

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 07-029888- -00003-0000

Fecha: 2009-02-24 16:25:35 Dep. 2020 NUECREACIONE
Tra. 11 PATENTEYII Eve: 378 FASENACIONALI
Act. 538 PETICION Folios: 2

Señora

Alix Carmenza Céspedes de Verge

Jefe de División de Nuevas Creaci

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

E. S. D.

DPT/LM

Referencia: Expediente No. 07.029.888

Solicitud de Patente de Invención titulada: "Mezclas fungicidas de derivados de tiofeno"

Solicitante: E.I, Du pont de Nemours and Company

SOLICITUD DE EXAMEN DE PATENTABILIDAD SEGÚN EL ARTÍCULO 44 DE LA DECISIÓN

486. GACETA NO. 595

ÁLVARO CORREA ORDÓÑEZ, mayor de edad y vecino de Bogotá D.C., identificado según aparece al pie de mi firma, en mi condición de apoderado de la sociedad arriba mencionada, solicito que se examine la invención de la referencia según los requisitos de patentabilidad previstos en la Decisión 486 de la Comisión de la Comunidad Andina de Naciones. Adjunto recibo de caja por valor de Patente \$452.000 para cubrir la tasa correspondiente según la Resolución 55819 del 26 de diciembre de 2008.

Atentamente,


ÁLVARO CORREA ORDÓÑEZ
C.C.No.79.143.366 de Usaquén
T.P.20.281

Anexo: Recibo de caja No. 09-12,238 por valor de Patente \$452.000

2009/003

102

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

NIT : 800176089-2

RECIBO OFICIAL DE CAJA : 09 - 12,238
FECHA : FEBRERO 16 DE 2009

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 07-029888- -00003-0000

Fecha: 2009-02-24 16:25:35 Dep. 2020 NUECREACIONE
Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI
Act. 538 PETICION Folios: 2

***** CONSIGNACION *****

POSITANTE	TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PGO	Vr. PAGO
BAKER & MCKENZIE	CONSIGNACION	BANCO DE BOGOTA	062754387	14468145	13/02/2009	99,962,000.00

***** CONCEPTO *****

CANT.	RENTISTICO	CONCEPTO	TOTAL CONCEPTO
1	50005-01-01	SOLICITUDES	
		85 EXAMEN DE PATENTABILIDAD DE INVEN	452,000.00
		TOTAL :	\$ 452,000.00

SON: CUATROCIENTOS CINCUENTA Y DOS MIL PESOS

RESPONSABLE : _____

RECIBO DE CAJA APLICADO AL EXPEDIENTE No. _____

DIVISIÓN DE NUEVAS CREACIONES

RADICACIÓN EXPEDIENTE No. 07-29888

EL EXTRACTO DE LA PRESENTE SOLICITUD DE **PATENTE DE INVENCION**

FUE PUBLICADO EN LA GACETA DE PROPIEDAD INDUSTRIAL No **595** DE

FECHA **29 DE AGOSTO DE 2008** EL TÉRMINO HÁBIL SEÑALADO POR LA

LEY EXPIRA EL **26 DE NOVIEMBRE DE 2008**

NOTA: Dentro del plazo de los seis (6) meses siguientes a partir de la fecha de publicación en la gaceta de Propiedad Industrial, deberá solicitar y cancelar el examen de patentabilidad so pena de que la solicitud caiga en abandono, de acuerdo con lo establecido en el Artículo 44 de la Decisión 486/2000.

SE PRESENTARON OPOSICIONES POR PARTE DE TERCEROS.

SI _____

NO X



US005747518A

United States Patent [19]

Yoshikawa et al.

[11] **Patent Number:** 5,747,518[45] **Date of Patent:** May 5, 1998

[54] **SUBSTITUTED THIOPHENE DERIVATIVE
AND AGRICULTURAL AND
HORTICULTURAL FUNGICIDE
CONTAINING THE SAME AS ACTIVE
INGREDIENT**

[75] **Inventors:** Yukihiro Yoshikawa; Kanji Tomiya;
Hiroyuki Katsuta; Hideo Kawashima;
Osamu Takahashi; Shunichi Inami;
Yuji Yanase; Junro Kishi; Hitoshi
Shimotori; Naofumi Tomura, all of
Chiba-ken, Japan

