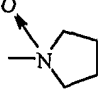
Formula I where D is H; when n is 1, T is oxygen; U is oxygen; R^2 is $1-R^4$; and Z is H unless otherwise noted

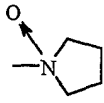
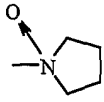
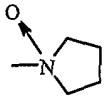
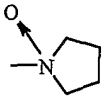
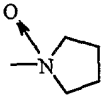
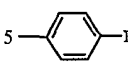
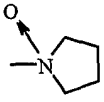
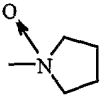
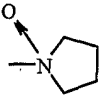
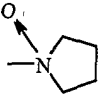
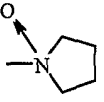
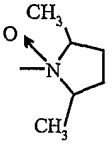
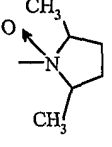
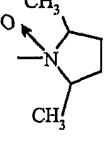


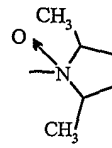
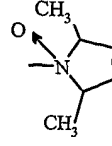
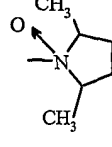
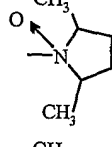
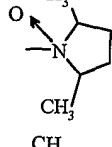
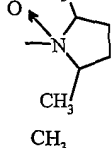
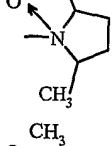
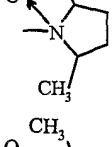
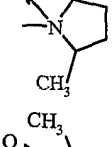
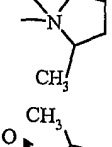
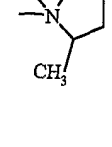
Cmpd No	m	n	B	R^1	X	Y
1	2	1	H		5-Cl	6-Cl
2	2	1	H		5-Cl	6-Cl
3	2	1	H		5-Cl	6-Cl
4	2	1	H		5-Cl	6-Cl
5	0	1	H		5-Cl	6-Cl
6	2	1	H		5-Cl	6-Cl
7	1	1	H		5-Cl	6-Cl
8	0	1	H		5-Cl	6-Cl
9	0	0	H		5-Cl	6-Cl
10	0	0	H		5-Cl	6-Cl

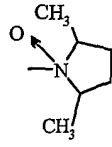
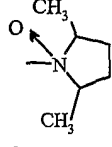
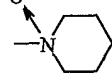
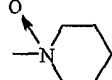
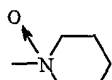
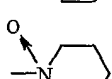
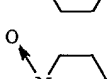
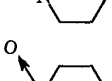
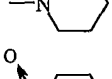
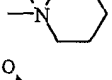
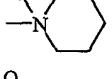
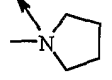
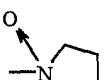
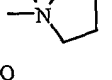
Cmpd No	m	n	B	R ¹	X	Y
11 Hydrochloride salt	0	0	H		5-Cl	6-Cl
12 Di-hydrochloride salt	0	0	H		5-Cl	6-Cl
13 Ethyl sulfonate salt	0	0	H		5-Cl	6-Cl
14 Di-ethyl sulfonate salt	0	0	H		5-Cl	6-Cl
15 t-Cinnamate salt	0	0	H		5-Cl	6-Cl
16	0	0	H		5-Cl	6-CH ₃
17	0	0	2-OCH ₃		5-Cl	6-Cl
18	0	0	2-OCH ₃		5-Cl	6-Cl
19	2	1	H		5-Cl	6-Cl
20	2	1	H		5-Cl	6-Cl
21	2	1	H		5-Cl	6-Cl
2	2	1	H		5-Cl	6-Cl
23	2	1	H		5-Cl	6-Cl

