624594

COMMONWEALTH of AUSTRALIA
Patents Act 1952

APPLICATION FOR A STANDARD PATENT

I/We

Eli Lilly and Company

of

Lilly Corporate Center, Indianapolis, Indiana, 46285, United States of America

hereby apply for the grant of a Standard Patent for an invention entitled:

Substituted quinolines and cinnolines

which is described in the accompanying complete specification.

Details of basic application(s):-

Number	Convention Country	Date
150366	United States of America	29 January 1988

The address for service is care of DAVIES & COLLISON, Patent Attorneys, of 1 Little Collins Street, Melbourne, in the State of Victoria, Commonwealth of Australia.

DATED this TWENTY FOURTH day of JANUARY 1989

To: THE COMMISSIONER OF PATENTS

.....
a member of the firm of
DAVIES & COLLISON for
and on behalf of the
applicant(s)

Davies & Collison, Melbourne

REPRINT OF RECEIPT
M006051 24/01/89

CASE: X-6076A

DAVIES & COLLISON

COMMONWEALTH OF AUSTRALIA

PATENTS ACT 1952

DECLARATION IN SUPPORT OF A
CONVENTION APPLICATION FOR A PATENT

In support of the Convention Application made for a patent for an invention entitled:
SUBSTITUTED QUINOLINES AND CINNOLINES
I, Mary Ann Tucker, Assistant Patent Counsel, Lilly Corporate Center, City of Indianapolis, State of Indiana 46285, United States of America do solemnly and sincerely declare as follows:

1. I am authorized by ELI LILLY AND COMPANY the applicant for the patent to make this declaration on its behalf.

2. The basic application as defined by Section 141 of the Act was/~~were~~ made in United States of America

on 29 January 1988

by Barry Allen Dreikorn and Glen Phil Jourdan

3. Barry Allen Dreikorn, Glen Phil Jourdan and Robert George Suhr of 9731 Trilobi Drive, Indianapolis, Indiana 46236, R.R. #1, Box 74B, Morristown, Indiana 46161 and 1522 Bruner Drive, Greenfield, Indiana 46140 United States of America respectively.

are the actual inventors of the invention and the facts upon which the applicant is entitled to make the application are as follows:

The said applicant is the assignee of the actual inventors, in respect of the invention.

4. The basic application(~~s~~) referred to in paragraph 2 of this Declaration was/~~were~~ the first application(~~s~~) made in a Convention country in respect of the invention(~~s~~) the subject of the said application.

DECLARED at Indianapolis, Indiana
this 8th day of December, 1988

ELI LILLY AND COMPANY

By 
Mary Ann Tucker
Assistant Patent Counsel

TO: THE COMMISSIONER OF PATENTS
AUSTRALIA

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(19) AUSTRALIAN PATENT OFFICE (10) Acceptance No. 624594

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SUBSTITUTED QUINOLINES AND CINNOLINES

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ELI LILLY AND COMPANY

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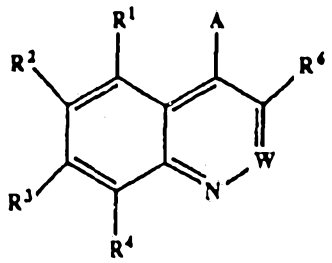
(56) Prior Art Documents
AU 28728/89 C07D 215/22 A61K 31/505
AU 28747/89 C07D 239/95 A01N 43/54 C07F 7/10
AU 28748/89 C07D 215/04 A01N 43/54

(57) Claim

1. A compound of the formula (1)



(1)

wherein:

R^1 to R^4 are independently

H, halo, (C_1-C_4) alkyl, branched (C_3-C_4) alkyl, halo (C_1-C_4) alkyl, (C_1-C_4) alkoxy, NO_2, or NH_2, at least two of R^1 to R^4 being H,

or one of R^2 to R^4 is $-NR^7$-Y-Ar or O-Y-Ar and the rest of R^1 to R^4 are H;

W is ~~N, or~~ CR^5;

R^5 is H, CH_3, Cl, O-Y-Ar, or $-NR^7$-Y-Ar;

R^6 is H, CH_3, Cl or Br;

A is -O-Alk or -X-Y-Ar;

Alk is a C_2-C_{18} saturated or unsaturated hydrocarbon chain, straight chain or branched, optionally substituted with halo, halo (C_1-C_4) alkoxy, (C_3-C_8) cyclo-

.../2

alkyl, hydroxy, or acetyl;

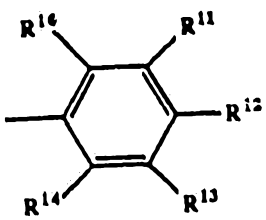
X is O, NR^7, or CR^8R^9, provided that if one of R^2 to R^5 is NR^7-Y-Ar or O-Y-Ar, then X-Y-Ar is an identical group;

R^7 is H, (C_1-C_4) alkyl, or acetyl;

R^8 and R^9 are independently H, (C_1-C_4) alkyl, (C_1-C_4) acyl, halo, or OH, or R^8 and R^9 combine to form a saturated or unsaturated carbocyclic ring comprising three to seven carbon atoms;

Y is an alkylene chain 2 to 8 carbon atoms long, optionally including an O, S, SO, SO_2, or NR^7 group or a saturated or unsaturated carbocyclic ring comprising three to seven carbon atoms, or substituted with (C_1-C_3) alkyl, (C_2-C_4) alkenyl, phenyl, (C_3-C_8) cycloalkyl, hydroxy, halo, or (C_1-C_4) acyl; and

Ar is
1,3-benzodioxolyl
fluorenyl,
pyridyl,
imidazolyl,
indolyl,
thienyl, optionally substituted with CH_3 or Cl,
thiazolyl,
cyclopentyl,
1-methylcyclopentyl,
cyclohexenyl (hexahydrophenyl),
cyclohexyl (tetrahydrophenyl),
naphthyl,
dihydronaphthyl,
tetrahydronaphthyl,
decahydronaphthyl, or
a group of the formula (2):



(2)

where

.../3

R^{10} to R^{14} are independently H, halo, I, (C_1-C_{10}) alkyl, branched (C_3-C_6) alkyl, halo (C_1-C_4) alkyl, (C_1-C_4) alkoxy, halo (C_1-C_4) alkoxy, phenoxy, substituted phenoxy, phenylthio, substituted phenylthio, phenyl, substituted phenyl, NO_2, NH_2, acetoxy, OH, CN, or $SiR^{15}R^{16}R^{17}$, $OSiR^{15}$, R^{16}, R^{17}, where R^{15}, R^{16}, and R^{17} are independently (C_1-C_4) alkyl or (C_3-C_4) branched alkyl provided that unless each of R^{10} to R^{14} is F, CH_3, or H, then at least two of R^{10} to R^{14} are H;

or an acid addition salt of a compound of formula (1)

or an N-oxide of a compound of formula (1) when W is CR^5

provided that the following compounds are excluded:

1) N-[4-(4-chlorophenyl)butyl]-7-chloro-4-quinolinamine; and

2) N-(2-phenylethyl)-4-quinolinamine, and

provided that if A is NR^7-Y-Ar, then Y is -$(CH_2)_2$- and Ar is a group of formula (2) wherein four of R^{10} to R^{14} are H and one of R^{10} to R^{14} is Cl, (C_1-C_4) alkyl, halo (C_1-C_4) alkyl, branched (C_3-C_6) alkyl, (C_1-C_4) alkoxy, halo (C_1-C_4) alkoxy, phenyl, substituted phenyl, phenoxy, or substituted phenoxy.

5. A fungicidal combination comprising at least 1% by weight of a compound of claim 1, or of N-(2-phenylethyl)-4-quinolinamine or N-[4-(4-chlorophenyl)-butyl]-7-chloro-4-quinolinamine in combination with a second fungicidal compound.

7. A fungicidal method which comprises applying to the locus of a plant pathogen a fungicidally effective but non-phytotoxic amount of a compound of claim 1, or of N-[4-(4-chlorophenyl)butyl]-7-chloro-4-quinolinamine or N-(2-phenylethyl)-4-quinolinamine.

10. An insecticide or miticide method which comprises applying to the locus of an insect or mite an insect- or mite-inactivating amount of a compound of claim 1.

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COMPLETE SPECIFICATION

NAME & ADDRESS
OF APPLICANT:

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United States of America

NAME(S) OF INVENTOR(S):

Barry Allen DREIKORN
Glen Phil JOURDAN
Robert George SUHR

ADDRESS FOR SERVICE:

DAVIES & COLLISON
Patent Attorneys
1 Little Collins Street, Melbourne, 3000.

COMPLETE SPECIFICATION FOR THE INVENTION ENTITLED:

Substituted quinolines and cinnolines

The following statement is a full description of this invention, including the best method of performing it known to me/us:-

Background of the Invention

Field of the Invention

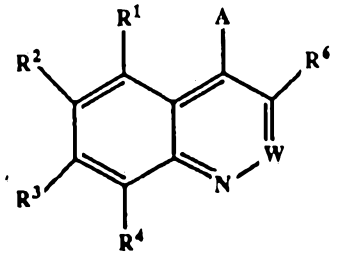
This invention provides new compounds that have excellent plant fungicide activity. Some of the compounds have also demonstrated insecticidal and miticidal activity. The invention also provides compositions and combination products that contain a compound of the invention as active ingredient. The invention also provides fungicidal, miticidal, and insecticidal methods.

There is an acute need for new fungicides, insecticides, and miticides, because target pathogens are rapidly developing resistance to currently used pesticides. Widespread failure of N-substituted azole fungicides to control barley mildew was observed in 1983, and has been attributed to the development of resistance. At least 50 species of fungi have developed resistance to the benzimidazole fungicides. The field performance of DMI (demethylation inhibitor) fungicides, which are now widely relied on to protect cereal crops from powdery mildew, has declined since they were introduced in the 1970's. Even recent fungicides, like the acylalanines, which initially exhibited excellent control of potato late blight and grape downy mildew in the field, have become less effective because of widespread resistance. Similarly,

mites and insects are developing resistance to the miticides and insecticides in current use. Resistance to insecticides in arthropods is widespread, with at least 400 species resistant to one or more insecticides. The development of resistance to some of the older insecticides, such as DDT, the carbamates, and the organophosphates, is well known. But resistance has even developed to some of the newer pyrethroid insecticides and miticides. Therefore a need exists for new fungicides, insecticides, and miticides.

Summary of the Invention

This invention provides compounds of the formula (1):



(1)

wherein:

R^1 to R^4 are independently

H, halo, (C_1-C_4) alkyl, branched (C_3-C_4) alkyl, halo (C_1-C_4) alkyl, (C_1-C_4) alkoxy, NO_2, or NH_2, at least two of R^1 to R^4 being H,

or one of R^2 to R^4 is $-NR^7$-Y-Ar or O-Y-Ar and the rest of R^1 to R^4 are H;

W is N, or CR^5;

R^5 is H, CH_3, Cl, O-Y-Ar, or $-NR^7$-Y-Ar;

R^6 is H, CH_3, Cl or Br;

A is -O-Alk or -X-Y-Ar;

Alk is a C_2-C_{18} saturated or unsaturated hydrocarbon chain, straight chain or branched, optionally substituted with halo, halo (C_1-C_4) alkoxy, (C_3-C_8) cycloalkyl, hydroxy, or acetyl;

X is O, NR^7, or CR^8R^9, provided that if one of R^2 to R^5 is NR^7-Y-Ar or O-Y-Ar, then X-Y-Ar is an identical group;

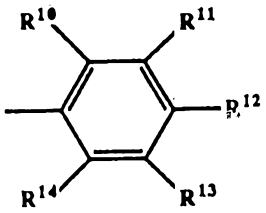
R^7 is H, (C_1-C_4) alkyl, or acetyl;

R^8 and R^9 are independently H, (C_1-C_4) alkyl, (C_1-C_4) acyl, halo, or OH, or R^8 and R^9 combine to form a saturated or unsaturated carbocyclic ring comprising three to seven carbon atoms;

Y is an alkylene chain 2 to 8 carbon atoms long, optionally including an O, S, SO, SO_2, or NR^7 group or a saturated or unsaturated carbocyclic ring comprising three to seven carbon atoms, or substituted with (C_1-C_3) alkyl, (C_2-C_4) alkenyl, phenyl, (C_3-C_8) cycloalkyl, hydroxy, halo, or (C_1-C_4) acyl; and

Ar is
1,3-benzodioxolyl
fluorenyl,
pyridyl,
imidazolyl,
indolyl,
thienyl, optionally substituted with CH_3 or Cl,
thiazolyl,
cyclopentyl,
1-methylcyclopentyl,
cyclohexenyl (hexahydrophenyl),

cyclohexyl (tetrahydrophenyl),
naphthyl,
dihydronaphthyl,
tetrahydronaphthyl,
decahydronaphthyl, or
a group of the formula (2):



(2)

where

R^{10} to R^{14} are independently H, halo, I, (C_1-C_{10}) alkyl, branched (C_3-C_6) alkyl, halo (C_1-C_4) alkyl, (C_1-C_4) alkoxy, halo (C_1-C_4) alkoxy, phenoxy, substituted phenoxy, phenylthio, substituted phenylthio, phenyl, substituted phenyl, NO_2, NH_2, acetoxy, OH, CN, or $SiR^{15}R^{16}R^{17}$, $OSir^{15}$, R^{16}, R^{17}, where R^{15}, R^{16}, and R^{17} are independently (C_1-C_4) alkyl or (C_3-C_4) branched alkyl, provided that unless each of R^{10} to R^{14} is F, CH_3, or H, then at least two of R^{10} to R^{14} are H;

or an acid addition salt of a compound of formula (1)

or an N-oxide of a compound of formula (1) when W is CR^5

provided that the following compounds are excluded:

1) N-[4-(4-chlorophenyl)butyl]-7-chloro-4-quinolinamine;

2) N-(2-phenylethyl)-4-quinolinamine, and

provided that if A is NR^7-Y-Ar, then Y is $-(CH_2)_2-$ and Ar is a group of formula (2) wherein four of R^{10} to R^{14} are H and one of R^{10} to R^{14} is Cl, (C_1-C_4) alkyl,halo (C_1-C_4) alkyl, branched (C_3-C_6) alkyl, (C_1-C_4) alkoxy, halo (C_1-C_4) alkoxy, phenyl, substituted phenyl, phenoxy, or substituted phenoxy.

The final provisos exclude compounds that are known per se or that could be considered similar to known compounds.

The fungicidal combinations of the invention comprise at least 1% by weight of a compound of formula (1), or N-[4-(4-chlorophenyl)butyl]-7-chloro-4-quinoline-amine or N-(2-phenylethyl)-4-quinolinamine, in combination with a second fungicidal compound.

The fungicidal compositions of the invention comprise a disease inhibiting and phtologically acceptable amount of a compound of formula (1), or N-[4-(4-chlorophenyl)butyl]-7-chloro-4-quinolinamine, or N-(2-phenylethyl)-4-quinolinamine, in combination with a phtologically-acceptable carrier.

The fungicidal method of the invention comprises applying to the locus of a plant pathogen a disease inhibiting and phytologically acceptable amount of a compound of formula (1), or N-[4-(4-chlorophenyl)butyl]-7-chloro-4-quinolinamine, or N-(2-phenylethyl)-4-quinolinamine.

The insecticidal or miticidal combinations of the invention comprise at least 1% by weight of a compound of formula (1) in combination with a second insecticide or miticide.

The insecticide or miticide compositions of the invention comprise an insect or mite inactivating amount of a compound of formula (1) in combination with a phtyologically-acceptable carrier.

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The insecticide and miticide methods of the invention comprise applying to a locus of an insect or mite an insect or mite inactivating amount of a compound of formula (1), or of a combination described above.

Detailed Description of the Invention

Throughout this document, all temperatures are given in degrees Celsius, and all percentages are weight percentages unless otherwise stated.

The terms "(C_1-C_3) alkyl", "(C_1-C_4) alkyl", and "(C_1-C_{10}) alkyl", when used alone, refer to straight chain alkyl radicals.

The terms "branched (C_3-C_4) alkyl", and "branched (C_3-C_6) alkyl" refer to all alkyl isomers containing the designated number of carbon atoms, excluding the straight chain isomers.

The term "(C_1-C_4) alkoxy" refers to straight or branched chain alkoxy groups.

The term "halo" used alone or in combination with other terms refers to F, Cl, or Br;

The term "halo (C_1-C_4) alkyl" refers to a (C_1-C_4) alkyl group, straight chain or branched, substituted with one or more halo groups.

The term "substituted phenyl" used alone or in combination with other terms, as in "substituted phenylthio" or "substituted phenylsulfonyl", refers to phenyl substituted with up to three groups selected from halo, I, (C_1-C_{10}) alkyl, branched (C_3-C_6) alkyl, halo (C_1-C_4) alkyl, hydroxy (C_1-C_4) alkyl, (C_1-C_4) alkoxy, halo (C_1-C_4) alkoxy, phenoxy, phenyl, NO_2, OH, CN, (C_1-C_4) alkanoyloxy, or benzyloxy.

The term "substituted phenoxy" refers to phenoxy substituted with up to three groups selected from halo, I, (C_1-C_{10}) alkyl, branched (C_3-C_6) alkyl, halo (C_1-C_4) alkyl, hydroxy (C_1-C_4) alkyl, (C_1-C_4) alkoxy, halo (C_1-C_4) alkoxy, phenoxy, phenyl, NO_2, OH, CN, (C_1-C_4) alkanoyloxy, or benzyloxy.

The term "unsaturated hydrocarbon chain" refers to a hydrocarbon chain containing one or two sites of unsaturation.

The term "HPLC" refers to high-performance liquid chromatography.

Compounds

While all of the compounds of the invention are useful fungicides, certain classes are preferred for reasons of greater efficacy or ease of synthesis, viz:

1. compounds of formula (1) where W is CR^5 (i.e., substituted quinolines);
2. compounds of preferred class (1) where R^5 is H;
3. compounds of formula (1) where R^6 is H;
4. compounds of formula (1) where at least three of R^1 to R^4 are H;
5. compounds of preferred class (4) where R^4 is F (i.e., 8-fluoroquinolines);
6. compounds of preferred class (4) where R^3 is F (i.e., 7-fluoroquinolines);

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7. compounds of preferred class (4) where R^3 is Cl (i.e., 7-chloroquinolines);

8. compounds of preferred class (4) where R^2 is F (i.e., 6-fluoroquinolines);

9. compounds of formula (1) where Y is an alkylene chain 2 to 4 carbon atoms long.