[73] **Assignee:** Mitsui Toatsu Chemicals, Inc., Tokyo,
Japan

[21] **Appl. No.:** 627,929

[22] **Filed:** Apr. 3, 1996

[30] **Foreign Application Priority Data**

Apr. 11, 1995 [JP] Japan 7-085601
Dec. 27, 1995 [JP] Japan 7-340480

[51] **Int. Cl.⁶** A61K 31/415; A61K 31/425;
A61K 31/38; A61K 31/44

[52] **U.S. Cl.** 514/403; 514/370; 514/365;
514/444; 514/445; 514/447; 514/448; 514/336;
514/255; 548/365.7; 548/200; 548/194;
549/59; 549/60; 549/61; 549/62; 549/63;
549/66; 549/69; 549/70; 549/71; 549/72;
549/73; 546/280.4

[58] **Field of Search** 548/365.7, 193,
548/194, 195, 198, 200; 549/69, 59, 60,
61, 63, 64, 66; 514/403, 447, 444, 445,
448, 365, 370, 336, 255; 546/280.4; 544/405,
406

[56] **References Cited****U.S. PATENT DOCUMENTS**

3,823,161 7/1974 Lesser 549/69

4,113,956 9/1978 Moon et al. 548/374
4,240,820 12/1980 Dickore et al. 549/69
4,472,425 9/1984 Sandmeier et al. 549/69
4,500,536 2/1985 Yosida et al. 514/397
4,767,758 8/1988 Breccia et al. 514/231.5
5,039,694 8/1991 Suzuki et al. 514/406
5,073,184 12/1991 Anthony et al. 549/69
5,330,995 7/1994 Eicken et al. 514/355
5,438,070 8/1995 Eicken et al. 514/403
5,480,897 1/1996 Eicken et al. 514/365

FOREIGN PATENT DOCUMENTS

545 099 11/1992 European Pat. Off. .
589 301 9/1993 European Pat. Off. .
639 574 8/1994 European Pat. Off. .

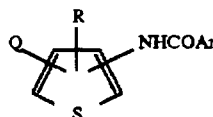
Primary Examiner—Richard L. Raymond

Assistant Examiner—Deborah Lambkin

Attorney, Agent, or Firm—Millen, White, Zelano, &
Branigan, P.C.

[57] **ABSTRACT**

The substituted thiophene derivative of the invention which is represented by the general formula (1) has a broad disease spectrum for a pathogenic fungus of various crops, exhibits an excellent controlling effect on disease such as gray mold, powdery mildew and rust in particular, and is also effective for a resistant fungus of conventional fungicides which has become a serious problem, and consequently is useful for an agricultural and horticultural fungicide.



(1)

17 Claims, No Drawings

SUBSTITUTED THIOPHENE DERIVATIVE AND AGRICULTURAL AND HORTICULTURAL FUNGICIDE CONTAINING THE SAME AS ACTIVE INGREDIENT

BACKGROUND OF THE INVENTION

1) Field of the Invention

The present invention relates to a novel substituted thiophene derivative, an agricultural and horticultural fungicide containing the same as in active ingredient and a method for controlling plant disease by the same.

2) Description of Related Art

Recently developed fungicides having selective mechanism of action differ from conventionally used, nonselective fungicides for exhibiting steady effect at low dosage. However, the recent fungicides have a problem of developing chemical tolerance and leading to reduction of efficacy. For example, a benzimidazole fungicide has a broad fungicidal spectrum and exhibits excellent effect also on gray mold disease. However, such fungicide caused a drastic reduction of efficacy due to appearance of a resistant fungus against said fungicide in the 1970's. A dicarboxyimide fungicide was focused attention as a replacement of the benzimidazole fungicide. Nevertheless, a resistant fungus also appeared against the dicarboxyimide fungicide in the 1980's. Consequently, the lack of the counter measure for controlling the resistant fungus of gray mold disease has become a serious problem in Japan and also in the world.

On the other hand, an azole fungicide has a broad fungicidal spectrum and is an excellent pesticide which exhibits efficacy at a previously unknown low dosage particularly for powdery mildew disease and rust disease of various crops and scab disease of apple and pear. However, a resistant fungus against this fungicide has recently appeared and also led to a problem of a sharp fall of the fungicide efficacy. Such occurrence of fungicide resistant fungus has become an inevitable problem for the selective fungicide, and accordingly development of a new fungicide is now an urgent subject.

Many aromatic aniline derivatives have conventionally been known to have fungicidal activity. For example, Japanese Laid-Open Patent Hei 5-221994 and 6-199803 have disclosed that various aniline derivatives have efficacy for gray mold disease. The present inventors have tested fungicidal activity against various plant-pathogenic fungi on the compounds disclosed in these patents. However, the disease control effect was low even in the case of gray mold disease and no efficacy was observed at all on powdery mildew disease and brown rust disease.