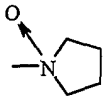
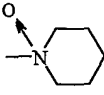
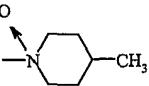
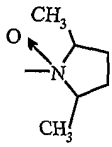
Cmpd No	m	n	B	R ¹	X	Y
24	2	1	H		5-Cl	6-Cl
25	2	1	H		5-Cl	6-Cl
26	2	1	H		5-Cl	6-Br
27	2	1	H		4-Cl	H
28*	2	1	H		4-Cl	5-Cl
29	2	1	H		4-Br	H
30	2	1	H		4-CF ₃	H
31	2	1	H		4-OC ₆ H ₅	H
32	2	1	H		4-C ₆ H ₅	H
33	2	1	H		4-CH ₃	H
34	2	1	H		4-CF ₃	H
35	2	1	H		4-Cl	H
36	2	1	H		4-Cl	H
37	2	1	H		4-Cl	H

Cmpd No	m	n	B	R ¹	X	Y
38	2	1	H		4-Br	H
39	2	1	H		4-CN	H
40	2	1	H		4-CF ₃	H
41	2	1	H		5-Cl	6-Cl
42	2	1	H		4-NO ₂	H
43	2	1	H		4-CN	H
44	2	1	H		4-OCH ₃	H
45	2	1	H		5-OCH ₃	H
46	2	1	H		5-I	H
47	2	1	H		5-CF ₃	H
48	2	1	H		5-OCF ₃	H
49	2	1	H		5-CN	H
50	2	1	H		5-Br	H

Cmpd No	m	n	B	R ¹	X	Y
51	2	1	H		5-F	H
52	2	1	H		5-OC ₂ H ₄ CH ₃	H
53	2	1	H		5-NO ₂	H
54	2	1	H		5-SCH ₃	H
55	2	1	H		5- 	H
56	2	1	H		5-OCH ₂ CH ₃	H
57	2	1	H		5-CF ₂ CF ₃	H
58	2	1	H		5-OCH(CH ₃) ₂	H
59	2	1	H		5-OCHF ₂	H
60	2	1	H		5-OSO ₂ CF ₃	H
61	2	1	H		6-Cl	H
62	2	1	H		6-CF ₃	H
63	2	1	H		6-Br	H

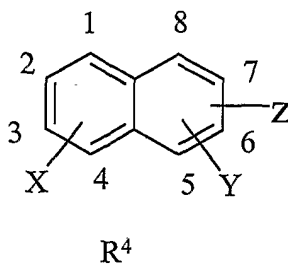
Cmpd No	m	n	B	R ¹	X	Y
64	2	1	H		6-I	H
65	2	1	H		6-OCF ₃	H
66	2	1	H		6-F	H
67	2	1	H		5-OCH ₃	6-Cl
68	2	1	H		5-I	6-Cl
69	2	1	H		5-Cl	6-Br
70	2	1	H		5-Cl	6-I
71	2	1	H		5-Cl	6-OCH ₃
72	2	1	H		5-CF ₃	6-Cl
73	2	1	H		5-Br	6-Br
74	2	1	H		5-Cl	6-OCH ₂ CH ₃

Cmpd No	m	n	B	R ¹	X	Y
75	2	1	H		5-Cl	6-OCH(CH ₃) ₂
76	2	1	H		5-OCHF ₂	6-Cl
77	2	1	H		5-OCH ₃	6-Cl
78	2	1	H		5-I	6-Cl
79	2	1	H		5-Cl	6-Br
80	2	1	H		5-CF ₃	6-Cl
81	2	1	H		5-Br	6-Br
82	2	1	H		5-Cl	6-OCH ₂ CH ₃
83	2	1	H		5-Cl	6-OCH(CH ₃) ₂
84	2	1	H		5-OCHF ₂	6-Cl
85 Hydrochloride salt	2	1	H		5-Cl	6-Cl
86 Trifluoroacetic salt	2	1	H		5-Cl	6-Cl
87 sulfonate salt	2	1	H		5-Cl	6-Cl
88 4-Methyl benzenesulfonate salt	2	1	H		5-Cl	6-Cl
89 Ethylsulfonate salt	2	1	H		5-Cl	6-Cl