10. compounds of preferred class (9) where Y is $-(CH_2)_2-$;

11. compounds of formula (1) where Ar is naphthyl;

12. compounds of formula (1) where Ar is thienyl;

13. compounds of formula (1) where Ar is thiazolyl;

14. compounds of formula (1) where Ar is cyclohexenyl;

15. compounds of formula (1) where Ar is a substituted phenyl group of formula (2);

16. compounds of preferred class (15) where at least three of R^{10} to R^{14} are H;

17. compounds of preferred class (15) where four of R^{10} to R^{14} are H;

18. compounds of preferred class (17) wherein one of R^{10} to R^{14} is Cl;

19. compounds of preferred class (18) where R^{12} is Cl;

20. compounds of preferred class (17) wherein one of R^{10} to R^{14} is CF_3;

21. compounds of preferred class (17) wherein one of R^{10} to R^{14} is (C_1-C_4) alkyl;

22. compounds of preferred class (21) wherein one of R^{10} to R^{14} is methyl;

23. compounds of preferred class (22) wherein R^{12} is methyl;

24. compounds of preferred class (17) wherein one of R^{10} to R^{14} is branched (C_3-C_6) alkyl;

25. compounds of preferred class (24) wherein R^{12} is t-butyl;

26. compounds of preferred class (24) wherein R^{12} is i-propyl;

27. compounds of preferred class (17) wherein one of R^{10} to R^{14} is phenyl or substituted phenyl;

28. compounds of preferred class (27) wherein R^{12} is phenyl;

29. compounds of preferred class (17) wherein one of R^{10} to R^{14} is phenoxy or substituted phenoxy;

30. compounds of preferred class (29) wherein R^{12} is phenoxy.

Compounds exhibiting particularly excellent activity against downy mildew include:

8-fluoro-N-(2-phenylethyl)-4-quinolinamine;

8-fluoro-N-[2-(4-phenyl-2-thiazolyl)ethyl]-4-quinolinamine;

8-fluoro-N-[2-[2-(trifluoromethyl)phenyl]ethyl]-4-quinolinamine;

N-[2-(4-chlorophenyl)ethyl]-6-methyl-4-quinolinamine;

8-chloro-N-(2-phenylethyl)-4-quinolinamine;

8-fluoro-N-[2-(4-phenyl-2-thiazolyl)ethyl]-4-quinolinamine;

8-fluoro-N-[2-(2-naphthyl)ethyl]-4-quinolinamine;

8-fluoro-N-[2-[3-(trifluoromethyl)phenyl]ethyl]-4-quinolinamine;

7-chloro-N-[2-(1-cyclohexenyl)ethyl]-4-quinolinamine;

N-[2-[4-(1-methylethyl)phenyl]ethyl]-8-fluoro-4-quinolinamine;

8-fluoro-N-[2-(2-thienyl)ethyl]-4-quinolinamine;

4-[2-(3-chlorophenyl)ethoxy]-8-fluoroquinoline;

8-fluoro-4-[2-(3-(trifluoromethyl)phenyl)ethoxy]-quinoline;

4-[2-(4-methylphenyl)ethoxy]quinoline;

8-fluoro-4-[2-(4-methylphenyl)ethoxy]quinoline; and

4-[2-[4-(t-butyl)phenyl]ethoxy]-8-fluoroquinoline;

Compounds exhibiting particularly excellent activity against rice blast include:

N-[2-(4-chlorophenyl)ethyl]-N-(8-fluoro-4-quinolinyl)-acetamide;

N-[2-[4-(i-propyl)-phenyl]ethyl]-8-fluoro-4-quinolinamine;

8-fluoro-N-(2-phenylethyl)-4-quinolinamine;

N-[2-[4-(t-butyl)phenyl]ethyl]-8-fluoro-4-quinolinamine;

8-fluoro-N-[2-(1,1'-biphenyl)-4-yl-ethoxy]quinoline;

8-fluoro-4-[2-(3-(trifluoromethyl)phenyl)ethoxy]-quinoline;

8-fluoro-4-[2-(2-naphthyl)ethoxy]quinoline;

8-fluoro-4-[2-(4-methylphenyl)ethoxy]quinoline; and

8-fluoro-4-[3-(4-(t-butyl)phenyl)propyl]quinoline;

Compounds exhibiting particularly excellent activity against a broad spectrum of plant pathogens include:

8-fluoro-N-[2-(3-phenoxyphenyl)ethyl]-4-quinolinamine;

N-[2-[4-(i-propyl)phenyl]ethyl]-8-fluoro-4-quinolinamine;

N-[2-(1,1'-biphenyl)-3-ylethyl]-8-fluoro-4-quinolinamine;

N-[2-(2,4-dichlorophenyl)ethyl]-8-fluoro-4-quinolinamine;

8-fluoro-4-[3-(4-(t-butyl)phenyl)propyl]quinoline;

8-fluoro-4-[3-(4-(i-propyl)phenyl)propyl]quinoline;

8-fluoro-4-[2-(2-(trifluoromethyl)phenyl)ethoxy]-quinoline;

4-[2-(4-chlorophenyl)ethoxy]-8-fluoroquinoline;

4-[2-(4-methylphenyl)ethoxy]quinoline;

8-fluoro-4-[2-(4-methylphenyl)ethoxy]quinoline;

8-fluoro-4-(2-phenylethoxy)quinoline;

8-fluoro-4-[2-(3-methylphenyl)ethoxy]quinoline;

8-fluoro-4-[2-(2-fluorophenyl)ethoxy]quinoline;

8-fluoro-4-[2-(2-methoxyphenyl)ethoxy]quinoline; and

8-fluoro-4-[2-(4-(i-propyl)phenyl)ethoxy]quinoline;

Compounds exhibiting particularly excellent activity as miticides include:

8-fluoro-N-[2-(4-iodophenyl)ethyl]-4-quinolinamine;

N-[2-(4-bromophenyl)ethyl]-8-fluoro-4-quinolinamine;

N-[2-(4-chlorophenyl)ethyl)-8-fluoro-4-quinolinamine;

N-[2-(4-chlorophenyl)ethyl]-N-ethyl-8-fluoro-4-quinolinamine;

N-[3-(1,1'-biphenyl)-4-ylpropyl]-8-fluoro-4-quinolinamine;

8-fluoro-N-[2-(4-phenoxyphenyl)ethyl]-4-quinolinamine;

N-[2-[4-(t-butyl)phenyl]ethyl]-8-fluoro-4-quinolinamine;

N-[2-[4-(i-propyl)phenyl]ethyl]-8-fluoro-4-quinolinamine;

N-[2-(4-chlorophenyl)ethyl]-6-fluoro-4-quinolinamine;

8-fluoro-N-[2-(1,1'-biphenyl)-4-yl-ethoxy]quinoline;

4-[2-(3-chlorophenyl)ethoxy]-8-fluoroquinoline;

4-[2-[4-(t-butyl)phenyl]ethoxy]-8-fluoroquinoline;

8-fluoro-4-[2-(4-(i-propyl)phenyl)ethoxy]quinoline;

8-fluoro-4-[2-(3-(trifluoromethyl)phenyl)ethoxy]-quinoline;

8-fluoro-4-[2-(4-methoxyphenyl)ethoxy]quinoline;

8-fluoro-4-[2-(3-phenoxyphenyl)ethoxy]quinoline;

8-fluoro-4-[2-(2-naphthyl)ethoxy]quinoline;

8-fluoro-4-[2-(1,1'-biphenyl)-2-yl-ethoxy]quinoline;

7-chloro-4-[2-(1,1'-biphenyl)-4-yl-ethoxy]quinoline;

7-chloro-4-[2-(4-(t-butyl)phenyl)ethoxy]quinoline;

4-[2-(4-(t-butyl)phenyl)ethoxy]-7-fluoroquinoline;

4-[2-(1,1'-biphenyl)-4-ylethoxy]-7-fluoroquinoline;

8-fluoro-4-(3-phenylpropyl)quinoline;

8-fluoro-4-[3-(4-methylphenyl)propyl]quinoline; and

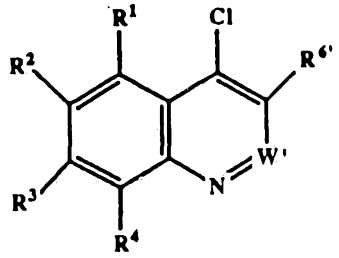
8-fluoro-4-[3-[3-(trifluoromethyl)phenyl]propyl]-quinoline.

Synthesis

The compounds of this invention are made using well known chemical procedures. The required starting materials are commercially available, or they are readily synthesized using standard procedures.

Synthesis of Compounds Wherein A is O-Y-Ar or -O-Alk

The compounds of formula (1) wherein A is O-Y-Ar or O-Alk were made by condensing a compound of formula (3):



(3)

where R^1 to R^4 are as previously defined, $R^{6'}$ is H or CH_3, and W' is N or $CR^{5'}$, where $R^{5'}$ is H, Cl, or CH_3, with an alcohol of the formula (4a or 4b):

HO-Y-Ar (4a)
HO-Alk (4b)

where

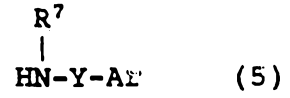
Y, Ar, and Alk are as previously defined.

The reaction is preferably carried out in the presence of a strong base, such as sodium hydride, in an inert organic solvent, such as DMF, at a temperature in the range of 0 to 25°C.

Synthesis of Compounds Wherein A is NR^7-Y-Ar

The compounds of formula (1) wherein A is NR^7-Y-Ar were prepared by condensing a compound of formula (3) with an amine of the formula (5)

$$\begin{array}{c} R^7 \\ | \\ HN\text{-}Y\text{-}Ar \end{array} \qquad (5)$$



where

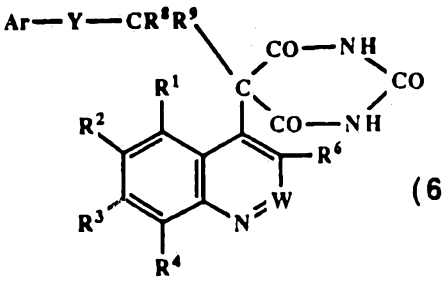
R^7 is H or (C_1-C_4) alkyl, and Y and Ar are as previously defined.

The chloride of formula (3) is allowed to react with an appropriate amine, preferrably at elevated temperature (100-180°C), and preferably in the presence of an acid acceptor, such as triethylamine. The reaction may be carried out neat, or in an inert organic solvent.

Compounds where R^7 is acetyl were prepared by reacting amines of formula (1) where R^7 is H, with an acylating agent, such as an acetyl chloride or acetic anhydride. In cases where the starting material of formula (3) is one wherein W' is CCl, a mixture of products is obtained, which are separable using HPLC.

Synthesis of Compounds Wherein A is CR^8R^9-Y-Ar

The compounds of formula (1) wherein A is CR^8R^9-Y-Ar can be made using the process described in J. Heterocyclic Chemistry, Vol. 14, p. 1081-1083 (1977) by A. Scoville and F. X. Smith. This process entails preparation of a 5-substituted-5-(4-quinolyl)barbituric acid of the formula (6)



(6)

which is then hydrolyzed and decarboxylated by dissolving the intermediate in a solution of sodium hydroxide and water, refluxing, then making the solution slightly acidic with hydrochloric acid and again refluxing.

Derivatives

The compounds of formula (1) wherein R^6 is Cl are prepared by halogenating a compound of formula (1) wherein R^6 is H with $POCl_3/PCl_5$.

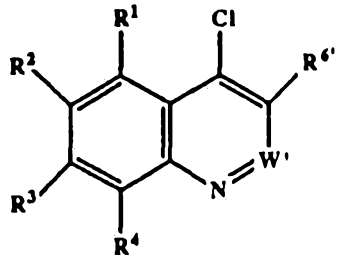
The compounds of formula (1) wherein R^6 is Br are prepared by reacting a compound of formula (1) wherein R^6 is H with Br_2 in acetic acid.

N-oxides of the compounds of formula (1) are prepared by reacting the compound of formula (1) with an oxidizing agent, such as 3-chloroperoxybenzoic acid or hydrogen peroxide, in a non-reactive organic solvent, such as methylene chloride or chloroform, at -20°C to room temperature, preferably at about 0°C.

The acid addition salts of compounds of formula (1) are obtained in the usual way.

Accordingly, the invention also provides a process for preparing a compound of formula (1) which comprises:

(a) condensing a compound of formula (3):



(3)

where R^1 to R^4 are as previously defined, $R^{6'}$ is H or CH_3, and W' is N or $CR^{5'}$, where $R^{5'}$ is H, Cl, or CH_3, with an alcohol of the formula (4a or 4b):

HO-Y-Ar (4a)
HO-Alk (4b)

where

Y, Ar, and Alk are as previously defined to provide a compound of formula (1) wherein A is O-Y-Ar or O-Alk; or

(b) condensing a compound of formula (3) with an amine of the formula (5)

$$\begin{array}{l} R^7 \\ | \\ HN\text{-}Y\text{-}Ar \end{array} \quad (5)$$

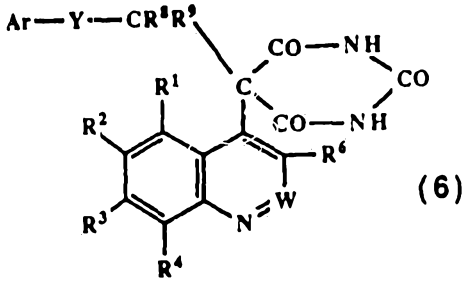
where

R^7 is H or $(C_1\text{-}C_4)$ alkyl, and Y and

Ar are as previously defined to provide a compound of formula (1) wherein A is $-NR^7$-Y-Ar; or

(c) reacting an amine of formula (1) where R^7 is H, with acetyl chloride or acetic anhydride to provide a compound of formula (1) wherein A is $-NR^7-Y-Ar$ where R^7 is acetyl; or

(d) hydrolyzing and decarboxylating a compound of the formula (6)



(6)

to provide a compound of formula (1) wherein A is $-CR^8R^9-Y-Ar$; or

(e) halogenating a compound of formula (1) wherein R^6 is H with $POCl_3/PCl_5$ to provide a compound of formula (1) wherein R^6 is Cl; or

(f) reacting a compound of formula (1) wherein R^6 is H with Br_2 in acetic acid to provide a compound of formula (1) wherein R^6 is Br; or

(g) oxidizing a compound of formula (1) wherein W is CR^5 to provide the corresponding N-oxide.

Preparation of Quinoline Starting Materials

Quinoline starting materials can be synthesized using a variety of known procedures.

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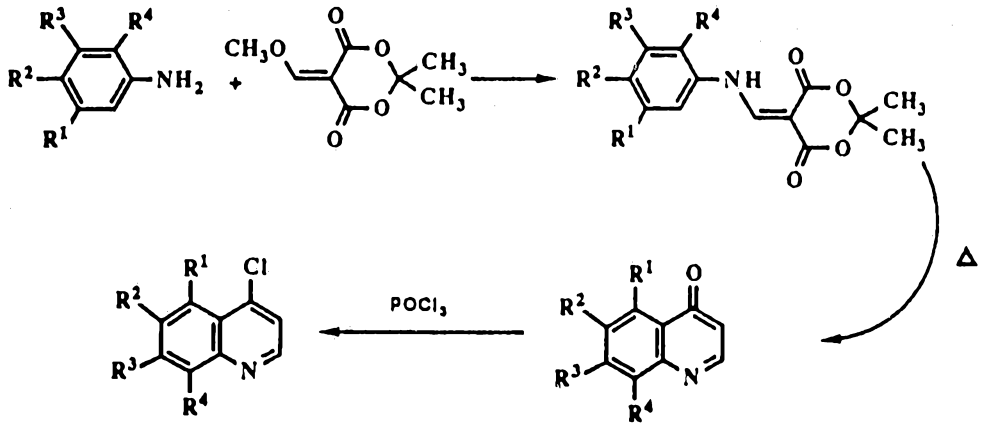
Organic Syntheses, collective volume 3, 1955, pp. 272-75, gives a procedure for preparing 4,7-dichloroquinoline, and other polysubstituted quinolines. Another general procedure is described in Tetrahedron, vol. 41, pp. 3033-36 (1985).

Many of the quinoline starting materials used in the following examples were prepared by the protocol shown in the following reaction scheme



In cases where mixtures of isomeric products were obtained, the mixture of substituted 4-quinolones was chlorinated under standard conditions, and the 4-chloroquinolines were separated by liquid chromatography.

~~Preparation of Cinnoline Starting Materials~~

Cinnoline analogs are prepared via published methods. (C. M. Atkinson and J. C. Simpson - J. Chem. Soc. London, 1947, 232). The substituted 2-amino-acetophenone is diazotized at 0-5°C in water using sodium

nitrite and mineral acid, and the intermediate diazonium salt is trapped by the enolic component of the ketone to provide the requisite 4-hydroxycinnoline. Routine chlorination provides the desired intermediates.

EXAMPLES 1 TO 295

Tables 1-12 identify compounds actually prepared by the above described general procedures, and give each compound's melting point. Specific illustrative preparations of the compounds of Examples 4, 10, 25, 69, 97, 154, 159, 173, 181, 186, 209, 212, 221, 238, 251, and 261 follow the table.

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TABLE 1
N-(2-phenylethyl)-4-quinolinamines

EXAMPLE NUMBER	COMPOUND	M.P.
1	6-methoxy-N-(2-phenylethyl)-4-quinolineamine	
2*	N-(2-phenylethyl)-4-quinolinamine	159-160°C
3	6-ethyl-N-(2-phenylethyl)-4-quinolinamine	119-120°C
4	N-ethyl-N-(2-phenylethyl)-4-quinolinamine	oil
5	8-fluoro-N-(2-phenylethyl)-4-quinolinamine	149-150°C
6	2-methyl-N-(2-phenylethyl)-4-quinolinamine	153-154°C
7	6,8-difluoro-N-(2-phenylethyl)-4-quinolinamine	196-197°C
8	7-fluoro-N-(2-phenylethyl)-4-quinolinamine	160-161°C
9	6-fluoro-N-(2-phenylethyl)-4-quinolinamine	163-164°C
10	N-[2-(4-chlorophenyl)ethyl]-N-(8-fluoro-4-quinolinyl)-acetamide	oil
11	8-fluoro-N-[2-(4-iodophenyl)ethyl]-4-quinolinamine	221-223°C
12	N-[2-(4-bromophenyl)ethyl]-6,8-difluoro-4-quinolinamine	235-238°C

* not a compound claimed per se, but one used in the claimed compositions and methods.