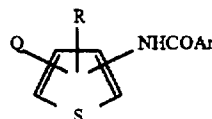
Consequently, the object of the invention is to provide a novel agricultural and horticultural fungicide which has a broad spectrum for pathogenic fungus of various crops and can also solve the resistant fungus which has become a serious problem.

SUMMARY OF THE INVENTION

As a result of an intensive research on the bioactivity of various heterocyclic amine derivatives, the present inventors have found that some kinds of aminothiophene derivative have powerful controlling effect on various plant disease and exhibit excellent controlling activity for not only a sensitive fungus but a resistant fungus of benzimidazole and dicarboxyimide fungicides, and further for the sensitive fungus and resistant fungus of an azole fungicide and that such

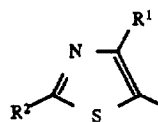
aminothiophene derivative has high safety for crops and consequently can attain the above object. Thus the present invention has been completed.

That is, the aspect of the invention is a substituted thiophene derivative represented by the general formula (1), an agricultural and horticultural fungicide comprising the same as an active ingredient and a method for controlling plant disease by the same.

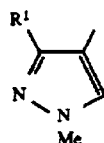


(1)

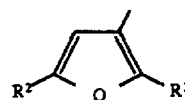
wherein Q is a hydrogen atom, fluorine atom, chlorine atom, bromine atom, iodine atom, methyl group, trifluoromethyl group, methoxy group, methylthio group, methylsulfonyl group, methylsulfoxy group, cyano group, acetyl group, nitro group, alkoxycarbonyl group or amino group; R is a straight or branched alkyl group having 1-12 carbon atoms, straight or branched halogenoalkyl group having 1-12 carbon atoms, straight or branched alkenyl group having 2-10 carbon atoms, straight or branched halogenoalkenyl group having 2-10 carbon atoms, alkoxyalkyl group having 2-12 carbon atoms, alkylthioalkyl group having 2-10 carbon atoms, cycloalkyl group having 3-10 carbon atoms, halogen substituted cycloalkyl group having 3-10 carbon atoms, or a phenyl group which can be substituted with 1-3 substituents; the substituent of said phenyl group is a hydrogen atom, alkyl group having 1-4 carbon atoms, alkenyl group having 2-4 carbon atoms, alkynyl group having 2-4 carbon atoms, cycloalkyl group having 3-6 carbon atoms, alkoxy group having 1-4 carbon atoms, halogenoalkoxy group having 1-4 carbon atoms, alkylthio group having 1-4 carbon atoms, alkylsulfoxy group having 1-4 carbon atoms, alkylsulfonyl group having 1-4 carbon atoms, halogen atom, cyano group, acyl group having 2-4 carbon atoms, alkoxycarbonyl group having 2-4 carbon atoms, amino group or amino group substituted with alkyl group having 1-3 carbon atoms; R and the group —NHCOAr are adjacent to each other; and Ar is a group represented by (A1) to (A8) below:



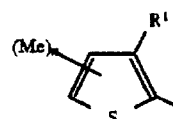
(A1)



(A2)



(A3)

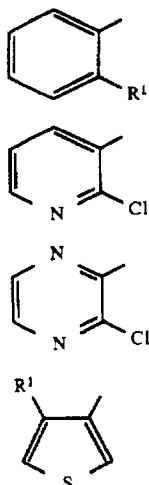


(A4)

5,747,518

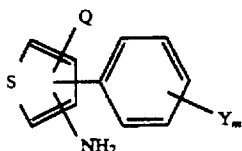
3

-continued

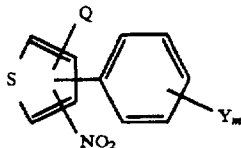


wherein R^1 is a trifluoromethyl group, difluoromethyl group, methyl group, ethyl group, chlorine atom, bromine atom or iodine atom. R^2 is a hydrogen atom, methyl group, trifluoromethyl group or amino group, and n is an integer of 0-2.

Another aspect of the invention is intermediates of the substituted thiophene derivative represented by the general formula (1), that is, an aminothiophene derivative represented by the general formula (2):



wherein Q is a hydrogen atom, fluorine atom, chlorine atom, bromine atom, iodine atom, methyl group, trifluoromethyl group, methoxy group, methylthio group, methylsulfonyl group, methylsulfoxy group, cyano group, acetyl group, nitro group, alkoxycarbonyl group or amino group; Y is a hydrogen atom, alkyl group having 1-4 carbon atoms, alkenyl group having 2-4 carbon atoms, cycloalkyl group having 3-6 carbon atoms, alkoxy group having 1-4 carbon atoms, halogenoalkoxy group having 1-4 carbon atoms, alkylthio group having 1-4 carbon atoms, alkylsulfoxy group having 1-4 carbon atoms, alkylsulfonyl group having 1-4 carbon atoms, halogen atom, cyano group, acyl group having 2-4 carbon atoms, alkoxycarbonyl group having 2-4 carbon atoms, amino group or amino group substituted with alkyl group having 1-3 carbon atoms, m is an integer of 1-3, and a phenyl group and amino group are adjacent to each other; and a nitrothiophene derivative represented by the general formula (3)