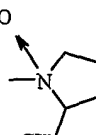
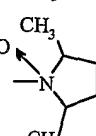
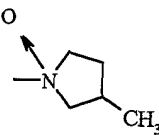
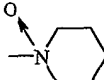
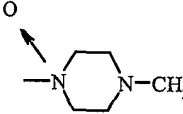
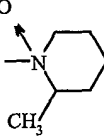
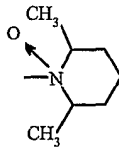
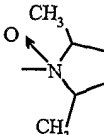
Cmpd No	m	n	B	R ¹	X	Y
90 Citrate salt	2	1	H		5-Cl	6-Cl
91 Sulfonate salt	2	1	H		5-Cl	6-Cl
92 Sulfonate salt	2	1	H		5-Cl	6-Cl
93 Sulfonate salt	2	1	H		5-Cl	6-Cl

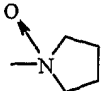
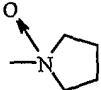
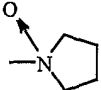
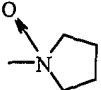
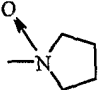
* Z is 6-Cl

Formula I where m is 2; n is 1; T is oxygen; B and D are H; U is nitrogen; R² is 1-R⁴; and Z is H unless otherwise noted



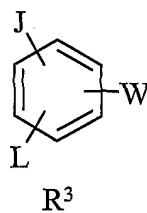
Cmpd No	R ¹	X	Y
94		4-Cl	H
95		4-Br	H
96		4-CF ₃	H
97		4-CN	H
98		5-Cl	H
99		5-CF ₃	H
100		5-Br	H
101		5-OCF ₃	H
102		5-Cl	6-Cl
103		5-Cl	6-OCH ₃
104		5-Cl	6-CF ₃

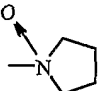
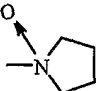
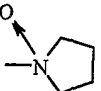
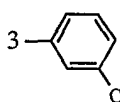
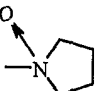
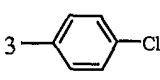
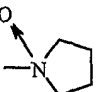
Cmpd No	R ¹	X	Y
105		5-Cl	6-OCF ₃
106*		4-Cl	5-Cl
107		5-Cl	5-Cl
108		5-Cl	6-Cl
109		5-Cl	6-Cl
110		5-Cl	6-Cl
111		5-Cl	6-Cl
112		5-Cl	6-Cl
113		5-Cl	6-Cl
114		4-Cl	5-Cl
115		5-Cl	6-CF ₃
116		6-CF ₃	H

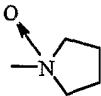
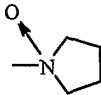
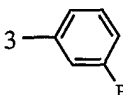
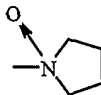
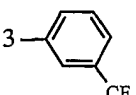
Cmpd No	R ¹	X	Y
117		6-OCF ₃	H
118		6-CN	H
119		6-Br	H
120		6-I	H
121		6-OCH(CH ₃) ₂	H

* Z is 6-Cl

5 Formula I where m is 2; n is 1; T is oxygen; B and D are H; U is oxygen; R² is 1-R³; and W is H unless otherwise noted



Cmpd No	R ¹	J	L
122		3-C ₆ H ₅	H
123		3-CH=C(Cl) ₂	H
124			H
125			H
126		3-I	H

Cmpd No	R ¹	J	L
127		3-Cl	4-Cl
128			H
129			H

The following table sets forth physical characterizing data for certain compounds of formula I of the present invention:

5

Table 2
Insecticidal Heterocyclic 1,4-Disubstituted Benzene N-Oxides
Compound Characterization