TABLE 1
N-(2-phenylethyl)-4-quinolinamines

EXAMPLE NUMBER	COMPOUND	M.P.
13	N-[2-(4-bromophenyl)ethyl]-8-(trifluoromethyl)-4-quinolinamine	188-190°C
14	N-[2-(4-chlorophenyl)ethyl]-6-methyl-4-quinolinamine	123-125°C
15	N-[2-(4-chlorophenyl)ethyl]-6,8-dimethyl-4-quinolinamine	113-115°C
16	N-[2-(4-chlorophenyl)ethyl]-6-methoxy-4-quinolinamine	155-157°C
17	N-(2-phenylethyl)-7-(trifluoromethyl)-4-quinolinamine	138-139°C
18	N-[2-(4-bromophenyl)ethyl]-4-quinolinamine	176-177°C
19	N-[2-(4-methylphenyl)ethyl]-4-quinolinamine	159-160°C
20*	N-[2-(4-chlorophenyl)ethyl]-4-quinolinamine	162-163°C
21	N-(2-phenylpropyl)-4-quinolinamine	126-127°C
22	N-[2-(4-methoxyphenyl)-ethyl]-4-quinolinamine	127-128°C
23	N-(2,2-diphenylethyl)-4-quinolinamine	154-155°C
24	N-(1-methyl-2-phenylethyl)-4-quinolinamine	132-133°C

* not a compound claimed per se, but one used in the claimed compositions and methods.

TABLE 1
N-(2-phenylethyl)-4-quinolinamines

EXAMPLE NUMBER	COMPOUND	M.P.
25	2-chloro-N-(2-phenylethyl)-4-quinolinamine	132-133°C
26	α-[(4-quinolinylamino)-methyl]benzenemethanol	195-197°C
27	8-methyl-N-(2-phenylethyl)-4-quinolinamine	127-128°C
28	6,8-dimethyl-N-(2-phenylethyl)-4-quinolinamine	114-115°C
29	8-ethyl-N-(2-phenylethyl)-4-quinolinamine	98-99°C
30	6-methyl-N-(2-phenylethyl)-4-quinolinamine	124-125°C
31	7-chloro-N-(2-phenylethyl)-4-quinolinamine	137-138°C
32	7,8-dimethyl-N-(2-phenylethyl)-4-quinolinamine	183-185°C
33	8-chloro-N-(2-phenylethyl)-4-quinolinamine	156-157°C
34	N-(2,2-diphenylpropyl)-4-quinolinamine	110-111°C
35	N-[2-(4-fluorophenyl)ethyl]-4-quinolinamine	121-122°C
36	8-fluoro-N-[2-(4-methoxyphenyl)ethyl]-4-quinolinamine	165-167°C
37	7-chloro-N-[2-(4-chlorophenyl)ethyl]-4-quinolinamine	190-192°C

TABLE 1
N-(2-phenylethyl)-4-quinolinamines

EXAMPLE NUMBER	COMPOUND	M.P.
38	N-[2-(3,4-dimethoxyphenyl)-ethyl]-8-fluoro-4-quinolin-amine	127-130°C
39	8-fluoro-N-[2-(3-phenoxy-phenyl)ethyl]-4-quinolin-amine	83-85°C
40	6,8-difluoro-N-(2-[1,1'-biphenyl]-4-ylethyl)-4-quinolinamine	216-218°C
41	N-[2-(4-chlorophenyl)ethyl]-6,8-difluoro-4-quinolinamine	218-220°C
42	N-[2-(4-methoxyphenyl)ethyl]-7-(trifluoromethyl)-4-quinolin-amine	107-109°C
43	7-chloro-N-[2-(3-methoxy-phenyl)ethyl]-4-quinolinamine	155-158°C
44	7-chloro-N-[2-(2,4-dichloro-phenyl)ethyl]-4-quinolinamine	168-170°C
45	7-chloro-N-[2-(3,5-di-methoxyphenyl)ethyl]-4-quinolinamine	117-120°C
46	N-[2-(4-methoxyphenyl)-ethyl]-6-methyl-4-quinolin-amine	120-123°C
47	N-[2-(4-chlorophenyl)ethyl]-7-(trifluoromethyl)-4-quinolin-amine	153-155°C
48	N-[2-(3,4-dimethoxyphenyl)-ethyl]-7-(trifluoromethyl)-4-quinolinamine	oil

TABLE 1
N-(2-phenylethyl)-4-quinolinamines

EXAMPLE NUMBER	COMPOUND	M.P.
49	N-[2-(3-chlorophenoxy)ethyl]-8-fluoro-4-quinolinamine	161-163°C
50	7-chloro-N-[2-(4-methylphenyl)ethyl]-4-quinolinamine	155-158°C
51	8-chloro-N-[2-(4-fluorophenyl)ethyl]-4-quinolinamine	194-196°C
52	N-[2-(2,4-dichlorophenyl)-ethyl]-8-(trifluoromethyl)-4-quinolinamine	158-160°C
53	N-[2-(2,4-dichlorophenyl)-ethyl]-6-methyl-4-quinolinamine	180-182°C
54	7-chloro-6-methoxy-2-methyl-N-(2-phenylethyl)-4-quinolinamine	180-181°C
55	N-[2-(2-methoxyphenyl)-ethyl]-4-quinolinamine	127-128°C
56	N-[2-(4-chlorophenyl)ethyl]-6-fluoro-4-quinolinamine	134-138°C
57	N-[2-(4-chlorophenyl)ethyl]-2-methyl-6-fluoro-4-quinolinamine	104-106°C
58	6-methyl-N-[2-(4-methylphenyl)ethyl]-4-quinolinamine	122-124°C
59	5,7-dichloro-N-[2-(4-chlorophenyl)ethyl]-4-quinolinamine	113-115°C
60	7-chloro-N-[2-(3-phenoxyphenyl)ethyl]-4-quinolinamine	128-130°C

TABLE 1
N-(2-phenylethyl)-4-quinolinamines

EXAMPLE NUMBER	COMPOUND	M.P.
61	8-methyl-N-[2-(4-chloro-phenyl)ethyl]-4-quinolinamine	118-120°C
62	8-fluoro-N-(2-cyclohexyl-2-phenylethyl)-4-quinolinamine	74-75°C
63	8-fluoro-N-[2-(2-phenoxyphenyl)-ethyl]-4-quinolinamine	131-133°C
64	7,8-dimethyl-N-[2-(2-phenoxyphenyl)-ethyl]-4-quinolinamine	124-126°C
65	N-[2-(2,6-difluorophenyl)-ethyl]-8-fluoro-4-quinolin-amine	203-204°C
66	8-fluoro-N-[2-(3-fluoro-phenyl)ethyl]-4-quinolinamine	174-175°C
67	N-[2-(3,5-dimethoxyphenyl)-ethyl]-4-quinolinamine	122-123°C
68	8-fluoro-N-[2-(2-methoxy-phenyl)ethyl]-4-quinolinamine	163-164°C
69	3-chloro-N-(2-chloro-2-phenylethyl)-4-quinolinamine	oil
70	N-(2-phenylethyl)-5,7-bis-(trifluoromethyl)-4-quinolin-amine	oil
71	8-fluoro-N-[2-(4-methyl-phenyl)ethyl]-4-quinolin-amine	176-177°C
72	N-[2-(1,1'-biphenyl)-3-ylethyl]-8-fluoro-4-quinolinamine	140-142°C

TABLE 1
N-(2-phenylethyl)-4-quinolinamines

EXAMPLE NUMBER	COMPOUND	M.P.
73	8-fluoro-4-[(2-phenylethyl)-amino]-3-quinolinemethanol	107-108°C
74	N-[2-(3-chlorophenyl)ethyl]-8-fluoro-4-quinolinamine	191-192°C
75	N-[2-(3,4-dichlorophenyl)-ethyl]-8-fluoro-4-quinolin-amine	204-206°C
76	N-[2-(2,4-dichlorophenyl)-ethyl]-8-fluoro-4-quinolin-amine	187-189°C
77	8-fluoro-N-(2-phenylpropyl)-4-quinolinamine	136-137°C
78	8-fluoro-N-[2-(4-fluoro-phenyl)ethyl]-4-quinolinamine	171-173°C
79	N-[2-(4-chlorophenyl)-propyl]-8-fluoro-4-quinolin-amine	126-127°C
80	N-(2,2-diphenylpropyl)-8-fluoro-4-quinolinamine	56-58°C
81	8-fluoro-N-(2-phenylbutyl)-4-quinolinamine	114-116°C
82	N-[2-(2-chlorophenyl)ethyl]-8-fluoro-4-quinolinamine	175-177°C
83	8-fluoro-N-[2-[4-(trifluoro-methyl)phenyl]ethyl]-4-quinolinamine	205-206°C
84	7-chloro-N-[2-(4-methoxy-phenyl)ethyl]-4-quinolinamine	122-124°C

TABLE 1
N-(2-phenylethyl)-4-quinolinamines

EXAMPLE NUMBER	COMPOUND	M.P.
85	8-chloro-N-[2-(4-chlorophenyl)ethyl]-4-quinolinamine	185-187°C
86	N-[2-(4-chlorophenyl)ethyl]-8-(trifluoromethyl)-4-quinolinamine	192-194°C
87	8-chloro-N-[2-(4-methylphenyl)ethyl]-4-quinolinamine	184-186°C
88	N-[2-(4-chlorophenyl)ethyl]-7,8-dimethyl-4-quinolinamine	177-179°C
89	8-fluoro-N-[2-(4-methylphenyl)ethyl]-4-quinolinamine	153-154°C
90	8-fluoro-N-[2-(4-phenoxyphenyl)ethyl]-4-quinolinamine	109-111°C
91	3-bromo-8-fluoro-N-(2-phenylethyl)-4-quinolinamine	95-97°C
92	8-fluoro-N-(1-methyl-2-phenylethyl)-4-quinolinamine	166-168°C
93	2,8-dichloro-N-(2-phenylethyl)-4-quinolinamine	190-192°C
94	N-[2-(4-bromophenyl)ethyl]-8-fluoro-4-quinolinamine	198-199°C
95	8-fluoro-N-[2-[3-(trifluoromethyl)phenyl]ethyl]-4-quinolinamine	161-162°C
96	N-[2-(4-chlorophenyl)ethyl)-8-fluoro-4-quinolinamine	176-177°C

TABLE 1
N-(2-phenylethyl)-4-quinolinamines

EXAMPLE NUMBER	COMPOUND	M.P.
97	8-fluoro-N-[2-[2-(trifluoromethyl)phenyl]ethyl]-4-quinolinamine	157-158°C
98	2-chloro-N-[2-(2,4-dichlorophenyl)ethyl]-8-fluoro-4-quinolinamine	199-200°C
99	N-(2-phenylethyl)-8-(trifluoromethyl)-4-quinolinamine	151-152°C
100	7-chloro-N-[2-(2-methoxyphenyl)ethyl]-4-quinolinamine	140-142°
101	7-chloro-N-[2-(3,4-dichlorophenyl)ethyl]-4-quinolinamine	128-130°C
102	N-[2-(4-chlorophenyl)ethyl]-2-methyl-4-quinolinamine	176-178°C
103	N-[2-(2-chloro-6-fluorophenyl)ethyl]-8-fluoro-4-quinolinamine	198-201°C
104	N-[2-(2,4-dichlorophenyl)-ethyl]-7-(trifluoromethyl)-4-quinolinamine	175-177°C
105	N-[2-(4-chlorophenyl)ethyl]-N-ethyl-8-fluoro-4-quinolinamine	oil
106	7-chloro-N-(4-fluorophenyl)-N-methyl-4-quinolinamine	83-85°C
107	7-chloro-N-[2-[3-(trifluoromethyl)phenyl]ethyl]-4-quinolinamine	184-186°C

TABLE 1
N-(2-phenylethyl)-4-quinolinamines

EXAMPLE NUMBER	COMPOUND	M.P.
108	N-[2-(3-bromophenyl)ethyl]-8-fluoro-4-quinolinamine	206-208°C
109	N-[2-(4-chlorophenyl)ethyl]-5,8-dimethyl-4-quinolinamine	oil
110	N(4)-[2-(4-chlorophenyl)ethyl]-4,8-quinolinediamine	oil
111	N-[2-[4-(t-butyl)phenyl]ethyl]--8-fluoro-4-quinolinamine	198-200°C
112	N-[2-(2,3,4,5,6-tetramethylphenyl)ethyl]-8-fluoro-4-quinolinamine	204-207°C
113	N-[2-(1,1-biphenyl)-4-ylethyl]-8-fluoro-4-quinolinamine	178-180°C
114	N-[2-[4-(i-propyl)phenyl]ethyl]--8-fluoro-4-quinolinamine	157-159°C
115	N-[2-(2-chlorophenyl)ethyl]-8-chloro-4-quinolinamine	205-207°C
116	2-chloro-8-fluoro-N-(2-phenylethyl)-4-quinolinamine	158-159°C
117	8-fluoro-N-[2-(4-nitrophenyl)ethyl]-4-quinolinamine	234-236°C
118	N-[2-(2,6-dichlorophenyl)-ethyl]-8-fluoro-4-quinolinamine	222-224°C

TABLE 1
N-(2-phenylethyl)-4-quinolinamines

EXAMPLE NUMBER	COMPOUND	M.P.
119	N-[2-(3,5-dimethoxyphenyl)-ethyl]-8-fluoro-4-quinolin-amine	131-132°C
120	N-(2-phenylcyclopropyl)-4-quinolinamine	147-148°C
121	N-[2-(4-chlorophenyl)ethyl]-N-(6-fluoro-4-quinolinyl)acetamide	87-88°C
122	N-[2-(4-methylphenyl)ethyl]-N-(6-methyl-4-quinolinyl)acetamide	97-98°C
123	8-fluoro-N-(2-phenylcyclopropyl)-4-quinolinamine	204-205°C
124	N-[2-(4-chlorophenyl)ethyl]-N-(7-chloro-4-quinolinyl)acetamide	oil
125	N-(7-chloro-4-quinolinyl)-N-[2-(4-methoxyphenyl)ethyl]acetamide	oil
126	N-(7-chloro-4-quinolinyl)-N-[2-[3-(trifluoromethyl)phenyl]ethyl]-acetamide	oil
127	N-[2-(2,4-dichlorophenyl)ethyl]-N-[7-(trifluoromethyl)-4-quinolinyl]-acetamide	oil
128	N-[4-(t-butyl)phenyl]ethyl-N-(8-fluoro-4-quinolinyl)acetamide	126-128°C
129	N-[2-[4-(i-propyl)phenyl]ethyl]-N-(8-fluoro-4-quinolinyl)acetamide	82-84°C
130	N-[2-(1,1'-biphenyl)-4-ylethyl]-N-(8-fluoro-4-quinolinyl)acetamide	oil

TABLE 1
N-(2-phenylethyl)-4-quinolinamines

EXAMPLE NUMBER	COMPOUND	M.P.
131	N-[2-(pentamethylphenyl)ethyl]-N-(8-fluoro-4-quinolinyl)acetamide	oil
132	N-[2-(2-chlorophenyl)ethyl]-N-(8-chloro-4-quinolinyl)acetamide	104-106°C
133	N-[2-(4-methoxyphenyl)ethyl]-7,8-dimethyl-4-quinolinamine	183-185°C

TABLE 2
N-(3-phenylpropyl)-4-quinolinamines

EXAMPLE NUMBER	COMPOUND	M.P.
134	7-chloro-N-[3-(1,1'-biphenyl)-4-ylpropyl]-4-quinolinamine	122-124°C
135	N-[3-(4-chlorophenyl)propyl]-8-fluoro-4-quinolinamine	134-136°C
136	N-[3-(4-chlorophenyl)propyl]-7-chloro-4-quinolinamine	177-179°C
137	N-[3-(1,1'-biphenyl)-4-ylpropyl]-8-fluoro-4-quinolinamine	124-127°C
138	8-fluoro-N-(1-methyl-3-phenylpropyl)-4-quinolinamine	164-166°C
139	N-(3-phenylpropyl)-4-quinolinamine	96-97°C

TABLE 3
N-(4-phenylbutyl)-4-quinolinamines

EXAMPLE NUMBER	COMPOUND	M.P.
140	8-fluoro-N-[4-(4-chlorophenyl)-butyl]-4-quinolinamine	110-112°C
141	N-[4-(4-chlorophenyl)butyl]-N-(8-fluoro-4-quinolinyl)acetamide	oil

N-(Ar)alkyl TABLE 4
~~N-Arylalkyl~~-4-quinolinamines

EXAMPLE NUMBER	COMPOUND	M.P.
142	N-[2-(1-cyclohexenyl)ethyl]-5,8-dimethyl-4-quinolinamine	78-81°C
143	N-[2-(1-cyclohexenyl)ethyl]-8-fluoro-4-quinolinamine	153-155°C
144	N-[2-(1-cyclohexenyl)ethyl]-6,8-dimethyl-4-quinolinamine	114-116°C
145	N-[2-(1-cyclohexenyl)ethyl]-6-ethyl-4-quinolinamine	135-137°C
146	N-[2-(1-cyclohexenyl)ethyl]-N-(6-fluoro-4-quinolinyl)acetamide	66-68°C
147	N-[2-(2-thienyl)ethyl]-4-quinolinamine	153-154°C
148	N-[2-(3-thienyl)ethyl]-4-quinolinamine	156-157°C
149	6,8-difluoro-N-[2-(2-thienyl)ethyl]-4-quinolinamine	175-176°C
150	6,8-difluoro-N-[2-(3-thienyl)ethyl]-4-quinolinamine	191-192°C

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TABLE 4
N-Arylalkyl-4-quinolinamines

EXAMPLE NUMBER	COMPOUND	M.P.
151	N-[2-(1-naphthyl)ethyl]-4-quinolinamine	149-150°C
152	N-[2-(2-naphthyl)ethyl]-4-quinolinamine	160-161°C
153	N-[2-(2-thienyl)ethyl]-7-(trifluoromethyl)-4-quinolinamine	131-132°C
154	8-fluoro-N-[2-(4-phenyl-2-thiazolyl)ethyl]-4-quinolinamine	134-135°C
155	8-chloro-N-[2-(1-naphthyl)ethyl]-4-quinolinamine	205-206°C
156	8-chloro-N-[2-(2-naphthyl)ethyl]-4-quinolinamine	206-208°C
157	α-[[(8-fluoro-4-quinolinyl)amino]-methyl]-2-naphthalenemethanol	182-185°C
158	8-fluoro-N-[2-(1-naphthyl)ethyl]-4-quinolinamine	152-153°C
159	8-fluoro-N-[2-(2-naphthyl)ethyl]-4-quinolinamine	173-174°C
160	N-[2-(1-cyclohexenyl)ethyl]-N-(5,8-dimethyl-4-quinolinyl)acetamide	oil
161	N-(2-cyclohexylethyl)-N-(8-fluoro-4-quinolinyl)acetamide	oil
162	8-fluoro-N-[2-(5-methyl-2-thienyl)ethyl]-4-quinolinamine	161-163°C
163	N-[2-(5-chloro-2-thienyl)ethyl]-8-fluoro-4-quinolinamine	167-168°C