wherein Q is a hydrogen atom, fluorine atom, chlorine atom, bromine atom, iodine atom, methyl group, trifluoromethyl group, methoxy group, methylthio group, methylsulfonyl group, methylsulfoxy group, cyano group, acetyl group, nitro group, alkoxycarbonyl group or amino group, Y is a hydrogen atom, alkyl group having 1-4 carbon atoms, alkenyl group having 2-4

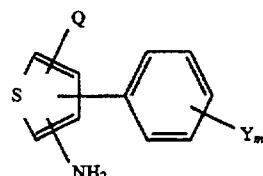
4

- (A5) carbon atoms, cycloalkyl group having 3-6 carbon atoms, alkoxy group having 1-4 carbon atoms, halogenoalkoxy group having 1-4 carbon atoms, alkylthio group having 1-4 carbon atoms, alkylsulfoxy group having 1-4 carbon atoms, alkylsulfonyl group having 1-4 carbon atoms, halogen atom, cyano group, acyl group having 2-4 carbon atoms, alkoxycarbonyl group having 2-4 carbon atoms, amino group or amino group substituted with alkyl group having 1-3 carbon atoms, m is an integer of 1-3, and a phenyl group and nitro group are adjacent to each other.
- (A6)
- (A7)

DETAILED DESCRIPTION OF THE INVENTION

- Examples of the substituent R of the thiophene derivative represented by the general formula (1) in the invention specifically include isopropyl, sec-butyl, tert-butyl, 1-methylbutyl, 1-methylhexyl, 1-ethylpropyl, 1,2-dimethylbutyl, 1,3-dimethylbutyl, 1-ethyl-3-methylbutyl, 1,2-dimethylhexyl, 1,3-dimethyloctyl, 3-methylbutyl, 3-methylpentyl, 4-methyloctyl, 1,2,2,3-tetramethylbutyl, 1,3,3-trimethylbutyl, 1,2,3-trimethylbutyl, 1,3-dimethylpentyl, 1,3-dimethylhexyl, 5-methyl-3-hexyl, 2-methyl-4-heptyl, 2,6-dimethyl-4-heptyl, 1-methyl-2-cyclopropylethyl, n -butyl, n -hexyl and other straight or branched alkyl groups having 1-12 carbon atoms; 3-chloro-1-methylbutyl, 2-chloro-1-methylbutyl, 1-chlorobutyl, 3,3-dichloro-1-methylbutyl, 3-chloro-1-methylbutyl, 1-methyl-3-trifluoromethylbutyl, 3-methyl-1-trifluoromethylbutyl and other straight or branched halogenoalkyl groups having 1-12 carbon atoms; propenyl, 1-methyl-1-propenyl, 1-ethyl-1-butenyl, 2,4-dimethyl-1-pentenyl, 2,4-dimethyl-2-pentenyl and other straight or branched alkenyl groups having 2-10 carbon atoms; 2-chloro-1-methyl-1-butenyl and other halogenoalkenyl groups having 2-10 carbon atoms; cyclopropyl, cyclohexyl, 2-ethylcyclohexyl, 2-isopropylcyclohexyl and other cycloalkyl groups having 3-10 carbon atoms; methoxymethyl, 1-methoxyethyl, 1-ethoxyethyl, 1-methoxypropyl, 1-isopropoxyethyl and other alkoxyalkyl groups having 2-10 carbon atoms; methylthiomethyl, 1-methylthioethyl, 1-ethylthioethyl, 1-methylthiopropyl, 1-isopropylthioethyl and other alkylthioalkyl groups having 2-10 carbon atoms; 2-chlorocyclohexyl, 3-chlorocyclohexyl and other halogen substituted cycloalkyl groups having 3-10 carbon atoms; and phenyl groups which can be substituted with 1-3 substituents. Exemplary substituents of the phenyl group specifically include a hydrogen atom, methyl, ethyl, propyl, isopropyl, sec-butyl, tert-butyl and other alkyl groups having 1-4 carbon atoms; vinyl, isopropenyl, 1-methylpropenyl and other alkenyl groups having 2-4 carbon atoms; ethynyl, 1-propynyl and other alkynyl groups having 2-4 carbon atoms; cyclopropyl, cyclopentyl, cyclohexyl and other cycloalkyl groups having 3-6 carbon atoms; methoxy, ethoxy, butoxy and other alkoxy groups having 1-4 carbon atoms; trifluoromethoxy, 1,1,2,2,2-pentafluoroethoxy and other halogenoalkoxy groups having 1-4 carbon atoms; methylthio, ethylthio and other alkylthio groups having 1-4 carbon atoms; methylsulfoxy, butylsulfoxy and other alkylsulfoxy groups having 1-4 carbon atoms; methylsulfonyl, isopropylsulfonyl and other alkylsulfonyl groups having 1-4 carbon atoms; a halogen atom such as fluorine, chlorine, bromine and iodine, cyano group; acetyl, propionyl and other acyl groups having 2-4 carbon atoms; methoxycarbonyl, ethoxycarbonyl and other alkoxycarbonyl groups having 2-4 carbon atoms; an amino group; and dimethylamino, diethylamino, propylamino and other substituted amino groups having alkyl groups of 1-3 carbon