	Molecular Formula	Melting Point (°C) of Solids Or Physical State
1	C ₂₃ H ₂₃ Cl ₂ NO ₃	157-159
2	C ₂₄ H ₂₅ Cl ₂ NO ₃	130-131
3	C ₂₅ H ₂₇ Cl ₂ NO ₃	VISCOUS OIL
4	C ₂₅ H ₂₇ Cl ₂ NO ₃	111.5-113.5
5	C ₂₃ H ₂₃ Cl ₂ NO ₃	145.5-148
6	C ₂₄ H ₂₅ Cl ₂ NO ₃	147-148
7	C ₂₃ H ₂₃ Cl ₂ NO ₃	VISCOUS OIL
8	C ₂₄ H ₂₅ Cl ₂ NO ₃	FOAM
9	C ₂₃ H ₂₄ Cl ₂ N ₂ O ₂	SOLID
10	C ₂₃ H ₂₄ Cl ₂ N ₂ O ₃	SOLID
11	C ₂₃ H ₂₅ Cl ₂ N ₂ O ₂ Cl	SOLID
12	C ₂₃ H ₂₆ Cl ₂ N ₂ O ₂ 2Cl	SOLID
13	C ₂₃ H ₂₅ Cl ₂ N ₂ O ₂ C ₂ H ₅ O ₃ S	SOLID
14	C ₂₃ H ₂₅ Cl ₂ N ₂ O ₂ 2C ₂ H ₅ O ₃ S	SOLID
15	C ₂₃ H ₂₅ Cl ₂ N ₂ O ₂ C ₉ H ₇ O ₂	SOLID
16	C ₂₄ H ₂₇ ClN ₂ O ₂	SOLID
17	C ₂₄ H ₂₆ Cl ₂ N ₂ O ₃	SOLID
18	C ₂₄ H ₂₆ Cl ₂ N ₂ O ₄	SOLID

10

Candidate insecticides were evaluated for activity against the tobacco budworm (*Heliothis virescens* [Fabricius]) in a surface-treated diet test.

In this test one mL of molten (65-70°C) wheat germ-based artificial diet was pipetted into each well of a four by six (24 well) multi-well plate (ID# 430345-15.5 mm dia. x 17.6 mm deep; Corning Costar Corp., One Alewife Center, Cambridge, MA 02140). The diet was allowed to cool to ambient temperature before treatment
5 with candidate insecticide.

For a determination of insecticidal activity, solutions of the candidate insecticides were prepared for testing using a Packard 204DT Multiprobe[®] Robotic System (Packard Instrument Company, 800 Research Parkway, Meriden, CT 06450), in which the robot first diluted a standard 50 millimolar DMSO solution of
10 candidate insecticide with a 1:1 water/acetone solution (V/V) in a ratio of 1:7 stock solution to water/acetone. The robot subsequently pipetted 40 microliters of the so-prepared solution onto the surface of the diet in each of three wells in the 24 multi-well plate. The process was repeated with solutions of seven other candidate insecticides. Once treated, the contents of the multi-well plate were allowed to dry,
15 leaving 0.25 millimoles of candidate insecticide on the surface of the diet, or a concentration of 0.25 millimolar. Appropriate untreated controls containing only DMSO on the diet surface were also included in this test.

For evaluations of the insecticidal activity of a candidate insecticide at varying rates of application, the test was established as described above using sub-
20 multiples of the standard 50 millimolar DMSO solution of candidate insecticide. For example, the standard 50 millimolar solution was diluted by the robot with DMSO to give 5, 0.5, 0.05, 0.005, 0.0005 millimolar, or more dilute solutions of the candidate insecticide. In these evaluations there were six replicates of each rate of application placed on the surface of the diet in the 24 multi-well plate, for a total of
25 four rates of application of candidate insecticide in each plate.

In each well of the test plate was placed one second instar tobacco budworm larvea, each weighing approximately five milligrams. After the larvae were placed in each well, the plate was sealed with clear polyfilm adhesive tape. The tape over each well was perforated to ensure an adequate air supply. The plates were then
30 held in a growth chamber at 25 °C and 60% relative humidity for five days (light 14 hours/day).