TABLE 4
N-Arylalkyl-4-quinolinamines

EXAMPLE NUMBER	COMPOUND	M.P.
164	8-fluoro-N-[2-(1H-imidazol-4-yl)-ethyl]-4-quinolinamine	230°C
165	7-chloro-N-[2-(1-cyclohexenyl)-ethyl]-4-quinolinamine	161-163°C
166	7-chloro-N-[2-(2-naphthyl)-ethyl]-4-quinolinamine	156-158°C
167	N-[2-(1-cyclohexenyl)ethyl]-7-(trifluoromethyl)-4-quinolinamine	158-160°C
168	N-[2-(1-cyclohexenyl)ethyl]-6-fluoro-4-quinolinamine	129-131°C
169	N-[2-(2-naphthyl)ethyl]-7-(trifluoromethyl)-4-quinolinamine	127-130°C
170	8-fluoro-N-[1-methyl-2-(2-thienyl)-ethyl]-4-quinolinamine	217-219°C
171	N-[1-methyl-2-(2-thienyl)ethyl]-4-quinolinamine	167-168°C
172	8-chloro-N-[2-(2-thienyl)ethyl]-4-quinolinamine	161-162°C
173	8-fluoro-N-[2-(2-thienyl)ethyl]-4-quinolinamine	157-158°C
174	N-[2-(2,3-dihydro-1,4-benzodioxin-2-yl)ethyl]-8-fluoro-4-quinolinamine	170-171°C
175	8-fluoro-N-[2-(3-thienyl)ethyl]-4-quinolinamine	163-164°C
176	8-fluoro-N-[2-(1H-indol-3-yl)ethyl]-4-quinolinamine	205-206°C

TABLE 4
N-Arylalkyl-4-quinolinamines

EXAMPLE NUMBER	COMPOUND	M.P.
177	N-(2-cyclohexylethyl)-8-fluoro-4-quinolinamine	145-147°C
178	N-(2-cyclohexylethyl)-6,8-dimethyl-4-quinolinamine	155-157°C
179	N-[2-(1-cyclohexenyl)ethyl]-N-(6,8-dimethyl-4-quinolinyl)acetamide	oil
180	8-fluoro-N-[2-(2-pyridinyl)ethyl]-4-quinolinamine	143-144°C

TABLE 5
Bis[2-phenylethyl]quinolinediamines

EXAMPLE NUMBER	COMPOUND	M.P.
181	N,N'-bis(2-phenylethyl)-2,4-quinolinediamine	70-71°C
182	N,N'-(2,4-quinolinediyl)bis[N-[2-(4-chlorophenyl)ethyl]acetamide]	oil
183	8-fluoro-N,N'-bis(2-phenylethyl)-2,4-quinolinediamine	oil
184	N,N'-bis(2-phenylpropyl)-2,4-quinolinediamine	oil
185	N,N'-bis[2-(4-chlorophenyl)ethyl]-4,6-quinolinediamine	135-137°C
186	N,N'-bis[2-(4-chlorophenyl)ethyl]-4,7-quinolinediamine	55-60°C
187	N,N'-bis[2-(4-methoxyphenyl)ethyl]-4,7-quinolinediamine	140-150°C
188	N,N'-bis[2-(4-chlorophenyl)ethyl]-8-fluoro-2,4-quinolinediamine	oil
189	N,N'-bis(2-phenylethyl)-4,8-quinolinediamine	83-84°C
190	N,N'-bis[2-(2,4-dichlorophenyl)ethyl]-8-fluoro-2,4-quinolinediamine	116-117°C
191	N,N'-(4,7-quinolinediyl)bis[N-[2-(4-chlorophenyl)ethyl]acetamide]	oil

TABLE 6
Bis[2-arylethyl]quinolinediamines

EXAMPLE NUMBER	COMPOUND	M.P.
192	N,N'-bis[2-(1-cyclohexen-yl)ethyl]-4,6-quinolinediamine	129-131°C

TABLE 7
4-(2-phenylethoxy)quinolines

EXAMPLE NUMBER	COMPOUND	M.P.
193	2-chloro-8-fluoro-4-[2-(4-methylphenyl)ethoxy]quinoline	76-77°C
194	5,7-dichloro-4-[2-(1,1'-biphenyl)-4-ylethoxy]quinoline	100-102°C
195	4-[2-(3-methoxyphenyl)ethoxy]-8-fluoroquinoline	90-91°C
196	8-fluoro-4-[2-(4-methoxyphenyl)-ethoxy]quinoline	70-71°C
197	8-fluoro-4-[2-(3-phenoxyphenyl)-ethoxy]quinoline	73-75°C
198	8-bromo-4-[2-(4-(t-butyl)phenyl)-ethoxy]quinoline	115-118°C
199	4-[2-(3,4-dimethoxyphenyl)ethoxy]-8-fluoroquinoline	113-114°C
200	8-fluoro-N-[2-(1,1'-biphenyl)-4-yl-ethoxy]quinoline	141-142°C
201	4-[2-(3-chlorophenyl)ethoxy]-8-fluoro-quinoline	76-77°C
202	7-chloro-4-(2-phenylethoxy)quinoline	oil
203	8-fluoro-4-[2-(3-(trifluoromethyl)-phenyl)ethoxy]quinoline	98-99°C
204	7-chloro-4-[2-(4-methylphenyl)ethoxy]-quinoline	87-88°C
205	8-fluoro-4-[2-(2-methylphenyl)ethoxy]-quinoline	72°C
206	8-fluoro-4-[2-(2-(trifluoromethyl)-phenyl)ethoxy]quinoline	60°C

TABLE 7
4-(2-phenylethoxy)quinolines

EXAMPLE NUMBER	COMPOUND	M.P.
207	8-chloro-4-(2-phenylethoxy)quinoline	73-74°C
208	4-(2-phenylethoxy)quinoline	oil
209	4-[2-(4-chlorophenyl)ethoxy]-8-fluoro-quinoline	138-140°C
210	4-[2-(4-methylphenyl)ethoxy]quinoline	59-60°C
211	4-[2-(4-chlorophenyl)ethoxy]quinoline	106-107°C
212	8-fluoro-4-[2-(4-methylphenyl)ethoxy]-quinoline	89-90°C
213	4-(1-methyl-2-phenylethoxy)quinoline	oil
214	8-fluoro-4-[1-(phenylmethyl)ethoxy]-quinoline	oil
215	8-bromo-4-[2-(4-chlorophenyl)ethoxy]-quinoline	112-114°C
216	8-chloro-4-[2-(2-chlorophenyl)ethoxy]-quinoline	90-92°C
217	8-fluoro-4-[2-(2-(1-methylethyl)phenyl)-ethoxy]quinoline	oil
218	8-fluoro-4-[2-(3-(phenylthio)phenyl)-ethoxy]quinoline	oil
219	8-fluoro-4-(2-phenylethoxy)quinoline	63-65°C
220	4-(2-phenylpropoxy)-8-fluoroquinoline	oil
221	4-[2-[4-(t-butyl)phenyl]ethoxy]-8-fluoroquinoline	81-82°C
222	8-fluoro-4-[2-(4-fluorophenyl)-ethoxy]quinoline	126-127°C

TABLE 7
4-(2-phenylethoxy)quinolines

EXAMPLE NUMBER	COMPOUND	M.P.
223	4-[2-(4-bromophenyl)ethoxy]-8-fluoroquinoline	130°C
224	8-fluoro-4-[2-(3-methylphenyl)ethoxy]-quinoline	92°C
225	8-fluoro-4-[2-(2-fluorophenyl)ethoxy]-quinoline	75°C
226	7-chloro-4-[2-(4-chlorophenyl)ethoxy]-quinoline	96-97°C
227	8-fluoro-4-[2-(2,4,6-trimethylphenyl)-ethoxy]quinoline	
228	8-fluoro-4-[2-(2-methoxyphenyl)ethoxy]-quinoline	74-75°C
229	4-[2-(2-methoxyphenyl)ethoxy]quinoline	oil
230	7-chloro-4-[2-(1,1'-biphenyl)-4-yl-ethoxy]quinoline	95-96°C
231	7-chloro-4-[2-(4-(t-butyl)phenyl)-ethoxy]quinoline	123-124°C
232	4-[2-(4-(t-butyl)phenyl)ethoxy]-7-fluoroquinoline	98-99°C
233	4-[2-(1,1'-biphenyl)-4-ylethoxy]-7-fluoroquinoline	73-75°C
234	4-[2-(4-chlorophenyl)ethoxy]-7-fluoro-quinoline	81-82°C
235	7-fluoro-4-[2-(4-methylphenyl)ethoxy]-quinoline	85-86°C
236	7-chloro-4-[2-(4-fluorophenyl)ethoxy]-quinoline	80°C

TABLE 7
4-(2-phenylethoxy)quinolines

EXAMPLE NUMBER	COMPOUND	M.P.
237	8-fluoro-4-[2-(1,1'-biphenyl)-2-yl-ethoxy]quinoline	55-60°C
238	8-fluoro-4-[2-(4-(i-propyl)phenyl)-ethoxy]quinoline	59-60°C
239	4-(2-phenylethoxy)-7-(trifluoro-methyl)quinoline	55-57°C
240	8-chloro-4-[2-(4-fluorophenyl)-ethoxy]quinoline	125-127°C

TABLE 8
4-(3-phenylpropoxy)quinolines

EXAMPLE NUMBER	COMPOUND	M.P.
241	8-fluoro-4-[3-[4-(t-butyl)phenyl]-propoxy]quinoline	103-105°C
242	8-chloro-4-[3-(4-chlorophenyl)-propoxy]quinoline	117-119°C
243	8-fluoro-4-[(3-phenyl-2-propenyl)-oxy]quinoline	128-130°C

TABLE 9
4-(2-Arylethoxy)quinolines

EXAMPLE NUMBER	COMPOUND	M.P.
244	8-fluoro-4-[2-(1-naphthyl)-ethoxy]quinoline	121-122°C
245	4-[2-(2-thienyl)ethoxy]-quinoline	oil
246	8-fluoro-4-[2-(2-thienyl)-ethoxy]quinoline	77-79°C
247	8-fluoro-4-[2-(2-naphthyl)ethoxy]-quinoline	123-124°C
248	5-chloro-4-(2-cyclohexylethoxy)-2,8-dimethylquinoline	100-102°C
249	6-fluoro-4-(2-cyclohexylethoxy)-2-methylquinoline	113-115°C

TABLE 10
Bis(2-phenylethoxy)quinolines

EXAMPLE NUMBER	COMPOUND	M.P.
250	8-fluoro-2,4-bis[2-(4-methyl-phenyl)ethoxy]quinoline	125-126°C
251	4,8-bis[2-(4-methylphenyl)ethoxy]-quinoline	142-143°C

TABLE 11
4-(3-Arylpropyl)quinolines

EXAMPLE NUMBER	COMPOUND	M.P.
252	4-(3-phenylpropyl)quinoline	
253	8-fluoro-4-(3-phenylpropyl)quinoline	43-45°C
254	4-(3-phenylpropyl)-7-(trifluoromethyl)quinoline	oil
255	8-chloro-4-(3-phenylpropyl)quinoline	70-71°C
256	8-fluoro-4-[3-(4-(i-propyl)phenyl)-propyl]quinoline	oil
257	4-[3-(1,1'-biphenyl)-4-ylpropyl]-8-fluoroquinoline	oil
258	8-fluoro-4-[3-(4-methylphenyl)propyl]-quinoline	oil
259	8-fluoro-4-[3-[3-(trifluoromethyl)-phenyl]propyl]quinoline	65-66°C
260	4-[3-[4-(t-butyl)phenyl]propyl]-8-fluoroquinoline	oil
261	4-[3-(4-chlorophenyl)propyl]-8-fluoro-quinoline	97°C

TABLE 12
Additional Compounds

EXAMPLE NUMBER	COMPOUND	M.P.
262	4-[2-[4-(t-butyl)phenyl]ethoxy]-quinoline	67-69°C
263	8-fluoro-4-[2-(1,1'-biphenyl)-4-yl-ethoxy]quinoline	97-99°C
264	8-fluoro-4-[(2-phenylethyl)sulfinyl]-quinoline	NA
265	8-fluoro-4-[2-[4-(2-hydroxyethyl)-phenyl]ethoxy]quinoline	NA
266	8-fluoro-4-[3-methoxybutoxy]-quinoline	oil
267	8-fluoro-4-(4-pentenoxy)quinoline	75-78°C
268	8-fluoro-N-(4-phenylbutyl)-4-quinolinamine	104-106°C
269	4-[2-(2-chlorophenyl)ethoxy]-8-fluoroquinoline	78-80°C
270	4-[2-[1,1'-biphenyl]-4-ylbutoxy]-8-fluoroquinoline	oil
271	N-[3-[4-(t-butyl)phenyl]propyl]-8-fluoro-4-quinolinamine	oil
272	8-fluoro-4-(4-phenoxybutoxy)quinoline	87-89°C
273	N-[2-(4-acetoxyphenyl)ethyl]-N-(8-fluoro-4-quinolinyl)acetamide	oil
274	8-fluoro-4-(3,5,5-trimethylhexyloxy)-quinoline	oil
275	8-fluoro-4-[2-(2,4-difluorophenyl)-ethoxy]quinoline	98-100°C

TABLE 12
Additional Compounds

EXAMPLE NUMBER	COMPOUND	M.P.
276	7-chloro-4-[2-(2,4-difluorophenyl)-ethoxy]quinoline	103-105°C
277	5,7-dichloro-4-[2-(4-ethoxyphenyl)-ethoxy]quinoline	104-105°C
278	4-[2-(4-butoxyphenyl)ethoxy]-8-fluoroquinoline	80-82°C
279	6-ethoxy-2-methyl-4-[3-(phenyl-methoxy)propoxy]quinoline	38-40°C
280	8-chloro-N-[2-(3-phenoxyphenyl)-ethyl]-4-quinolinamine	145-147°C
281	8-chloro-N-(4-phenylbutyl)-4-quino-linamine	134-136°C
282	8-fluoro-4-[3-(4-phenoxyphenyl)pro-poxy]quinoline	94-96°C
283	7-chloro-N-[2-(4-chlorophenyl)-propyl]-4-quinolinamine	145-147°C
284	4-[(4,5-dibromopentyl)oxy]-8-fluoro-quinoline	70-73°C
285	8-fluoro-4-[(8-phenoxyoctyl)oxy]-quinoline	80-81°C
286	6-chloro-2-methyl-4-[2-[4-(t-butyl)-phenyl]ethoxy]quinoline	83-86°C
287	8-fluoro-4-[(6-phenoxyhexyl)oxy]-quinoline	NA
288	8-chloro-N-(2-methyl-2-phenylpropyl)-4-quinolinamine	137-139°C

TABLE 12
Additional Compounds

EXAMPLE NUMBER	COMPOUND	M.P.
289	8-fluoro-N-(2-methyl-2-phenylpropyl)-4-quinolinamine	136-138°C
290	6-methoxy-2-methyl-N-[2-(3-phenoxyphenyl)ethyl]-4-quinolinamine	NA
291	8-fluoro-N-[2-[4-(phenylmethoxy)-phenyl]ethyl]-4-quinolinamine	157-159°C
292	7-fluoro-4-[2-(4-bromophenoxy)-ethoxy]quinoline	127-129°C
293	N-[2-(4-hydroxyphenyl)ethyl]-8-fluoro-4-quinoline	249-251°C
294	8-fluoro-4-[3-[3-(trifluoromethyl)-phenyl]propoxy]quinoline	67-69°C
295	8-fluoro-4-(2-phenylcyclohexyloxy)-quinoline	NA

The procedures described in the following detailed Examples are representative of the procedures used to prepare the compounds of the other Examples.

Example 4
N-Ethyl-N-(2-phenylethyl)-4-quinolinamine

To a suspension of 0.59 g of lithium aluminum hydride in 100 mL of dry ether was added, dropwise, a solution of 2.3 g of N-(2-phenylethyl)-N-(4-quinolinyl)-acetamide dissolved in 50 mL of dry ether. The mixture was heated to reflux for seven hours. Excess lithium aluminum hydride was then destroyed by adding 100 mL of water to the mixture. The solvent was then removed, and the residue was dissolved in chloroform. After washing with water, the mixture was then dried and concentrated. Using HPLC (silica gel, CH_2Cl_2 → EtOAc), 0.80 g of the title product was isolated. Yield 36.7%. M.P. oil.

Example 10
N-[2-(4-Chlorophenyl)ethyl]-N-[8-fluoro-4-quinolinyl]acetamide

A mixture of 2.0 g of N-[2-(4-chlorophenyl)-ethyl]-8-fluoro-4-quinolinamine and 5.0 mL of acetic anhydride was refluxed overnight. The mixture was then cooled, and solvents were removed by reducing pressure. The residue was washed with water and then dried. The resulting oil was passed over a silica gel column with ethyl acetate, and the front running spot was collected, producing 0.8 g of the title product as a thick oil.

Example 25
2-Chloro-N-(2-phenylethyl)-4-quinolinamine

To .6 g of 2-hydroxy-N-(2-phenylethyl)-4-quinolinamine was added 15 mL of $POCl_3$. The mixture was heated to reflux overnight, then cooled and concentrated to dryness. A mixture of ammonium hydroxide in water was added, then the product was extracted into CH_2Cl_2. This solution was concentrated to dryness, and the product was recrystallized from pentane/CH_2Cl_2, giving .55 g of the title product. Yield 85.9%. M.P. 132-133°C.

Example 69
3-Chloro-N-(2-chloro-2-phenylethyl)-4-quinolinamine

A mixture of 4.1 g of 1-phenyl-2-(4-quinolinylamino)ethanol, 100 mL of $POCl_3$ and 6.5 g of PCl_5 was heated to reflux for 18 hours, then cooled and concentrated to dryness. An ice/water mixture was added, then the product was extracted into CH_2Cl_2. This solution was concentrated to dryness, and the residue was purified by HPLC (silica gel column eluted with pentane/CH_2Cl_2 (50:50)). Fractions containing the product were combined and concentrated to dryness producing .433 g of the title product. Yield 8.7%. M.P. oil.