TABLE 4-continued

(phenyl-substituted aminothiophene derivatives)					
(2)					
					
Ym	Position of amino group	Position of phenyl group	M.P. (°C.)	¹ H-NMR(CDCl ₃ , δ-value, J:Hz)	
2,4-Cl ₂	3-	2-	oil	3.60(2H, brs), 6.65(1H, d, J=5.1), 7.22(1H, d, J=5.1), 7.28(1H, dd, J=8.1, 2.2), 7.40(1H, d, J=8.1), 7.50(1H, d, J=2.2)	
3,4-Cl ₂	3-	2-	oil	3.82(2H, brs), 6.64(1H, d, J=5.1), 7.15(1H, d, J=5.1), 7.35(1H, dd, J=8.1, 2.2), 7.45(1H, d, J=8.1), 7.62(1H, d, J=2.2)	
3,5-Cl ₂	3-	2-	oil	3.86(2H, brs), 6.64(1H, d, J=5.9), 7.16(1H, d, J=5.9), 7.22(1H, t, J=1.5), 7.41(2H, d, J=1.5)	
3,4-F ₂	3-	2-	oil	3.77(2H, brs), 6.64(1H, d, J=5.9), 7.12(1H, d, J=5.9), 7.15-7.24(2H, m), 7.31-7.38(2H, m)	
3,5-Me ₂	3-	2-	oil	2.35(6H, s), 3.79(2H, brs), 6.65(1H, d, J=5.1), 6.90(1H, s), 7.09(1H, d, J=5.1), 7.14(2H, s)	
3-F-4-Me	3-	2-	oil	2.28(3H, d, J=1.4), 3.85(2H, brs), 6.62(1H, d, J=5.8), 7.09(1H, d, J=5.8), 7.18(1H, d, J=8.1), 7.18(1H, s), 7.20(1H, d, J=8.1)	
4-F-3-Me	3-	2-	oil	2.31(3H, s), 3.72(2H, brs), 6.62(1H, d, J=5.4), 7.03(1H, t, J=8.8), 7.09(1H, d, J=5.4), 7.25-7.32(2H, m)	
4-Cl-3-CF ₃	3-	2-	oil	3.82(2H, brs), 6.64(1H, d, J=5.1), 7.16(1H, d, J=5.1), 7.52(1H, d, J=8.8), 7.62(1H, dd, J=8.8, 2.2), 7.84(1H, d, J=2.2)	
4-Cl-3-F	3-	2-	oil	3.83(2H, brs), 6.63(1H, d, J=5.1), 7.13(1H, d, J=5.1), 7.23-7.43(3H, m)	
3-Cl-4-F	3-	2-	oil	3.77(2H, brs), 6.64(1H, d, J=5.1), 7.06-7.21(2H, m), 7.32-7.40(1H, m), 7.56(1H, d, J=7.3)	
4-Cl-3-Me	3-	2-	oil		
2-i-Pr	3-	2-	oil		
3-OCF ₃	3-	2-	oil		
2,5-Cl ₂	3-	2-	oil		
2-Et	3-	2-	oil		
2-Me	3-	2-	oil	2.30(3H, s), 3.41(2H, brs), 6.66(1H, d, J=5.1), 7.14(1H, d, J=5.1), 7.19-7.34(4H, m)	
4-ethynyl	3-	2-	oil		

These compounds shown by "" were unstable, so they were used for next reaction without separation from reaction solution of catalytic reduction.