After the five-day exposure period insecticidal activity for each rate of application of candidate insecticide was assessed as percent inhibition of insect weight relative to the weight of insects from untreated controls, and percent mortality when compared to the total number of insects infested.

5 Insecticidal activity data at selected rates of application from this test are provided in Table 3. The test compounds of formula I are identified by numbers that correspond to those in Table 1.

Table 3
Insecticidal Activity of Certain Heterocyclic 1,4-disubstituted benzene N-Oxides
When Applied to the Surface of the Diet of Tobacco Budworm (*Heliothis virescens*
[Fabricius])

Cmpd No.	Percent Mortality	Percent Growth Inhibition	Cmpd No.	Percent Mortality	Percent Growth Inhibition
1	100	100	2	100	100
3	100	100	4	100	100
5	100	100	6	100	100
7	100	100	8	100	100
9	100	100	10	100	100
11	100	100	12	100	100
14	100	100	16	100	100

15 Concentration of the candidate insecticide applied to the surface of the diet is 0.25 millimolar.

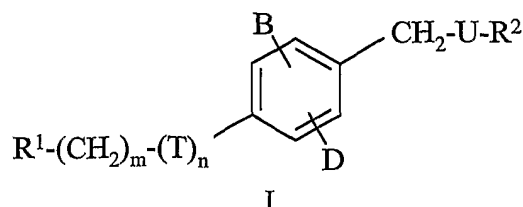
As set forth in Table 3, all of the tested compounds of the present invention provided 100% mortality and/or 100% growth inhibition of the tobacco budworm.

While this invention has been described with an emphasis upon preferred
20 embodiments, it will be understood by those of ordinary skill in the art that
variations of the preferred embodiments may be used and that it is intended that the
invention may be practiced otherwise than as specifically described herein.
Accordingly, this invention includes all modifications encompassed within the spirit
and scope of the invention as defined by the following claims.

25

WHAT IS CLAIMED IS:

1. A compound of formula I:



wherein:

R^1 is a non-aromatic heterocyclic N-oxide, where the heterocyclic N-oxide moiety is comprised of one or more nitrogen atoms, where at least one of the nitrogen atoms is oxidized, and where the heterocyclic N-oxide is optionally substituted with a halogen, hydroxyl, alkyl, haloalkyl, alkoxy, haloalkoxy, alkylthio, alkylsulfonyl, alkoxycarbonyl, aryl, aryloxy, arylcarbonyl, benzyl, alkenyl, alkynyl or alkylamino;

m is an integer selected from 0, 1, or 2;

n is an integer selected from 0 or 1,

and when n is 1;

T is selected from oxygen or sulfur;

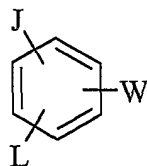
U is selected from $-CH_2-$, $-OCH_2-$, oxygen, sulfur, sulfonyl, oxyalkyloxy, alkenylamino, carbonylamino, or NR^5 where R^5 is selected from hydrogen, hydroxyl, alkyl, haloalkyl, sulfonylalkyl, carbonylamino, and carbonylalkyl;

R^2 is an optionally substituted aryl, an optionally substituted alkylpolycyclyl or an optionally substituted heterocyclyl, where the optional substituents are independently selected from the group consisting of hydrogen, halogen, cyano, nitro, amino, carboxyl, alkyl, haloalkyl, alkylthio, haloalkylthio, alkenyl, alkoxy, haloalkoxy, aminoalkoxy, carbonyl, alkylcarbonyl, haloalkylcarbonyl, alkoxycarbonyl, haloalkoxycarbonyl, aryl, aryloxy, and heterocyclyl; where the aryl and heterocyclyl moieties are optionally substituted with one or more substituents selected from the group consisting of halogen, haloalkyl, alkoxy, and haloalkoxy;

B and D are independently selected from hydrogen, halogen, alkyl, haloalkyl, alkoxy, and haloalkoxy;

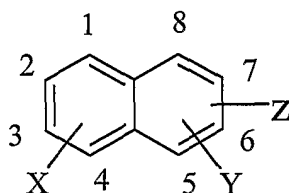
and the corresponding agriculturally acceptably salts thereof.