Example 97

8-Fluoro-N-[2-(2-trifluoromethyl)phenyl]-4-quinolinamine

To 2.0 g of 4-chloro-8-fluoroquinoline was added 4.1 g of 2-[2-(trifluoromethyl)phenyl]ethylamine. The mixture was stirred and heated to 160-165°C under nitrogen for two hours, then cooled, and 200 mL of a 50:50 mixture of ammonium hydroxide and water was added. The product was extracted into CH_2Cl_2, which was concentrated to dryness. Recrystallization from a pentane/CH_2Cl_2 mixture yielded 1.5 g of the title product. Yield 41.6%.

Example 154

8-Fluoro-N-[2-(4-phenyl-2-thiazolyl)ethyl]-4-quinolinamine

To 1.0 g of 4-chloro-8-fluoroquinoline was added 2.6 g of 2-β-aminoethyl-4-phenylthiazole monohydrochloride. The mixture was stirred under nitrogen and heated to 170-175°C for one hour. The mixture was then cooled and 250 mL of a 50:50 mixture of ammonium hydroxide and water was added. The product was extracted into CH_2Cl_2, which was then concentrated to dryness. Recrystallizing from pentane/CH_2Cl_2 gave .410 g of the title product. Yield 21.6%. M.P. 134-135°C.

Example 159

8-Fluoro-N-[2-(2-naphthyl)ethyl]-4-quinolinamine

A mixture of 2.0 g of 4-chloro-8-fluoroquinoline and 3.8 g of 2-(2-naphthyl)ethyl amine was heated under nitrogen to 160-165°C for one hour. Then 200 mL of a 50:50 mixture of ammonium hydroxide in water was added. The product was extracted from the mixture into CH_2Cl_2, which was then concentrated to dryness. The residue was recrystallized from pentane/ethyl acetate to give 1.4 g of the title product. Yield 41.2%. M.P. 173-174°C.

Example 173

8-Fluoro-N-[2-(2-thienyl)ethyl]-4-quinolinamine

A mixture of 2.0 g of 4-chloro-8-fluoroquinoline and 2.8 g of 2-(2-thienyl)ethyl amine was heated under nitrogen to 160-165°C for two hours, then cooled and combined with 200 mL of a 50:50 mixture of ammonium hydroxide and water. The product was extracted into CH_2Cl_2, which was then concentrated to dryness. The residue was recrystallized from pentane/CH_2Cl_2 to give 1.0 g of the title product. Yield 34.5%. M.P. 157-158°C.

Example 181

Bis[2-phenylethyl]-2,4-quinolinediamine

To 2.0 g of 2,4-dichloroquinoline was added 4.8 g of 2-phenylethylamine, and the mixture was heated to 150-160°C under nitrogen for 18 hours. The mixture

was then cooled and a solution of ammonium hydroxide and water was added. The product was extracted into CH_2Cl_2, which was then concentrated to dryness, giving an oil. To the oil, 100 mL of pentane and CH_2Cl_2 was added and the oil went into solution. This solution was cooled, and the title product crystallized. Yield 44.4%. M.P 70-71°C.

Example 186

N,N'-Bis[2-(4-chlorophenyl)ethyl]-2,7-quinolinediamine

A mixture of 2.0 g of 4-chloro-7-fluoroquinoline and 3.5 g of 2-(4-chlorophenyl)ethyl amine was heated neat until fuming began. The mixture was then cooled. The product was extracted into a $CHCl_3$/ammonium hydroxide solution, which was then washed with water. Solvent was removed by reducing pressure. The residue was placed on a silica gel column with acetone, then flushed with ethanol. Solvent was removed by reducing pressure, giving the title product as a yellow-brown foam. Yield 1.1 g. M.P. 55-60°C.

Example 209

4-[2-(4-Chlorophenyl)ethoxy]-8-fluoroquinoline

To 1.2 g of sodium hydride in 50 mL of DMF was added 3.9 g of 2-(4-chlorophenyl)ethyl alcohol. The mixture was stirred at room temperature for one hour, then 4.5 g of 4-chloro-8-fluoroquinoline in 10 mL of DMF was added, the the mixture was heated to reflux for two hours. Then the mixture was allowed to cool to room temperature

while it was stirred for four hours, after which it was poured into an ice/water mixture. The mixture was filtered, and the filter cake was washed with H_2O. Recrystallization from pentane/ethyl acetate gave .840 g of the title product. Yield 11.2%. M.P. 139-140°C.

Example 221

4-[2-[4-(t-Butyl)phenyl]ethoxy]-8-fluoroquinoline

To a mixture of 1.1 g of sodium hydride in 50 mL of DMF was added 4.0 g of 2-[4-(1,1-dimethylethyl)-phenyl]ethyl alcohol, and the mixture was stirred for one hour at room temperature. Then 4.0 g of 4-chloro-8-fluoroquinoline in 20 mL of DMF were added, and the mixture was stirred at room temperature overnight. Then the mixture was poured into an ice/water mixture, and the solid was collected and recrystallized from ethyl acetate/pentane to give 2.3 g of the title product. Yield 32.4%. M.P. 81-82°C.

Example 238

8-Fluoro-4-[2-[4-(i-propyl)phenyl]ethoxy]quinoline

To a suspension of .96 g of sodium hydride in 10 mL of dry DMF was added 3.6 g of 4-chloro-8-fluoroquinoline. The mixture was cooled in an ice/water bath, and 3.3 g of 2-[4-(1-methylethyl)phenyl]ethyl alcohol was added. The mixture was stirred overnight, then diluted with ice and water. The pH was adjusted to 7, then the product was extracted into CH_2Cl_2. The CH_2Cl_2 layer was

separated, filtered, and evaporated in vacuo. An azeotrope with xylene was formed to facilitate removal of residual DMF. The residue was chromatographically purified on a silica gel column, eluting with CH_2Cl_2, → 5% EtOAc/CH_2Cl_2 → 10% EtOAc/CH_2Cl_2. The fractions containing product were combined and evaporated to give an oil, which crystallized on adding ether. Recrystallization yielded 2.5 g of title product. M.P. 56-60°C.

Examples 212 and 251

8-fluoro-4-[2-(4-methylphenyl)ethoxy]quinoline,
4,8-Bis[2-(4-methylphenyl)ethoxy]quinoline

To a solution of 1.2 g of sodium hydride in 50 ml of DMF was added 3.4 g of 2-(4-methylphenyl)ethanol, and the mixture was stirred for one hour at room temperature. Then 4.5 g of 4-chloro-8-fluoroquinoline were added, the mixture was heated to reflux for five hours, and then cooled to room temperature, and poured into a mixture of ice in water. The solid phase was collected and dried. TLC showed three products. These were separated by HPLC (silica gel, 70% pentane/30% EtOAc) giving

1.84 g of 8-fluoro-4-[2-(4-methylphenyl)ethoxy]quinoline (Yield: 26.3%; M.P. 89-90°C)

0.610 g of 4-chloro-8-[2-(4-methylphenyl)ethoxy]quinoline (Yield: 8.7%; M.P. 74-75°C); and

0.450 g of 4,8-bis[2-(4-methylphenyl)ethoxy]quinoline (Yield: 6.4%; M.P. 142-143°C).

Example 261

4-[3-(4-chlorophenyl)propyl]-8-fluoroquinoline

A mixture of 3.63 g of 4-chloroquinoline and 5.3 g of 5-[2-(4-chlorophenyl)ethyl]barbituric acid was heated to 150°C for 1¼ hours, to form 5-[2-(4-chlorophenyl)ethyl]-5-(4-quinolinyl)barbituric acid. This compound was hydrolyzed, without isolation, by adding 4 g of NaOH in 40 ml of water and refluxing for four hours. The mixture was cooled, acidified with HCl and refluxed for several hours, cooled, and neutralized with dilute NaOH. The desired product was extracted into CH_2Cl_2, which was then filtered through phase separating paper and evaporated to dryness. The residue was absorbed onto silica gel and chromatographed over silica gel using CH_2Cl_2. Fractions containing product were combined to give 2.69 g of crystalline material. This was recrystallized from a petroleum ether/CH_2Cl_2 mixture to give 2.35 g of the title product. Yield: 39%. M.P. 97°C.

Utility

Plant Pathology

The compounds of the present invention have been found to control fungi, particularly plant pathogens. When employed in the treatment of plant fungal diseases, the compounds are applied to the plants in a disease inhibiting and "phytologically acceptable amount". The term "disease inhibiting" and "phytologically acceptable

amount," as used herein, refers to an amount of a compound of the invention which kills or inhibits the plant disease for which control is desired, but is not significantly toxic to the plant. This amount will generally be from about 1 to 1000 ppm, with 10 to 500 ppm being preferred. The exact concentration of compound required varies with the fungal disease to be controlled, the type formulation employed, the method of application, the particular plant species, climate conditions and the like. The compounds of the invention may also be used to protect stored grain and other non-plant loci from fungal infestation.

Greenhouse Tests

The following experiments were performed in the laboratory to determine the fungicidal efficacy of the compounds of the invention.

Test 1

This screen was used to evaluate the efficacy of the present compounds against a variety of different organisms that cause plant diseases.

The test compounds were formulated for application by dissolving 50 mg of the compound into 1.25 ml of solvent. The solvent was prepared by mixing 50 ml of "Tween 20" with 475 ml of acetone and 475 ml of ethanol. The solvent/compound solution was diluted to 125 ml with deionized water. The resulting formulation contains 400 ppm test chemical. Lower concentrations were obtained by serial dilution with the solvent-surfactant mixture.

The formulated test compounds were applied by foliar spray. The following plant pathogens and their corresponding plants were employed.

Pathogen	Designation in Following Tables	Host
Erysiphe graminis tritici (powdery mildew)	POWD MDEW	wheat
Pyricularia oryzae (rice blast)	RICE BLAS	rice
Puccinia recondita tritici (leaf rust)	LEAF RUST	wheat
Botrytis cinerea (gray mold)	GRAY MOLD	grape berries
Pseudoperonospora cubensis (downy mildew)	DOWN MDEW	squash
Cercospora beticola (leaf spot)	LEAF SPOT	sugar beet
Venturia inaequalis (apple scab)	APPL SCAB	apple seedling
Septoria tritici (leaf blotch)	LEAF BLOT	wheat

The formulated technical compounds were sprayed on all foliar surfaces of the host plants (or cut berry) to past run-off. Single pots of each host plant were placed on raised, revolving pedestals in a fume hood. Test solutions were sprayed on all foliar surfaces. All treatments were allowed to dry and the plants were inoculated with the appropriate pathogens within 2-4 hours.

The effectiveness of test compounds in controlling disease was rated on the following scale:

0	=	not tested against specific organism
-	=	0-19% control at 400 ppm
+	=	20-89% control at 400 ppm
++	=	90-100% control at 400 ppm
+++	=	90-100% control at 100 ppm.

Table 13 gives the results.

TABLE 13

EX. NO.	POWD MDEW	RICE BLAST	LEAF RUST	GRAY MOLD	DOWN MDEW	LEAF SPOT	APPL SCAB	LEAF BLOT
1	+	+	+	+	++	0	-	-
2	-	-	-	-	+++	0	-	-
3	-	++	+	-	+++	0	-	-
4	+	+	++	-	++	0	-	-
5	++	++	+++	-	+++	0	-	+++
6	++	+	+	+	++	0	-	-
7	+	+	+++	-	+++	-	-	+++
8	+	++	+	-	+++	+++	-	+
9	+	+	+	-	+++	-	-	-
10	++	+++	+++	-	++	+++	-	+++
11	-	++	+++	-	++	+++	-	-
12	+	++	+++	-	++	+++	-	++
13	-	++	++	-	++	-	-	-
14	-	+	+	-	+++	+++	-	-
15	-	+	+	-	+++	+++	+	-
16	-	+	+	-	+++	+++	-	-
17	++	+	++	-	++	0	-	-
18	+	++	++	-	++	0	-	-
19	+	++	++	-	+++	0	-	-
20	+	+	+	-	+++	0	-	-
21	+	+	+	-	++	0	-	-
22	+	+	+	-	+++	0	-	-
23	+	+	+	-	+++	0	-	-
24	+	+	+	-	+++	0	-	-
25	+	+	++	-	+++	0	-	-
26	+	+	-	-	+++	0	-	-
27	+	++	+	-	+++	0	-	-
28	+	++	+	-	+++	0	-	-
29	-	+	+	-	-	0	0	0
30	-	+	+	-	+++	0	-	-
31	++	+	+	-	+++	0	-	-
32	+	+	-	-	+++	0	-	-
33	-	+	+	-	+++	0	-	-
34	+	+	++	-	+++	+	-	-
35	+	+	+	-	+++	+++	-	-
36	+	+++	+++	-	+++	+++	-	+++
37	+	-	+	-	+	0	0	0
38	+	-	++	-	+++	+	-	-
39	+++	+++	+++	-	+++	0	0	0
40	-	++	+++	-	+	0	0	0

TABLE 13

EX. NO.	POWD MDEW	RICE BLAST	LEAF RUST	GRAY MOLD	DOWN MDEW	LEAF SPOT	APPL SCAB	LEAF BLOT
41	+	++	+++	-	++	+++	-	+
42	+++	+	++	-	+++	+++	-	-
43	+	+	-	-	++	+++	-	-
44	+++	+	+	-	+++	+++	+	-
45	+	++	+	-	++	+++	-	-
46	+	++	+	-	++	+++	+	+
47	+	-	+	-	+	0	0	0
48	+	+	+	-	++	+	-	-
49	-	+	+	-	+	0	0	0
50	+++	-	++	-	+++	-	-	-
51	-	+	+	-	+++	+++	-	-
52	-	+	+	-	+++	+	-	+++
53	+++	+	+	-	+++	+++	-	+
54	-	++	+	-	+++	+++	-	+
55	+	++	+	-	++	+++	-	-
56	-	++	++	-	+++	+++	-	+
57	-	++	+	-	++	+++	-	-
58	-	-	+	-	+++	0	0	0
59	+	+	-	-	[illegible]	0	0	0
60	++	+++	++	-	+++	0	0	0
61	-	++	++	-	+++	0	0	0
62	-	++	++	-	+++	-	-	+
63	-	+	+++	-	++	0	0	0
64	+	-	+	-	+++	0	0	0
65	+	+	++	-	+++	-	-	+
66	+	++	+++	-	+++	+++	-	+
67	-	+	+	-	++	+	-	-
68	+	+	+++	-	++	-	-	+++
69	+	+	+	-	+++	-	-	-
70	+++	+	+	-	-	-	-	-
71	+	+	+++	-	+++	+++	-	+
72	++	+++	+++	-	+++	0	0	0
73	-	+	-	-	++	-	-	-
74	+	+	+++	-	+++	+++	-	-
75	+	+	++	-	+++	-	-	+
76	++	+++	+++	-	+++	-	+	+++
77	+	+	++	-	+++	-	+	-
78	+	++	+++	-	+++	+++	-	+
79	+	++	++	-	+++	+++	-	+
80	+	++	++	-	+++	+	-	-

TABLE 13

EX. NO.	POWD MDEW	RICE BLAST	LEAF RUST	GRAY MOLD	DOWN MDEW	LEAF SPOT	APPL SCAB	LEAF BLOT
81	+	++	++	-	+++	+	-	-
82	+	+++	+++	-	+++	+	-	+++
83	+	++	+++	+++	++	+	-	-
84	+++	++	++	-	++	+	-	-
85	-	-	+	-	-	0	0	0
86	-	-	+	-	+	0	0	0
87	-	-	+	-	+++	-	-	-
88	-	-	++	-	++	+	-	-
89	-	-	+	-	+++	0	0	0
90	-	+++	+++	-	+++	0	0	0
91	+	+	-	-	++	-	-	-
92	+	++	+++	-	++	+	-	+++
93	-	-	-	-	-	+	-	+
94	+	+++	+++	-	+++	+++	-	+
95	+	++	+++	+	+++	+	+	+++
96	+	+++	+++	-	+++	+++	-	+++
97	+	+++	+++	-	+++	+++	-	+++
98	-	+	++	-	++	-	-	-
99	-	++	+++	-	+++	+	-	-
100	+	+	+	-	+	0	0	0
101	+++	-	+	-	+++	+++	+	-
102	+	+	-	-	-	0	0	0
103	+	++	++	-	+++	+	+++	+
104	-	-	-	-	++	+	+	-
105	+++	++	+++	-	+++	+	-	+
106	++	+	+	-	+	+	-	+
107	++	+	+	-	+++	-	-	-
108	+	+	++	-	+	-	-	+++
109	+	+	++	-	+++	0	0	0
110	-	+	++	-	++	0	0	0
111	+	++	+++	-	+++	-	-	+++
112	-	-	+	-	+++	-	-	-
113	+	+++	+++	-	+++	-	-	+++
114	+++	+++	+++	-	+++	+++	-	+++
115	-	+	-	-	+	0	0	0
116	-	+	+++	-	+++	+	+	-
117	+	+	+	-	+++	+	-	-
118	-	+	-	-	-	-	-	-
119	+	+	+	-	++	-	+	+
120	-	+	+	-	++	+++	-	-

TABLE 13

EX. NO.	POWD MDEW	RICE BLAST	LEAF RUST	GRAY MOLD	DOWN MDEW	LEAF SPOT	APPL SCAB	LEAF BLOT
121	+	-	++	-	+	0	0	0
122	-	++	+	-	++	-	-	-
123	-	+	+	-	+++	-	-	-
124	+++	+	+	-	-	-	-	-
125	+	-	-	-	-	0	0	0
126	++	+++	+	-	+	-	-	+
127	+	+	+	-	+	0	0	0
128	-	+	+	-	-	0	0	0
129	-	+	++	-	+	-	+	-
130	-	-	-	-	-	0	0	0
131	-	-	-	-	+	0	0	0
132	-	-	-	-	-	0	0	0
133	-	+	+	-	+	0	0	0
134	+	++	+	-	+++	0	0	0
135	-	-	-	-	+++	-	-	+
136	+	-	-	-	+++	-	-	-
137	+	+++	+	-	+++	0	0	0
138	-	+	+	-	+++	0	0	0
139	+	+	+	-	++	-	-	-
140	+	+++	+++	-	+++	+++	+	+++
141	-	++	+	-	+	0	0	0
142	-	++	++	-	+++	0	0	0
143	++	++	+++	-	+++	+	-	+
144	-	+	++	-	+++	+	+	-
145	-	+	+	-	+++	+	-	-
146	-	-	-	-	+	0	0	0
147	-	+	+	-	+++	-	-	-
148	-	+	+	-	++	+	-	-
149	+	+	++	-	++	+++	-	+
150	+	+	++	-	++	+++	-	+++
151	+	+	++	-	+++	+	-	+
152	++	+++	++	-	+++	+++	-	+++
153	+	+	++	-	+	-	-	-
154	++	+	+++	-	+++	+	+	+
155	-	+	-	-	+++	-	-	-
156	-	+	+	-	+++	-	-	-
157	-	++	++	-	+++	0	0	0
158	+	+++	+++	-	+++	+	-	+++
159	++	+++	+++	-	+++	+	-	+++
160	-	+	-	-	-	0	0	0