The agricultural and horticultural fungicide which comprises the compound represented by the general formula (1) of the invention as an active ingredient has an excellent disease control effect on rice diseases such as Blast (*Piricularia oryzae*), Helminthosporium leaf spot (*Cochliobolus miyabeanus*), Sheath blight (*Rhizoctonia solani*), "Bakanae" disease (*Gibberella fujikuroi*), Wheat Powdery mildew (*Erysiphe graminis* f.sp. *hordei*; f.sp. *tritici*), Leaf stripe (*Pyrenophora graminea*), Net blotch (*Pyrenophora teres*), Fusarium blight (*Gibberella zeae*), Stripe rust (*Puccinia striiformis*, Stem rust (*P. graminis*), Brown rust (*P. recondita*), Brown rust (*P. hordei*), Snow rot

(*Typhula* sp.; *Micronectriella nivalis*). Loose smut (*Ustilago tritici*; *U. nuda*), Eye spot (*Pseudocercospora herpotrichoides*), Rhynchosporium leaf blotch (*Rhynchosporium secalis*), Septoria leaf blotch (*Septoria tritici*), Glume blotch (*Leptosphaeria nodorum*), Grape Powdery mildew (*Uncinula necator*), Anthracnose (*Elsinoe ampelina*), Ripe rot (*Glomerella cingulata*), Rust (*Phakopsora ampelopsidis*), Apple Powdery mildew (*Podosphaera leucotricha*), Scab (*Venturia inaequalis*), Alternaria leaf spot (*Alternaria mali*), Rust (*Gymnosporangium yamadae*), Blossom blight (*Sclerotinia mali*), Canker (*Valsa mali*), Pear Black spot (*Alternaria kikuchiana*), Scab (*Venturia nashicola*), Rust (*Gymnosporangium haraeaeum*), Peach Brown rot (*Sclerotinia cinerea*), Scab (*Cladosporium carpophilum*), Phomopsis rot (*Phomopsis* sp.), Persimmon Anthracnose (*Gloeosporium kaki*), Angular leaf spot (*Cercospora kaki*; *Mycosphaerella nawae*), Melon Powdery mildew (*Sphaerotheca fuliginea*), Anthracnose (*Colletotrichum lagenarium*), Gummy stem blight (*Mycosphaerella melonis*), Tomato Early blight (*Alternaria solani*), leaf mold (*Cladosporium fulvum*), Eggplant Powdery mildew (*Erysiphe cichoracearum*), Alternaria leaf spot (*Alternaria japonica*), White spot (*Cercospora barassicae*), Leak Rust (*Puccinia allii*), Beans Purple spec (*Cercospora kikuchii*), Sphaceloma scab (*Elsinoe glycines*), Pod and stem blight (*Diaporthe phaseololum*), Beans Anthracnose (*Colletotrichum lindemuthianum*), Leaf spot (*Mycosphaerella personatum*), Brown leaf spot (*Cercospora arachidicola*), Powdery mildew (*Erysiphe pisi*), Early blight (*Alternaria solani*), Net blister blight (*Exobasidium reticulatum*), White scab (*Elsinoe leucospila*), Brown spot (*Alternaria longipes*), Beans Powdery mildew (*Erysiphe cichoracearum*), Anthracnose (*Colletotrichum tabacum*), Cercospora leaf spot (*Cercospora beticola*), Black spot (*Diplocarpon rosae*), Powdery mildew (*Sphaerotheca pannosa*), Leaf blotch (*Septoria chrysanthemi-indici*), Rust (*Puccinia horiana*), Powdery mildew (*Sphaerotheca humuli*), Gray mold (*Botrytis cinerea*) and Sclerotinia rot (*Sclerotinia sclerotiorum*)

When the compound represented by the general formula (1) of the invention is used as an agricultural and horticultural fungicide, the technical compound can be applied as intact to the plant to be treated. However, the technical compound is generally mixed with an inert liquid carrier or solid carrier and used in the form of a dust formulation, wettable powder, flowable formulation, emulsifiable concentrate, granule and other commonly used formulations. Adjuvant can also be added when necessary in view of formulation.

The term "carrier" means a synthetic or natural, inorganic or organic material which is formulated in order to assist reach of the effective ingredient to the portion to be treated and also to make storage, transport and handling of the effective ingredient compound easy. Any solid or liquid material can be used for the carrier so long as the material is commonly used for agricultural and horticultural formulations. No particular restriction is imposed on the carrier.

Solid carriers which can be used include, for example, montmorillonite, kaolinite and other clays; diatomaceous earth, China clay, talc, vermiculite, gypsum, calcium carbonate, silica gel, ammonium sulfate and other inorganic materials; soy bean powder, saw dust, wheat powder and other plant organic materials and urea.