2. The compound of claim 1, wherein R^2 is 1- R^3 , 1- R^4 , or 2- R^4 ; where:
 R^3 is



where J, L, and W are independently selected from hydrogen, halogen, cyano, nitro, amino, carboxyl, alkyl, haloalkyl, alkenyl, alkoxy, haloalkoxy, aminoalkoxy, carbonyl, alkylcarbonyl, haloalkylcarbonyl, alkoxycarbonyl, haloalkoxycarbonyl, aryl, aryloxy, and heterocyclyl; and

R^4 is



where X, Y, and Z are independently selected from hydrogen, halogen, cyano, nitro, amino, alkyl, haloalkyl, alkylthio, haloalkylthio, alkenyl, alkoxy, haloalkoxy, carbonyl, haloalkoxycarbonyl, aryl, aryloxy, and heterocyclyl; where the aryl and heterocyclyl moieties are optionally substituted with one or more substituents selected from the group consisting of halogen, haloalkyl, alkoxy, and haloalkoxy.

3. The compound of claim 2, wherein R^1 is a non-aromatic heterocyclic N-oxide, where the heterocyclic N-oxide moiety is comprised of one or more nitrogen atoms, where at least one of the nitrogen atoms is oxidized, and where the heterocyclic N-oxide is optionally substituted with a halogen, alkyl, haloalkyl, haloalkoxy, alkylthio, alkylsulfonyl, alkoxycarbonyl, aryl, aryloxy, arylcarbonyl, benzyl, alkenyl or alkynyl;

R^5 is selected from hydrogen, alkyl, haloalkyl and carbonylamino;

J, L, and W are independently selected from hydrogen, halogen, cyano, nitro, carboxyl, alkyl, haloalkyl, haloalkoxy, alkylcarbonyl, alkoxycarbonyl, aryl, arlyoxy, and heterocyclyl;

X, Y, and Z are independently selected from hydrogen, halogen, cyano, nitro, alkyl, haloalkyl, alkylthio, haloalkylthio, alkoxy, haloalkoxy, aryl and aryloxy; where the aryl moiety is optionally substituted with one or more substituents selected from the group consisting of halogen and haloalkyl; and

B and D are independently selected from hydrogen, halogen, alkyl, haloalkyl and alkoxy.

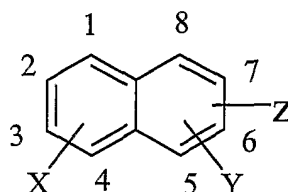
4. The compound of claim 3, wherein R^1 is a non-aromatic heterocyclic N-oxide, where the heterocyclic N-oxide moiety is comprised of one or more nitrogen atoms, where at least one of the nitrogen atoms is oxidized, and where the heterocyclic N-oxide is optionally substituted with an alkyl or alkoxycarbonyl;

T is oxygen;

U is oxygen;

R^2 is 1- R^4 where

R^4 is



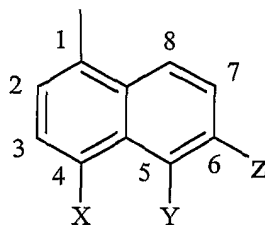
where X, Y, and Z are independently selected from hydrogen, halogen, cyano, nitro, alkyl, haloalkyl, alkylthio, haloalkylthio, alkoxy, haloalkoxy, aryl and aryloxy; where the aryl moiety is optionally substituted with one or more substituents selected from the group consisting of halogen and haloalkyl; and

B and D are independently selected from hydrogen and alkoxy.