TABLE 13

EX. NO.	POWD MDEW	RICE BLAST	LEAF RUST	GRAY MOLD	DOWN MDEW	LEAF SPOT	APPL SCAB	LEAF BLOT
161	+	+	-	-	+	0	0	0
162	+	+	++	-	+++	-	-	-
163	++	+	+++	-	++	+++	-	-
164	-	+	+	+	++	+	-	-
165	+	++	++	-	+++	+++	+	-
166	+	+	+	-	+++	-	-	+
167	+	-	-	-	+	0	0	0
168	+	++	++	-	+++	-	-	-
169	+	++	+	-	++	-	-	-
170	+	+	++	-	+	-	-	-
171	-	+	+	-	+	+	-	+
172	+	+	+	-	+	-	-	-
173	+	+	++	-	+++	+++	-	+
174	+	+	++	-	+++	-	-	+
175	+	+	+++	-	+++	-	-	+
176	+	+	+	-	++	+	-	-
177	++	+++	+++	-	+++	0	0	0
178	-	+	++	-	+++	0	0	0
179	-	-	-	-	++	+	+	-
180	++	+	-	-	++	+	-	+
181	+	+	+	-	+++	0	-	-
182	-	+	-	-	-	0	0	0
183	-	++	++	-	+++	+	+	-
184	-	+	++	-	++	-	-	-
185	-	+	+	-	+	0	0	0
186	-	-	+	-	+++	+	-	+
187	-	+	+	-	+++	-	-	-
188	-	++	+	-	++	0	0	0
189	-	+	+	-	+	-	-	-
190	-	+	+++	-	-	-	-	-
191	-	+	++	-	-	0	0	0
192	-	-	++	-	+++	-	-	+
193	-	-	+	-	-	0	0	0
194	+	-	-	-	-	0	0	0
195	+++	+++	+++	-	+++	0	0	0
196	+++	+++	+++	-	+++	0	0	0
197	+++	+++	+++	-	+	0	0	0
198	-	-	-	-	-	0	0	0
199	++	++	+++	-	+++	0	0	0
200	+++	+++	+++	-	+	+	+	+++

TABLE 13

EX. NO.	POWD MDEW	RICE BLAST	LEAF RUST	GRAY MOLD	DOWN MDEW	LEAF SPOT	APPL SCAB	LEAF BLOT
201	+++	+	+++	-	+++	+++	+	+++
202	+++	+	++	-	++	+	-	+
203	+	+++	+++	-	++	+	+	++
204	+	-	+	-	+	0	0	0
205	++	+++	+++	-	+++	0	0	0
206	+++	+++	+++	-	+++	0	0	0
207	++	+++	+++	-	+++	+	+	+++
208	++	+++	+++	-	+++	+	-	+
209	+++	+++	+++	-	+++	+++	+	+++
210	++	+++	+++	-	+++	+	-	+++
211	++	+++	+++	-	+++	+++	-	+++
212	++	+++	+++	-	+++	-	+++	+++
213	+	++	++	-	+++	-	+	+
214	+	+++	+	-	++	0	0	0
215	-	+	+	-	++	0	0	0
216	++	++	++	-	++	0	0	0
217	+++	+++	+++	-	+++	0	0	0
218	+++	+++	+++	-	+++	0	0	0
219	++	+++	+++	-	+++	+	+	+
220	++	+	++	-	++	-	+	-
221	+	-	+++	-	+++	+++	+	+++
222	+	+	+++	-	+++	+	+++	+++
223	++	+++	+++	-	-	0	0	0
224	++	+++	+++	-	+++	0	0	0
225	++	+++	+++	-	+++	0	0	0
226	+	-	+	-	+	0	0	0
227	-	+	+	-	-	0	0	0
228	++	+++	+++	-	+++	+	+++	+++
229	+	+++	++	-	+++	-	-	+
230	++	-	+	-	-	-	-	-
231	+	-	-	-	-	0	0	0
232	-	-	-	-	-	0	0	0
233	+	++	++	-	+	-	-	+
234	+	+	++	-	+	+	-	+
235	+	++	++	-	+	-	-	+
236	+++	-	+	-	-	-	-	-
237	++	++	+	-	-	0	0	0
238	+++	+++	+++	+	++	0	0	0
239	+++	++	++	-	++	0	0	0
240	-	+	++	-	-	0	0	0

TABLE 13

EX. NO.	POWD MDEW	RICE BLAST	LEAF RUST	GRAY MOLD	DOWN MDEW	LEAF SPOT	APPL SCAB	LEAF BLOT
241	-	-	-	-	-	0	0	0
242	-	-	-	-	-	0	0	0
243	-	-	-	-	-	0	0	0
244	+	++	+	-	+	-	-	+
245	+	++	++	-	++	-	-	-
246	++	+++	+++	-	+++	+	+++	+++
247	++	+++	+++	-	+	-	-	+++
248	+	-	-	-	-	0	0	0
249	-	-	-	-	-	0	0	0
250	-	-	+	-	+	0	0	0
251	-	+	-	-	+	-	-	-
252	++	++	+++	-	++	-	+	+
253	+++	++	+++	-	++	+	+++	+
254	++	++	-	-	-	0	0	0
255	+	+++	+++	-	+	0	0	0
256	+++	+++	+++	-	++	0	0	0
257	+++	+	+++	-	+++	0	0	0
258	++	+++	++	-	++	+	-	+
259	+	+++	+++	+	+++	-	+++	+++
260	++	+++	+++	-	+++	+	-	+++
261	+	+	+++	-	+	-	+	+
262	-	++	+++	-	+++	0	0	0
263	+	+	+	-	-	0	0	0
264	-	-	+	-	0	0	0	0
265	-	++	++	-	-	0	0	0
266	-	-	-	-	-	0	0	0
267	++	+++	++	-	+	0	0	0
268	+	+++	+++	-	+++	0	0	0
269	++	+++	+++	-	+++	0	0	0
270	-	+	-	-	-	0	0	0
271	-	+++	+	-	+++	0	0	0
272	-	+	-	-	+	0	0	0
273	+	++	+	-	+	0	0	0
274	++	++	++	-	+	0	0	0
275	+++	+++	+++	-	+++	0	0	0
276	+++	-	+	-	-	0	0	0
277	++	-	-	-	-	0	0	0
278	+++	+++	+++	-	+++	0	0	0
279	-	++	++	-	++	0	0	0
280	+++	+++	+++	-	+++	0	0	0

TABLE 13

EX. NO.	POWD MDEW	RICE BLAST	LEAF RUST	GRAY MOLD	DOWN MDEW	LEAF SPOT	APPL SCAB	LEAF BLOT
281	+	+++	+	-	+++	0	0	0
282	-	+	-	-	-	0	0	0
283	+	+	++	-	++	0	0	0
284	-	+++	++	-	+	0	0	0
285	-	-	-	-	-	0	0	0
286	+	-	+	-	-	0	0	0
287	-	-	+	-	++	0	0	0
288	-	+	-	-	+	0	0	0
289	+	++	++	-	+++	0	0	0
290	-	+++	+	-	+++	0	0	0
291	+++	+++	+++	-	+++	0	0	0
292	-	-	-	-	-	0	0	0
293	-	-	++	-	-	0	0	0
294	-	-	-	-	-	0	0	0
295	+	+	+	-	++	0	0	0

Field Tests

Selected compounds were field tested against a variety of plant pathogens. The following table reports pathogens against which compounds of the invention showed activity in these tests.

TABLE 14

COMPOUND EX. NO.	CROP	PATHOGEN
2	barley	Pyrenophora teres
5	potato	Phytophthora infestans
	tomato	Phytophthora infestans
5	barley	Pyrenophora teres
		Rhynchosporium secalis
	cucumber	Sphaerotheca fuliginea
	grape	Plasmopara viticola
	potato	Phytophthora infestans
	rape	Alternaria brassica
	tomato	Phytophthora infestans
10	barley	Rhynchosporium secalis
		Pyrenophora teres
		Erysiphe graminis hordei
	cucumber	Sphaerotheca fuliginea
	wheat	Pseudocercosporella herpotrichoides
		Erysiphe graminis tritici
97	grape	Plasmopara viticola
159	barley	Rhynchosporium secalis
	grape	Plasmopara viticola
	wheat	Puccinia recondita
173	grape	Plasmopara viticola

TABLE 14

COMPOUND EX. NO.	CROP	PATHOGEN
200	barley	Rhynchosporium secalis
		Pyrenophora teres
		Erysiphe graminis hordei
	cucumber	Sphaerotheca fuliginea
	wheat	Pseudocercosporella herpotrichoides
		Erysiphe graminis tritici
212	apple	Podosphaera leucotricha
	barley	Pyrenophora teres
	grape	Uncinula necator
		Plasmopara viticola
	rape	Alternaria brassica
	rice	Piricularia oryzae
212	barley	Rhynchosporium secalis
		Pyrenophora teres
		Erysiphe graminis hordei
	cucumber	Sphaerotheca fuliginea
	wheat	Pseudocercosporella herpotrichoides
		Erysiphe graminis tritici
219	barley	Rhynchosporium secalis
		Pyrenophora teres
		Erysiphe graminis hordei
	cucumber	Sphaerotheca fuliginea
	wheat	Pseudocercosporella herpotrichoides
		Erysiphe graminis tritici
221	sugar beet	Erysiphe sp.

Combinations

Fungal disease pathogens are known to develop resistance to fungicides. When strains resistant to a fungicide do develop, it becomes necessary to apply larger and larger amounts of the fungicide to obtain desired results. To retard the development of resistance to new fungicides, it is desirable to apply the new fungicides in combination with other fungicides. Use of a combination product also permits the product's spectrum of activity to be adjusted.

Accordingly, another aspect of the invention is a fungicidal combination comprising at least 1% by weight of a compound of formula (1) in combination with a second fungicide.

Contemplated classes of fungicides from which the second fungicide may be selected include:

1) N-substituted azoles, for example propiconazole, triademefon, flusilazol, diniconazole, ethyltrianol, myclobutanil, and prochloraz;

2) pyrimidines, such as fenarimol and nuarimol;

3) morpholines, such as fenpropimorph and tridemorph;

4) piperazines, such as triforine; and

5) pyridines, such as pyrifenox.

Fungicides in these five classes all function by inhibiting sterol biosynthesis. Additional classes of contemplated fungicides, which have other mechanisms of action, include:

6) dithiocarbamates, such as maneb and mancozeb;

7) phthalimides, such as captafol;
8) isophthalonitrites, such as chlorothalonil;
9) dicarboximides, such as iprodione;
10) benzimidazoles, such as benomyl and carbendazim;
11) 2-aminopyrimidines, such as ethirimol;
12) carboxamides, such as carboxin; and
13) dinitrophenols, such as dinocap.

The fungicide combinations of the invention contain at least 1%, ordinarily 20 to 80%, and more typically 50 to 75% by weight of a compound of formula (1).

Combination Tests

Selected compounds were tested in the greenhouse in combination with other known fungicides against various plant pathogens. Results are reported in Tables 15 and 16. In the tables, the time given under "Time in hours" is the number of hours elapsing between treatment and inoculation. A negative time indicates that the pathogen was inoculated before treatment. In such cases, curative activity was being tested. A positive time indicates that the plants were treated before they were inoculated with pathogen. In such cases, residual or protectant activity was tested. The compounds were formulated and applied as foliar sprays as in Test 1. The results were evaluated on a 1-9 rating scale. These ratings represent the following percent disease control:

1 = 0-19%, 2 = 20-29%, 3 = 30-39%, 4 = 40-59%, 5 = 60-74%, 6 = 75-89%, 7 = 90-96%, 8 = 97-99%, and 9 = 100%.

TABLE 15

CUCURBIT DOWNY MILDEW

COMPOUND 1 PLUS COMPOUND 2	TIME IN HOURS	RATE CMPD 1 IN PPM	RATE CMPD 2 IN PPM	RESULTS
Ex. 5	4	48.00		8.0
		24.00		7.5
		12.00		7.0
		6.00		1.0
nuarimol	4	2.00		1.0
		1.00		1.0
		0.50		1.0
		0.25		1.0
nuarimol+Ex. 5	4	2.00	48.00	8.5
		1.00	24.00	7.5
		0.50	12.00	5.0
		0.25	6.00	1.0

TABLE 16

CUCURBIT POWDERY MILDEW

Ex. 5	4	48.00		6.0
		24.00		5.0
		12.00		1.0
		6.00		1.0
nuarimol	4	2.00		9.0
		1.00		8.0
		0.50		7.0
		0.25		6.0
nuarimol+Ex. 5	4	2.00	48.00	9.0
		1.00	24.00	9.0
		0.50	12.00	8.0
		0.25	6.00	6.0

Insecticide and Miticide Utility

The compounds of the invention are also useful for the control of insects and mites. Therefore, the present invention also is directed to a method for inhibiting an insect or mite which comprises applying to a locus of the insect or mite an insect- or mite-inhibiting amount of a compound of formula (1).

The compounds of the invention show activity against a number of insects and mites. More specifically, the compounds show activity against melon aphid, which is a member of the insect order Homoptera. Other members of the Homoptera include leafhoppers, planthoppers, pear pyslla, apple sucker, scale insects, whiteflies, spittle bugs as well as numerous other host specific aphid species. Activity has also been observed against greenhouse thrips, which are members of the order Thysanoptera. The compounds also show activity against Southern armyworm, which is a member of the insect order Lepidoptera. Other typical members of this order are codling moth, cutworm, clothes moth, Indianmeal moth, leaf rollers, corn earworm, European corn borer, cabbage worm, cabbage looper, cotton bollworm, bagworm, eastern tent caterpillar, sod webworm, and fall armyworm.

Representative mite species with which it is contemplated that the present invention can be practiced include those listed below.

FAMILY	SCIENTIFIC NAME	COMMON NAME
ACARIDAE		
	Aleurobius farinae	
	Rhizoglyphus echinopus	Bulb mite
	Rhizoglyphus elongatus	
	Rhizoglyphus rhizophagus	
	Rhizoglyphus sagittatae	
	Rhizoglyphus tarsalis	
ERIOPHYIDAE		
	Abacarus farinae	Grain rust mite
	Aceria brachytarsus	
	Acalitus essigi	Redberry mite
	Aceria ficus	
	Aceria fraaxinivorus	
	Aceria granati	
	Aceria parapopuli	
	Eriophyes sheldoni	Citrus bud mite
	Aceria tulipae	
	Aculus carnutus	Peach silver mite
	Aculus schlechtendali	Apple rust mite
	Colomerus vitis	Grape erineum mite
	Eriophyes convolvens	
	Eriophyes insidiosus	
	Eriophyes malifoliae	
	Eriophyes padi	
	Eriophyes pruni	
	Epitrimerus pyri	Pear leaf blister mite
	Eriophyes ramosus	

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FAMILY	SCIENTIFIC NAME	COMMON NAME
	Eriophyes sheldoni	Citrus bud mite
	Eriophyes ribis	
	Phyllocoptes gracilis	Dryberry mite
	Phyllocoptruta oleivora	Citrus rust mite
	Phytoptus ribis	
	Trisetacus pini	
	Vasates amygdalina	
	Vasates eurynotus	
	Vasates quadripedes	Maple bladdergall mite
	Vasates schlechtendali	
EUPODIDAE		
	Penthaleus major	Winter grain mite
	Linopodes spp.	
NALEPELLIDAE		
	Phylocoptella avellanae	Filbert bud mite
PENTHALEIDAE		
	Halotydeus destrustor	
PYEMOTIDAE		
	Pyemotes tritici	Straw itch mite
	Siteroptes cerealium	
TARSONEMIDAE		
	Polyphagotarsonemus latus	Broad mite
	Steneotarsonemus pallidus	Cyclamen mite

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FAMILY	SCIENTIFIC NAME	COMMON NAME
TENUIPALPIDAE		
	Brevipalpus californicus	
	Brevipalpus obovatus	Privet mite
	Brevipalpus lewisi	Citrus flat mite
	Dolichotetranychus floridanus	Pineapple flase spider mite
	Tenuipalpes granati	
	Tenuipalpes pacificus	
TETRANYCHIDAE		
	Bryobia arborea	
	Bryobia practiosa	Clover mite
	Bryobia rubrioculus	Brown mite
	Eotetranychus coryli	
	Eotetranychus hicoriae	Pecan deaf scorch mite
	Eotetranychus lewisi	
	Eotetranychus sexmaculatus	Sixspotted spider mite
	Eotetranychus willametti	
	Eotetranychus banksi	Texas citrus mite
	Oligonychus ilicis	Southern red mite
	Oligonychus pratensis	Banks grass mite
	Oligonychus ununguis	Spruce spider mite
	Panonychus citri	Citrus red mite
	Panonychus ulmi	European red mite
	Paratetranychus modestus	
	Paratetranychus pratensis	
	Paratetranychus viridis	
	Petrobia latens	Brown wheat mite

FAMILY	SCIENTIFIC NAME	COMMON NAME
	Schizotetranychus celarius	Bamboo spider mite
	Schizotetranychus pratensis	
5	Tetranychus canadensis	Fourspotted spider mite
	Tetranychus cinnabarinus	Carmine spider mite
	Tetranychus mcdanieli	McDaniel spider mite
	Tetranychus pacificus	Pacific spider mite
	Tetranychus schoenei	Schoene spider mite
10	Tetranychus urticae	Twospotted spider mite
	Tetranychus turkestani	Strawberry spider mite
	Tetranychus desertorum	Desert spider mite

The compounds are useful for reducing populations of insects and mites, and are used in a method of inhibiting an insect or mite population which comprises applying to a locus of the insect or arachnid an effective insect- or mite-inactivating amount of a compound of formula (1). The "locus" of insects or mites is a term used herein to refer to the environment in which the insects or mites live or where their eggs are present, including the air surrounding them, the food they eat, or objects which they contact. For example, plant-ingesting insects or mites can be controlled by applying the active compound to plant parts, which the insects or mites eat, particularly the foliage. It is contemplated that the compounds might also be useful to protect textiles, paper, stored grain, or seeds by applying an active compound to such substance. The term "inhibiting an insect or mite" refers to a decrease in the numbers of living insects or mites; or a decrease in the number of viable insect or mite eggs. The extent of reduction accomplished by a compound depends, of course, upon the application rate of the compound, the particular compound used, and the target insect or mite species. At least an insect-inactivating or mite-inactivating amount should be used. The terms "insect-inactivating amount" and "mite-inactivating amount" are used to describe the amount, which is sufficient to cause a measurable reduction in the treated insect or mite population. Generally an amount in the range from about 1 to about 1000 ppm active compound is used.