Exemplary liquid carriers include toluene, xylene, cumene and other aromatic hydrocarbons; kerosene, mineral oil and other paraffin hydrocarbons; acetone, methyl ethyl ketone and other ketones; dioxane, diethylene glycol dim-

ethyl ether and other ethers; methanol, ethanol, propanol, ethylene glycol and other alcohols; dimethylformamide, dimethyl sulfoxide and other aprotic solvents; and water.

In order to further enhance the effect of the compound in the invention, following adjuvant can also be used singly or as a mixture depending upon the object in view of the formulation and application place.

Adjuvant which can be used include surfactants and binders which are commonly used for agricultural and horticultural formulations, for example, ligninsulfonic acid, alginic acid, polyvinyl alcohol, gum arabic and sodium CMC, and stabilizers, for example, phenol compounds, thiophenol compounds and higher fatty acid ester for oxidation inhibition, phosphoric acid salts for pH regulation and light stabilizers in some cases. These adjuvant can be used singly or in combination, when needed. Further, an industrial fungicide or a bacteria proofing agent can also be added in a certain case in order to inhibit fungus and bacteria.

The adjuvants will be illustrated further in detail.

Exemplary adjuvants which can be used for the purpose of emulsification, dispersion, spreading, wetting, binding and stabilization include salt of ligninsulfonic acid, salt of alkylbenzenesulfonic acid, ester salt of alkylsulfate, polyoxyalkylenealkylsulfate, ester salt of polyoxyalkylenealkylphosphate and other anionic surface active agents; polyoxyalkylene alkyl ether, polyoxyalkylene alkyl aryl ether, polyoxyalkylene alkylamine, polyoxyalkylene alkylamide, polyoxyalkylene alkyl thioether, polyoxyalkylene fatty acid ester, glycerin fatty acid ester, sorbitan fatty acid ester, polyoxyalkylenesorbitan fatty acid ester, polyoxypropylene-polyoxyethylene block copolymer and other nonionic surface active agents; calcium stearate, wax and other lubricants, isopropyl hydrogen phosphate and other stabilizers; and other miscellaneous materials such as methylcellulose, carboxymethylcellulose, casein and gum arabic. However, no restriction is imposed upon these adjuvants.

The content of the compound represented by the general formula (1) in the agricultural and horticultural fungicide of the invention differs depending upon formulation and is usually 0.05–20% by weight in the dust formulation, 0.1–80% by weight in the wettable powder, 0.1–20% by weight in the granule, 1–50% by weight in the emulsifiable concentrate, 1–50% by weight in the flowable formulation, and 1–80% by weight in the dry flowable formulation. Preferred concentration is 0.5–5% by weight in the dust formulation, 5–80% by weight in the wettable powder, 0.5–8% by weight in the granule, 5–20 by weight in the emulsifiable concentrate, 5–50 by weight in the flowable formulation and 5–50% by weight in the dry flowable formulation.

The content of adjuvants is 0–80% by weight and the content of the carrier is quantity obtained by subtracting the total content of the active ingredient compound and the adjuvants from 100% by weight.

The methods for applying the composition of the invention include seed disinfection and foliage application. However, the composition can exhibit satisfactory activity by any application method utilized by those who are skilled in the art.

Application amount and application concentration, are variant depending upon object crops, object diseases, abundance of disease damage, formulation of compound, application method and various environmental conditions. The amount of active ingredient is usually 50–1000 g/hectare, preferably 100–500 g/hectare in spraying. When a wettable

powder, flowable formulation or emulsifiable concentrate is diluted with water and sprayed, the dilution is usually 200–20,000 times, preferably 1,000–5,000 times.

The agricultural and horticultural fungicide of the invention can of course be used in combination with other fungicides, insecticides, herbicides, plant-growth regulators and other agricultural chemicals; soil conditioners; or materials having fertilizer effect. A mixed formulation of the fungicide in the invention can also be prepared by using these materials.

Exemplary other fungicides include triadimefon, hexaconazole, prochloraz, triflumizole and other azole fungicides; metalaxyl, oxadixyl and other acyl alanine fungicides; thiophanate-methyl, benomil and other benzimidazole fungicides; manzeb and other dithiocarbamate fungicides; and TPN and sulphur.

Insecticides include, for example, fenitrothion, diazinon, pyridafenthion, chlorpyrifos, marathion, phenthoate, dimethoate, methyl thiometon, prothiofos, DDVP, acephate, salithion, EPN and other organophosphate insecticides; NAC, MTMC, BPMC, pirimicarb, carbosulfan, methomyl and other carbamate insecticides; and ethofenprox, permethrin, fenvalerate and other pyrethroid insecticides. However, no restriction is imposed upon these materials.