5. The compound of claim 2, wherein R^1 is a non-aromatic heterocyclic N-oxide, comprised of five or six members, wherein the heterocyclic N-oxide is optionally substituted with a halogen, alkyl, haloalkyl, alkoxy, alkylthio,

alkylsulfonyl, alkoxycarbonyl, aryl, or aryloxy; n is 1, T is oxygen; U is oxygen; R^2 is 1- R^4 ; and B and D are hydrogen;

6. The compound of claim 5, wherein R^1 is a non-aromatic heterocyclic N-oxide optionally substituted with an alkyl and R^2 is 1- R^4 ; where R^4 is

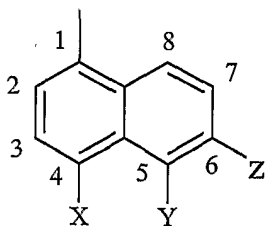


where X, Y, and Z are independently selected from hydrogen, halogen, alkyl, haloalkyl, alkoxy, and haloalkoxy.

7. The compound of claim 6, wherein m is 2 and R^1 is a non-aromatic heterocyclic N-oxide selected from pyrrolidin-1-yl 1-oxide or piperidin-1-yl 1-oxide.

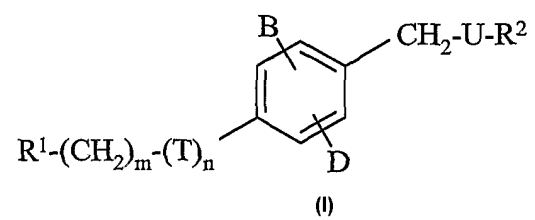
8. The compound of claim 2, wherein R^1 is a non-aromatic heterocyclic N-oxide, comprised of six members, wherein the heterocyclic N-oxide is optionally substituted with a halogen, alkyl, haloalkyl, alkoxy, alkylthio, alkylsulfonyl, alkoxycarbonyl, aryl, or aryloxy; m is 0; n is 0; U is oxygen and R^2 is 1- R^4 .

9. The compound of claim 8, wherein R^1 is a non-aromatic heterocyclic N-oxide optionally substituted with an alkyl and R^2 is 1- R^4 ; where R^4 is



where X, Y, and Z are independently selected from hydrogen, halogen, alkyl, haloalkyl, alkoxy, and haloalkoxy.

10. The compound of claim 9, wherein R^1 is a non-aromatic heterocyclic N-oxide selected from 1-ethylpiperazin-4-yl 1-oxide, 1-ethylpiperazin-4-yl 4-oxide, or 1-ethylpiperazin-4-yl 1,4-dioxide.



11. A composition comprising an insecticidally effective amount of a compound of claim 1 and at least one agriculturally acceptable extender or adjuvant.
12. The insecticidal composition of claim 11, further comprising one or more second compounds selected from the group consisting of pesticides, plant growth regulators, fertilizers and soil conditioners.
13. A method of controlling insects, comprising applying an insecticidally effective amount of a composition of claim 11 to a locus where insects are present or are expected to be present.
14. A method of controlling insects, comprising applying an insecticidally effective amount of a composition of claim 12 to a locus where insects are present or are expected to be present.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US06/01532

A. CLASSIFICATION OF SUBJECT MATTER

IPC: C07D 207/46(2006.01);C07D 211/94;C07D 241/04;A01N 25/02

USPC: 548/542;546/226,236;544/383;424/406

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 548/542;546/226,236;544/383;424/406

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
CAPLUS**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2004060865 A2 (DING et al) 22 April 2004.	1-3, 6, 11-14
A	US 6,753,429 A1 (THEODORIDIS et al) 22 June 2004.	1-14
A	BLUME, H. Arzneimittel-Forschung 1981, Vol 31. No. 10, pages 1731-1735.	1-3, 6

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

* Special categories of cited documents:

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

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document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

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Date of the actual completion of the international search

09 June 2006 (09.06.2006)

Date of mailing of the international search report

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