In a preferred embodiment, the present invention is directed to a method for inhibiting a mite which comprises applying to a plant an effective mite-inactivating amount of a compound of formula (1) in accordance with the present invention.

MITE/INSECT SCREEN

The compounds of Examples 1-295 were tested for miticidal and insecticidal activity in the following mite/insect screen.

Each test compound was formulated by dissolving the compound in acetone/alcohol (50:50) mixture containing 23 g of "TOXIMUL R" (sulfonate/nonionic emulsifier blend) and 13 g of "TOXIMUL S" (sulfonate/nonionic emulsifier blend) per liter. These mixtures were then diluted with water to give the indicated concentrations.

Twospotted spider mites (Tetranychus urticae Koch) and melon aphids (Aphis gossypii Glover) were introduced on squash cotyledons and allowed to establish on both leaf surfaces. Other plants in the same treatment pot were left uninfested. The leaves were then sprayed with 5 ml of test solution using a DeVilbiss atomizing sprayer at 10 psi. Both surfaces of the leaves were covered until runoff, and then allowed to dry for one hour. Two uninfested leaves were then excised and placed into a Petri dish containing southern armyworm (Spodopetra eridania Cramer).

After standard exposure periods, percent mortality was evaluated. Results are reported in Table 17, where the following abbreviations are used.

CRW refers to corn rootworm
SAW refers to Southern armyworm
SM refers to twospotted spider mites
MA refers to melon aphids.

TABLE 17
MITE/INSECT SCREEN

COMPOUND EX. NO.	CRW RATE PPM	CRW RESULTS %	SAW SM & MA RATE PPM	SAW RESULTS %	SM RESULTS %	MA RESULTS %
1	12.00	0	200	0	0	0
2	12.00	0	200	0	0	0
3	12.00	0	200	0	0	0
4	12.00	0	200	0	0	0
5	12.00	0	200	0	0	0
6	12.00	0	200	0	0	0
7	12.00	0	200	0	0	0
8	12.00	0	200	100	0	0
9	12.00	0	200	0	0	0
10	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
11	24.00	60	400	100	0	0
	12.00	0	200	80	0	0
12	24.00	40	400	100	0	0
	12.00	0	200	0	0	0
13	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
14	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
15	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
16	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
17	12.00	0	200	0	0	0
18	12.00	0	200	0	0	0
19	12.00	0	200	0	0	0
20	12.00	0	200	0	0	0
21	12.00	0	200	0	0	0
22	12.00	0	200	0	0	0
23	12.00	0	200	0	0	0
24	12.00	0	200	0	0	0
25	12.00	0	200	0	0	0
26	12.00	0	200	0	0	0
27	12.00	0	200	0	0	0
28	12.00	0	200	0	0	0
29	12.00	0	200	0	0	0
30	12.00	0	200	0	0	0
31	12.00	0	200	0	0	0

TABLE 17
MITE/INSECT SCREEN

COMPOUND EX. NO.	CRW RATE PPM	CRW RESULTS %	SAW SM & MA RATE PPM	SAW RESULTS %	SM RESULTS %	MA RESULTS %
32	12.00	0	200	0	0	0
33	12.00	0	200	0	0	0
34	12.00	0	200	0	0	0
35	12.00	0	200	0	0	0
36	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
	24.00	0	400	0	0	0
37	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
38	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
39	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
40	24.00	100	400	80	0	0
	12.00	0	200	0	0	0
41	24.00	0	400	40	0	0
	12.00	0	200	80	0	0
42	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
43	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
44	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
45	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
46	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
47	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
48	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
49	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
50	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
51	12.00	0	200	0	0	0
	24.00	0	400	20	0	0

TABLE 17
MITE/INSECT SCREEN
SAW

COMPOUND EX. NO.	CRW RATE PPM	CRW RESULTS %	SM & MA RATE PPM	SAW RESULTS %	SM RESULTS %	MA RESULTS %
52	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
53	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
54	12.00	0	200	0	0	0
55	12.00	0	200	0	0	0
56	24.00	0	400	80	0	0
	12.00	0	200	100	0	0
57	12.00	0	200	40	0	0
	24.00	0	400	50	0	0
58	24.00	0	400	0	0	0
59	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
60	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
61	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
62	24.00	0	400	0	0	0
63	24.00	0	400	0	0	0
64	24.00	0	400	0	0	0
	12.00	0	200	60	0	0
65	12.00	0	200	0	0	0
66	12.00	0	200	0	0	0
67	12.00	0	200	0	0	0
68	12.00	0	200	0	0	0
69	12.00	0	200	0	0	0
70	12.00	0	200	0	0	0
71	12.00	0	200	0	0	0
	12.00	60	200	0	0	0
72	24.00	0	400	0	0	0
73	12.00	0	200	0	0	0
74	12.00	0	200	20	0	0
	12.00	0	200	0	0	0
75	12.00	0	200	0	0	0
76	12.00	0	200	0	0	0
	12.00	0	200	90	0	0
77	12.00	0	200	0	0	0

TABLE 17
MITE/INSECT SCREEN

COMPOUND EX. NO.	CRW RATE PPM	CRW RESULTS %	SAW SM & MA RATE PPM	SAW RESULTS %	SM RESULTS %	MA RESULTS %
78	12.00	0	200	20	0	0
	12.00	0	200	20	0	0
79	12.00	0	200	10	0	0
	12.00	0	200	60	0	0
80	12.00	0	200	0	0	0
81	12.00	0	200	0	0	0
82	12.00	0	200	0	0	0
83	12.00	0	200	0	0	0
84	12.00	0	200	10	0	0
	24.00	0	400	0	0	0
85	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
86	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
87	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
88	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
89	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
90	24.00	0	400	0	0	0
	12.00	0	200	100	80	80
91	12.00	0	200	0	0	0
92	12.00	0	200	0	0	0
93	12.00	0	200	0	0	0
94	12.00	100	200	0	0	0
95	12.00	0	200	20	0	0
	12.00	0	200	40	0	0
96	12.00	0	200	100	0	0
	12.00	0	200	100	0	0
97	12.00	0	200	0	0	0
98	12.00	0	200	0	0	0
99	12.00	0	200	0	0	0
100	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
101	12.00	0	200	0	0	0
	24.00	0	400	0	0	0

TABLE 17
MITE/INSECT SCREEN

COMPOUND EX. NO.	CRW RATE PPM	CRW RESULTS %	SAW SM & MA RATE PPM	SAW RESULTS %	SM RESULTS %	MA RESULTS %
102	12.00	0	200	0	0	0
	24.00	0	400	50	0	0
103	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
104	12.00	0	200	0	0	0
	24.00	0	400	60	0	0
105	12.00	0	200	30	100	80
	24.00	0	400	0	0	50
106	24.00	0	400	0	0	0
107	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
108	12.00	0	200	0	0	0
109	24.00	0	400	0	0	0
110	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
111	12.00	0	200	20	90	0
	24.00	0	400	20	80	0
112	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
113	12.00	0	200	100	40	0
	24.00	100	400	70	0	0
114	24.00	0	400	70	100	30
115	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
116	12.00	0	200	0	0	0
117	12.00	0	200	0	0	0
	12.00	0	200	0	0	0
118	12.00	0	200	0	0	0
119	12.00	0	200	0	0	0
120	12.00	0	200	0	0	0
121	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
122	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
123	12.00	0	200	0	0	0
124	24.00	0	400	0	0	0
	12.00	0	200	0	0	0

TABLE 17
MITE/INSECT SCREEN

COMPOUND EX. NO.	CRW RATE PPM	CRW RESULTS %	SM & MA RATE PPM	SAW RESULTS %	SM RESULTS %	MA RESULTS %
125	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
126	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
127	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
128	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
129	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
130	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
131	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
132	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
133	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
134	24.00	0	400	0	0	0
135	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
136	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
137	24.00	0	400	100	80	80
138	24.00	0	400	0	0	0
139	12.00	0	200	0	0	0
140	24.00	0	400	60	0	0
	12.00	0	200	0	0	0
141	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
142	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
143	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
144	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
145	24.00	0	400	0	0	0
	12.00	0	200	0	0	0

TABLE 17
MITE/INSECT SCREEN

COMPOUND EX. NO.	CRW RATE PPM	CRW RESULTS %	SAW SM & MA RATE PPM	SAW RESULTS %	SM RESULTS %	MA RESULTS %
146	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
147	12.00	0	200	0	0	0
148	12.00	0	200	0	0	0
149	12.00	0	200	0	0	0
150	12.00	0	200	0	0	0
	12.00	0	200	0	0	0
151	12.00	0	200	0	0	0
152	12.00	0	200	0	0	0
	12.00	0	200	0	0	0
153	12.00	0	200	0	0	0
154	12.00	0	200	0	0	0
	12.00	0	200	0	0	0
155	12.00	0	200	0	0	0
156	12.00	0	200	0	0	0
	12.00	0	200	0	0	0
157	24.00	0	400	100	80	0
158	12.00	0	200	0	0	0
159	12.00	0	200	0	0	0
160	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
161	24.00	40	400	0	0	80
	12.00	0	200	0	0	0
162	12.00	0	200	0	0	0
163	12.00	0	200	0	0	0
164	12.00	0	200	0	0	0
165	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
166	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
167	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
168	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
169	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
170	12.00	0	200	0	0	0
171	12.00	0	200	0	0	0

TABLE 17
MITE/INSECT SCREEN

COMPOUND EX. NO.	CRW RATE PPM	CRW RESULTS %	SAW SM & MA RATE PPM	SAW RESULTS %	SM RESULTS %	MA RESULTS %
172	12.00	0	200	0	0	0
173	12.00	0	200	0	0	0
174	12.00	0	200	0	0	0
175	12.00	0	200	0	0	0
176	12.00	0	200	0	0	0
177	12.00	0	200	0	0	0
	24.00	100	400	0	0	0
178	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
179	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
180	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
181	12.00	0	200	0	0	0
182	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
183	12.00	0	200	0	0	0
184	12.00	0	200	0	0	0
185	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
186	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
187	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
188	24.00	0	400	0	0	0
189	12.00	0	200	0	0	0
190	12.00	0	200	0	0	0
191	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
192	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
193	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
194	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
195	24.00	0	400	0	0	0
196	24.00	0	400	0	100	100
197	24.00	0	400	80	90	80

TABLE 17
MITE/INSECT SCREEN
SAW

COMPOUND EX. NO.	CRW RATE PPM	CRW RESULTS %	SM & MA RATE PPM	SAW RESULTS %	SM RESULTS %	MA RESULTS %
198	24.00	0	400	0	90	80
199	24.00	100	400	0	0	0
200	24.00	0	400	50	100	100
	12.00	0	200	0	100	100
201	12.00	0	200	0	80	100
	24.00	0	400	0	80	100
202	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
203	12.00	0	200	10	0	100
	24.00	0	400	0	0	90
204	12.00	0	200	0	0	0
	24.00	0	400	100	0	50
205	24.00	0	400	0	0	0
206	24.00	0	400	0	0	0
207	12.00	0	200	0	0	0
208	12.00	0	200	0	10	10
209	12.00	0	200	10	0	0
	12.00	0	200	100	0	40
210	12.00	0	200	0	0	0
211	12.00	0	200	0	10	40
212	12.00	0	200	0	0	0
213	12.00	0	200	0	0	0
214	24.00	0	400	0	0	0
215	24.00	0	400	0	100	100
216	24.00	100	400	0	0	0
217	24.00	0	400	0	0	0
218	24.00	0	400	100	0	0
219	12.00	0	200	0	0	0
220	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
221	24.00	0	400	0	90	80
	12.00	40	200	0	90	90
222	24.00	0	400	0	0	40
	12.00	0	200	0	0	50
223	24.00	0	400	0	0	100
	12.00	80	200	0	0	80
224	24.00	0	400	0	0	0
225	24.00	0	400	0	0	0

TABLE 17
MITE/INSECT SCREEN

COMPOUND EX. NO.	CRW RATE PPM	CRW RESULTS %	SAW SM & MA RATE PPM	SAW RESULTS %	SM RESULTS %	MA RESULTS %
226	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
227	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
228	12.00	0	200	0	0	0
	24.00	0	400	0	0	80
229	12.00	0	200	0	50	50
	24.00	0	400	0	0	0
230	12.00	0	200	0	100	90
	24.00	0	400	0	80	0
231	12.00	0	200	0	90	0
	24.00	0	400	0	40	50
232	24.00	0	400	30	80	40
	12.00	0	200	0	100	70
233	12.00	0	200	0	100	50
	24.00	0	400	0	80	80
234	12.00	0	200	60	50	50
	24.00	0	400	0	30	100
235	24.00	0	400	0	0	50
	12.00	0	200	80	0	0
236	24.00	40	400	0	0	30
	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
237	24.00	0	400	0	100	0
	12.00	0	200	0	0	0
238	24.00	0	400	100	0	0
	12.00	0	200	0	100	100
239	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
240	24.00	0	400	0	0	0
241	24.00	0	400	0	0	0
242	24.00	0	400	0	0	0
	12.00	0	200	0	0	0
243	24.00	0	400	0	0	0
244	12.00	0	200	0	0	40
245	12.00	0	200	0	0	0
246	12.00	0	200	0	0	0

TABLE 17
MITE/INSECT SCREEN

COMPOUND EX. NO.	CRW RATE PPM	CRW RESULTS %	SAW SM & MA RATE PPM	SAW RESULTS %	SM RESULTS %	MA RESULTS %
247	24.00	0	400	50	0	0
	12.00	0	200	20	90	0
248	24.00	0	400	0	0	0
249	24.00	0	400	0	0	0
250	24.00	0	400	0	0	0
251	12.00	0	200	0	0	0
252	24.00	0	400	0	90	100
	12.00	0	200	0	90	100
253	24.00	0	400	0	100	100
	12.00	0	200	0	100	90
254	24.00	0	400	0	0	0
255	24.00	0	400	0	0	0
256	24.00	100	400	100	0	0
257	24.00	0	400	0	0	0
258	24.00	0	400	0	90	100
259	24.00	0	400	0	80	80
	12.00	0	200	0	100	90
260	24.00	40	400	40	0	0
	12.00	0	200	100	100	100
261	24.00	100	400	80	50	100
	12.00	0	200	100	90	100
262	12.00	0	200	0	100	100
	24.00	0	400	0	100	100
263	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
264	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
265	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
266	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
267	12.00	0	200	0	40	20
	24.00	0	400	0	100	100
268	12.00	0	200	0	0	0
	24.00	0	400	0	80	0
269	12.00	0	200	0		30
	24.00	40	400	0	0	0

TABLE 17
MITE/INSECT SCREEN

COMPOUND EX. NO.	CRW RATE PPM	CRW RESULTS %	SAW SM & MA RATE PPM	SAW RESULTS %	SM RESULTS %	MA RESULTS %
270	12.00	0	200	20	0	0
	24.00	0	400	0	80	0
271	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
272	12.00	0	200	0	0	0
	24.00	0	400	0	20	0
273	24.00	0	400	0	0	0
274	12.00	0	200	0	100	100
	24.00	0	400	0	0	100
275	12.00	0	200	0	0	90
	24.00	0	400	0	60	100
276	12.00	0	200	0	0	0
	24.00	0	400	0	60	80
277	24.00	0	400	0	0	0
278	12.00	0	200	0	60	90
	24.00	0	400	100	0	0
279	12.00	0	200	0	0	0
	24.00	0	400	0	0	80
280	12.00	0	200	60	0	0
	24.00	0	400	0	0	0
281	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
282	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
283	12.00	0	200	0	0	80
	24.00	0	400	0	80	0
284	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
285	12.00	0	200	0	40	80
	24.00	0	400	0	0	0
286	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
287	12.00	0	200	0	0	80
	24.00	0	400	0	0	0
288	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
289	12.00	0	200	0	0	0
	24.00	0	400	0	0	0

TABLE 17
MITE/INSECT SCREEN

COMPOUND EX. NO.	CRW RATE PPM	CRW RESULTS %	SAW SM & MA RATE PPM	SAW RESULTS %	SM RESULTS %	MA RESULTS %
290	12.00	0	200	0	80	80
	24.00	0	400	0	0	0
291	12.00	0	200	0	0	100
	24.00	0	400	0	0	0
292	12.00	0	200	0	0	30
	24.00	0	400	0	0	0
293	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
294	12.00	0	200	0	0	0
	24.00	0	400	0	0	0
295	12.00	0	200	0	0	0
	24.00	0	400	0	0	0

Field Trials

4-[2-[4-(t-Butyl)phenyl]ethoxy]-8-fluoroquinoline (Example 221) was evaluated in a number of field trials. The following table reports the host plants on which it was tested and the pest species against which it showed activity.

TABLE 18

HOST	PEST
alfalfa (Lucerne)	pea aphid, potato leaf hopper, tarnished plant bug, green cloverworm
apples	mites, apple aphid, European red mite, green peach aphid, white apple leafhopper, apple rust mite, rosy apple aphid
azaleas	greenhouse thrip
bean, faba broad	bean aphid
broccoli	twospotted spider mite
cotton	cotton aphid
grape (European)	grape thrip, grape leafhopper

TABLE 18 (cont.)

HOST	PEST
hops	Dawson-hop aphid
pea, garden (English)	pea aphid
pecan nut	yellow hickory aphid
privet	thrip
sugar beet	green peach aphid
wheat	wheat aphid

Compositions

The compounds of this invention are applied in the form of compositions which are important embodiments of the invention, and which comprise a compound of this invention and a phytologically-acceptable inert carrier. The compositions are either concentrated formulations which are dispersed in water for application, or are dust or granular formulations which are applied without further treatment. The compositions are prepared according to procedures and formulae which are conventional in the agricultural chemical art, but which are novel and important because of the presence therein of the compounds of this invention. Some description of the formulation of the compositions will be given, however, to assure that agricultural chemists can readily prepare any desired composition.

The dispersions in which the compounds are applied are most often aqueous suspensions or emulsions prepared from concentrated formulations of the compounds. Such water-soluble, water-suspendable or emulsifiable formulations are either solids usually known as wettable powders, or liquids usually known as emulsifiable concentrates or aqueous suspensions. Wettable powders, which may be compacted to form water dispersible granules, comprise an intimate mixture of the active compound, an inert carrier and surfactants. The concentration of the active compound is usually from about 10% to about 90% by weight. The inert carrier is usually chosen from among the attapulgite clays, the montmorillonite clays, the diatomaceous

earths, or the purified silicates. Effective surfactants, comprising from about 0.5% to about 10% of the wettable powder, are found among the sulfonated lignins, the condensed naphthalenesulfonates, the naphthalenesulfonates, the alkylbenzenesulfonates, the alkyl sulfates, and nonionic surfactants such as ethylene oxide adducts of alkyl phenols.

Emulsifiable concentrates of the compounds comprise a convenient concentration of a compound, such as from about 50 to about 500 grams per liter of liquid, equivalent to about 10% to about 50%, dissolved in an inert carrier which is either a water miscible solvent or a mixture of water-immiscible organic solvent and emulsifiers. Useful organic solvents include aromatics, especially the xylenes, and the petroleum fractions, especially the high-boiling naphthalenic and olefinic portions of petroleum such as heavy aromatic naphtha. Other organic solvents may also be used, such as the terpenic solvents including rosin derivatives, aliphatic ketones such as cyclohexanone, and complex alcohols such as 2-ethoxyethanol. Suitable emulsifiers for emulsifiable concentrates are chosen from conventional nonionic surfactants, such as those mentioned above.

Aqueous suspensions comprise suspensions of water-insoluble compounds of this invention, dispersed in an aqueous vehicle at a concentration in the range from about 5% to about 50% by weight. Suspensions are prepared by finely grinding the compound, and vigorously mixing it into a vehicle comprised of water and surfactants chosen from the same types discussed above. Inert

ingredients, such as inorganic salts and synthetic or natural gums, may also be added, to increase the density and viscosity of the aqueous vehicle. It is often most effective to grind and mix the compound at the same time by preparing the aqueous mixture, and homogenizing it in an implement such as a sand mill, ball mill, or piston-type homogenizer.

The compounds may also be applied as granular compositions, which are particularly useful for applications to the soil. Granular compositions usually contain from about 0.5% to about 10% by weight of the compound, dispersed in an inert carrier which consists entirely or in large part of clay or a similar inexpensive substance. Such compositions are usually prepared by dissolving the compound in a suitable solvent, and applying it to a granular carrier which has been pre-formed to the appropriate particle size, in the range of from about 0.5 to 3 mm. Such compositions may also be formulated by making a dough or paste of the carrier and compound, and crushing and drying to obtain the desired granular particle size.

Dusts containing the compounds are prepared simply by intimately mixing the compound in powdered form with a suitable dusty agricultural carrier, such as kaolin clay, ground volcanic rock and the like. Dusts can suitably contain from about 1% to about 10% of the compound.

It is equally practical, when desirable for any reason, to apply the compound in the form of a solution in an appropriate organic solvent, usually a bland petroleum oil, such as the spray oils, which are widely used in agricultural chemistry.

Insecticides and miticides are generally applied in the form of a dispersion of the active ingredient in a liquid carrier. It is conventional to refer to application rates in terms of the concentration of active ingredient in the carrier. The most widely used carrier is water.

The compounds of the invention can also be applied in the form of an aerosol composition. In such compositions the active compound is dissolved or dispersed in an inert carrier, which is a pressure-generating propellant mixture. The aerosol composition is packaged in a container from which the mixture is dispensed through an atomizing valve. Propellant mixtures comprise either low-boiling halocarbons, which may be mixed with organic solvents, or aqueous suspensions pressurized with inert gases or gaseous hydrocarbons.

The actual amount of compound to be applied to loci of insects and mites is not critical and can readily be determined by those skilled in the art in view of the examples above. In general, concentrations of from 10 ppm to 5000 ppm of compound are expected to provide good control. With many of the compounds, concentrations of from 100 to 1500 ppm will suffice. For field crops, such as soybeans and cotton, a suitable application rate for the compounds is about 0.5 to 1.5 lb/A, typically applied in 50 gal/A of spray formulation containing 1200 to 3600 ppm of compound. For citrus crops, a suitable application rate is from about 100 to 1500 gal/A spray formulation, which is a rate of 100 to 1000 ppm.

The locus to which a compound is applied can be any locus inhabited by an insect or arachnid, for example, vegetable crops, fruit and nut trees, grape vines, and ornamental plants. Inasmuch as many mite species are specific to a particular host, the foregoing list of mite species provides exemplification of the wide range of settings in which the present compounds can be used.

Because of the unique ability of mite eggs to resist toxicant action, repeated applications may be desirable to control newly emerged larvae, as is true of other known acaricides.

The following formulations of compounds of the invention have been prepared, and are typical of compositions useful in the practice of the present invention.

A. Aqueous Suspension

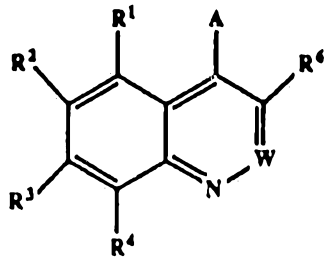
8-Fluoro-N-[2-(2-naphthyl)ethyl]-4-quinolinamine	12.5%
"TERGITOL TMN-6" (nonionic surfactant)	1.0%
"ZEOSYL 200" (silica)	1.0%
"AF-100" (silicon based antifoam agent)	0.2%
2% xanthan solution	10.0%
"MAKON 10" (10 moles ethyleneoxide nonylphenol surfactant)	9.0%
tap water	66.3%

B. Emulsifiable Concentrate

4-[2-[4-(t-Butyl)phenyl]ethoxy]-8-fluoroquinoline	12.4%
"EXXON 200" (naphthalene solvent)	83.6%
"TOXIMUL H" (nonionic/anionic surfactant blend)	2.0%
"TOXIMUL D" (nonionic/anionic surfactant blend)	2.0%

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A compound of the formula (1)



(1)

wherein:

R^1 to R^4 are independently

H, halo, (C_1-C_4) alkyl, branched (C_3-C_4) alkyl, halo (C_1-C_4) alkyl, (C_1-C_4) alkoxy, NO_2, or NH_2, at least two of R^1 to R^4 being H,

or one of R^2 to R^4 is $-NR^7$-Y-Ar or O-Y-Ar and the rest of R^1 to R^4 are H;

W is ~~N, or~~ CR^5;

R^5 is H, CH_3, Cl, O-Y-Ar, or $-NR^7$-Y-Ar;

R^6 is H, CH_3, Cl or Br;

A is -O-Alk or -X-Y-Ar;

Alk is a C_2-C_{18} saturated or unsaturated hydrocarbon chain, straight chain or branched, optionally substituted with halo, halo (C_1-C_4) alkoxy, (C_3-C_8) cycloalkyl, hydroxy, or acetyl;

X is O, NR^7, or CR^8R^9, provided that if one of R^2 to R^5 is NR^7-Y-Ar or O-Y-Ar, then X-Y-Ar is an identical group;

R^7 is H, (C_1-C_4) alkyl, or acetyl;

R^8 and R^9 are independently H, (C_1-C_4) alkyl, (C_1-C_4) acyl, halo, or OH, or R^8 and R^9 combine to form a saturated or unsaturated carbocyclic ring comprising three to seven carbon atoms;

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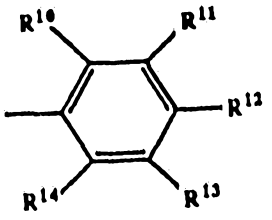
Y is an alkylene chain 2 to 8 carbon atoms long, optionally including an O, S, SO, SO_2, or NR^7 group or a saturated or unsaturated carbocyclic ring comprising three to seven carbon atoms, or substituted with (C_1-C_3) alkyl, (C_2-C_4) alkenyl, phenyl, (C_3-C_8) cycloalkyl, hydroxy, halo, or (C_1-C_4) acyl; and

Ar is
1,3-benzodioxolyl
fluorenyl,
pyridyl,
imidazolyl,
indolyl,
thienyl, optionally substituted with CH_3 or Cl,
thiazolyl,
cyclopentyl,
1-methylcyclopentyl,
cyclohexenyl (hexahydrophenyl),
cyclohexyl (tetrahydrophenyl),
naphthyl,
dihydronaphthyl,
tetrahydronaphthyl,
decahydronaphthyl, or
a group of the formula (2):



(2)

where

R^{10} to R^{14} are independently H, halo, I, (C_1-C_{10}) alkyl, branched (C_3-C_6) alkyl, halo (C_1-C_4) alkyl, (C_1-C_4) alkoxy, halo (C_1-C_4) alkoxy, phenoxy, substituted phenoxy, phenylthio, substituted phenylthio, phenyl, substituted phenyl, NO_2, NH_2, acetoxy, OH, CN, or $SiR^{15}R^{16}R^{17}$, $OSir^{15}$, R^{16}, R^{17}, where R^{15}, R^{16}, and R^{17} are independently (C_1-C_4) alkyl or (C_3-C_4) branched alkyl provided that unless each of R^{10} to R^{14} is F, CH_3, or H, then at least two of R^{10} to R^{14} are H;

or an acid addition salt of a compound of formula (1)

or an N-oxide of a compound of formula (1) when W is CR^5

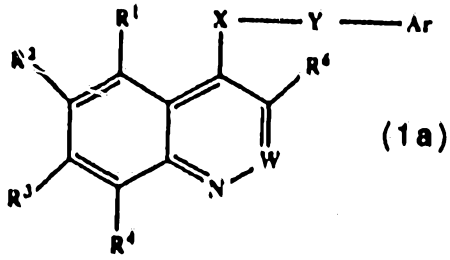
provided that the following compounds are excluded:

1) N-[4-(4-chlorophenyl)butyl]-7-chloro-4-quinolinamine; and

2) N-(2-phenylethyl)-4-quinolinamine, and

provided that if A is NR^7-Y-Ar, then Y is -$(CH_2)_2$- and Ar is a group of formula (2) wherein four of R^{10} to R^{14} are H and one of R^{10} to R^{14} is Cl, (C_1-C_4) alkyl, halo (C_1-C_4) alkyl, branched (C_3-C_6) alkyl, (C_1-C_4) alkoxy, halo (C_1-C_4) alkoxy, phenyl, substituted phenyl, phenoxy, or substituted phenoxy.

2. A compound of formula (1a):



(1a)

wherein:

R^1 to R^4 are independently

H, halo, (C_1-C_4) alkyl, branched (C_3-C_4) alkyl, halo (C_1-C_4) alkyl, (C_1-C_4) alkoxy, NO_2, or NH_2, at least two of R^1 to R^4 being H,

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or one of R^2 to R^4 is $-NR^7-Y-Ar$ or $O-Y-Ar$ and the rest of R^1 to R^4 are H;

W is ~~N, or~~ CR^5;

R^5 is H, CH_3, Cl, $O-Y-Ar$, or $-NR^7-Y-Ar$;

R^6 is H, CH_3, Cl or Br;

X is O, NR^7, or CR^8R^9, provided that if one of R^2 to R^5 is NR^7-Y-Ar or $O-Y-Ar$, then $X-Y-Ar$ is an identical group;

R^7 is H, (C_1-C_4) alkyl, or acetyl;

R^8 and R^9 are independently H, (C_1-C_4) alkyl, or (C_1-C_4) acyl or R^8 and R^9 combine to form a saturated or unsaturated carbocyclic ring comprising three to seven carbon atoms;

Y is an alkylene chain 2 to 6 carbon atoms long, optionally including a saturated or unsaturated carbocyclic ring comprising three to seven carbon atoms, or substituted with (C_1-C_3) alkyl, phenyl, (C_3-C_8) cycloalkyl, hydroxy, halo, or acetyl; and

Ar is

1,3-benzodioxolyl

fluorenyl,

pyridyl,

imidazolyl,

indolyl,

thienyl, optionally substituted with CH_3 or Cl,

thiazolyl,

cyclohexenyl (hexahydrophenyl),

cyclohexyl (tetrahydrophenyl),

naphthyl,

dihydronaphthyl,

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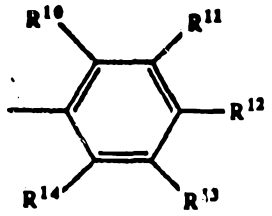
tetrahydronaphthyl,
decahydronaphthyl, or
a group of the formula (2):



(2)

where

R^{10} to R^{14} are independently H, halo, I, (C_1-C_{10}) alkyl, branched (C_3-C_6) alkyl, halo (C_1-C_4) alkyl, (C_1-C_4) alkoxy, halo (C_1-C_4) alkoxy, phenoxy, substituted phenoxy, phenylthio, substituted phenylthio, phenyl, substituted phenyl, NO_2, OH or CN, provided that unless each of R^{10} to R^{14} is F, CH_3, or H, then at least two of R^{10} to R^{14} are H;

or an acid addition salt of a compound of formula (1), or an N-oxide of a compound of formula (1) when W is CR^5;

provided that the following compounds are excluded:

1) N-[4-(4-chlorophenyl)butyl]-7-chloro-4-quinolinamine; and
2) N-(2-phenylethyl)-4-quinolinamine, and

provided that if X is NR^7, then Y is $-(CH_2)_2-$ and Ar is a group of formula (2) wherein four of R^{10} to R^{14} are H and one of R^{10} to R^{14} is Cl, (C_1-C_4) alkyl,halo (C_1-C_4) alkyl, branched (C_3-C_6) alkyl, (C_1-C_4) alkoxy, halo (C_1-C_4) alkoxy, phenyl, substituted phenyl, phenoxy, or substituted phenoxy.

3. A compound of claim 1 or 2 wherein
A is -X-Y-Ar,
Y is $-(CH_2)_2-$; and

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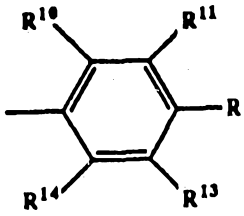
Ar is a group of formula (2)



(2)

wherein four of R^{10} to R^{14} are H and one of R^{10} to R^{14} is Cl, (C_1-C_4) alkyl, halo (C_1-C_4) alkyl, branched (C_3-C_6) alkyl, (C_1-C_4) alkoxy, halo (C_1-C_4) alkoxy, phenyl, substituted phenyl, phenoxy, or substituted phenoxy.

4. A compound of any one of claims 1 to 3 wherein R^4 is F.

5. A fungicidal combination comprising at least 1% by weight of a compound of claim 1, or of N-(2-phenylethyl)-4-quinolinamine or N-[4-(4-chlorophenyl)-butyl]-7-chloro-4-quinolinamine in combination with a second fungicidal compound.

6. A fungicidal composition comprising a disease inhibiting and phytologically acceptable amount of a compound of claim 1 in combination with a phytologically-acceptable carrier.

7. A fungicidal method which comprises applying to the locus of a plant pathogen a fungicidally effective but non-phytotoxic amount of a compound of claim 1, or of N-[4-(4-chlorophenyl)butyl]-7-chloro-4-quinolinamine or N-(2-phenylethyl)-4-quinolinamine.

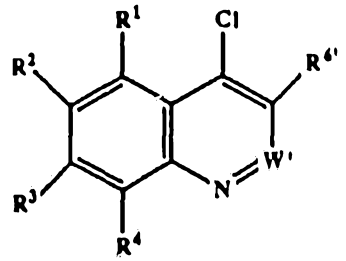
8. An insecticidal or miticidal combination which comprises at least 1% by weight of a compound of claim 1 or N-[4-(4-chlorophenyl)butyl]-7-chloro-4-quinolinamine or N-(2-phenylethyl)-4-quinolinamine in combination with a second insecticide or miticide.

9. An insecticide or miticide composition comprising an insect- or mite-inactivating amount of a compound of claim 1 in combination with a phytologically-acceptable carrier.

10. An insecticide or miticide method which comprises applying to the locus of an insect or mite an insect- or mite-inactivating amount of a compound of claim 1.

11. A process for preparing a compound of formula (1) as defined in claim 1 which comprises

(a) condensing a compound of formula (3):



(3)

where R^1 to R^4 are as previously defined, $R^{6'}$ is H or CH_3, and W' is ~~N or~~ $CR^{5'}$, where $R^{5'}$ is H, Cl, or CH_3, with an alcohol of the formula (4a or 4b):

HO-Y-Ar (4a)

HO-Alk (4b)

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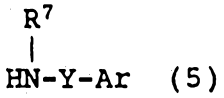
where

Y, Ar, and Alk are as previously defined to provide a compound of formula (1) wherein A is O-Y-Ar or O-Alk; or

(b) condensing a compound of formula (3) with an amine of the formula (5)



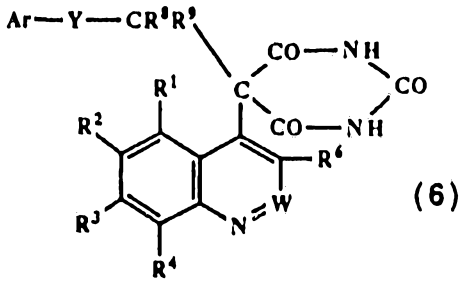
(5)

where

R^7 is H or (C_1-C_4) alkyl, and Y and Ar are as previously defined to provide a compound of formula (1) wherein A is -NR^7-Y-Ar; or

(c) reacting an amine of formula (1) where R^7 is H, with acetyl chloride or acetic anhydride to provide a compound of formula (1) wherein A is NR^7-Y-Ar and R^7 is acetyl; or

(d) hydrolyzing and decarboxylating a compound of the formula (6)



(6)

to provide a compound of formula (1) wherein A is -CR^8R^9-Y-Ar; or

(e) halogenating a compound of formula (1) wherein R^6 is H with $POCl_3/PCl_5$ to provide a compound of formula (1) wherein R^6 is Cl; or

(f) reacting a compound of formula (1) wherein R^6 is H with Br_2 in acetic acid to provide a compound of formula (1) wherein R^6 is Br; or

(g) oxidizing a compound of formula (1) wherein W is CR^5 to provide the corresponding N-oxide.

12. Compounds of formula (1) or processes for their preparation, substantially as hereinbefore described with reference to the Examples.

DATED this 23rd day of March, 1992
Eli Lilly and Company
By Its Patent Attorneys
DAVIES COLLISON CAVE

AUSTRALIAN PATENT OFFICE