EXAMPLES

The compound of the invention will be further specifically illustrated by way of examples.

Example 1

Preparation of N-[2-{3-(4-tolyl)}thienyl]-3-trifluoromethyl-1-methylpyrazole-4-carboxamide (Compound No. 3.9)

1) 2-nitro-3-(4-tolyl)thiophene

A mixture of 0.8 g of 3-bromo-2-nitrothiophene, 0.52 g of 4-tolylboric acid, 5 ml of a 2M-aqueous potassium carbonate solution, 2.5 ml of ethanol and 30 ml of toluene was stirred at room temperature for 30 minutes in a nitrogen atmosphere. Successively 0.15 g of $\text{Pd}(\text{PPh}_3)_4$ was added and refluxed by heating for 7 hours. After separating into two layers, the organic layer was washed with water and dried over anhydrous sodium sulfate. Solvent was distilled off under reduced pressure. The residue was purified by silica gel column chromatography to obtain 0.56 g (70% yield) of the product as a yellow crystal. $^1\text{H-NMR}(\text{CDCl}_3, \delta \text{ value}): 2.42(3\text{H, s}), 7.01(1\text{H, d, J}=5.1), 7.25(2\text{H, d, J}=8.1), 7.37(2\text{H, d, J}=8.1), 7.47(1\text{H, d, J}=5.1)$

2) 2-amino-3-(4-tolyl)thiophene

After dissolving 0.5 g of 2-nitro-3-(4-tolyl)thiophene in 20 ml of dioxane, 0.25 g of 5% Pd/C was added and catalytic reduction was carried out at room temperature for 5 hours. The solution obtained was filtered to recover the catalyst and the filtrate was used as intact for the next reaction.

3) N-[2-{3-(4-tolyl)}thienyl]-3-trifluoromethyl-1-methylpyrazole-4-carboxamide

To the filtrate obtained in the above 2), 0.73 of pyridine and 0.45 of 3-trifluoromethyl-1-methylpyrazolecarbonyl chloride was added and stirred at room temperature for an hour. The reaction mixture was extracted with ethyl acetate, washed with an aqueous saturated sodium carbonate solution and dried over anhydrous sodium sulfate. Solvent was distilled off under the reduced pressure and the residue was purified by silica gel column chromatography to obtain 0.4 g of the desired product. The yield was 47% based on 2-nitro-3-(4-tolyl) thiophene.

solution and dried over anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure and the residue was purified by silica gel column chromatography to obtain 0.43 g of the product as a crystal.

3) N-(2-(1,3-dimethylbutyl)-3-thienyl)-3-trifluoromethyl-1-methylpyrazole-4-carboxamide

The same procedures as described in Example 3 were carried out except that 3-amino-2-(4-chlorophenyl) thiophene was replaced by 3-amino-2-(1,3-dimethylbutyl) thiophene. The yield was 41%.

Example 15

Preparation of N-(2-isopropyl-3-thienyl)-3-trifluoromethyl-1-methylpyrazole-4-carboxamide (Compound No. 1.1)

1) 3-amino-2-isopropylthiophene (Process C)

In 10 ml of methylene chloride, 0.9 g of 2-(1-hydroxy-1-methyl) ethyl-3-t-butoxycarbonylaminothiophene (an intermediate in Example 6) was dissolved. 0.41 g of triethylsilane and 4 g of trifluoroacetic acid were added, and the mixture was stirred at the room temperature for 20 hours. Thereafter the reaction mixture was neutralized with a saturated aqueous sodium hydrogen carbonate solution and extracted with ethyl acetate. The ethyl acetate layer was washed with a saturated aqueous sodium chloride solution and dried over anhydrous magnesium sulfate. The solvent was distilled off under reduced pressure and the residue was

purified by silica gel column chromatography to obtain 0.29 g of the product as a crystal. The yield was 62%.

2) N-(2-isopropyl-3-thienyl)-3-trifluoromethyl-1-methylpyrazole-4-carboxamide

The same procedures as described in Example 3 were carried out except that 3-amino-2-(4-chlorophenyl) thiophene was replaced by 3-amino-2-isopropylthiophene. The yield was 53%.

Example 16

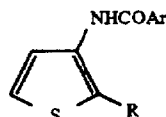
Preparation of N-(2-isopropyl-3-thienyl)-3-trifluoromethyl-1-methylpyrazole-4-carboxamide (Compound No. 1.1, Process D)

In 10 ml of methanol, 1 g of the compound prepared in Example 6 (Compound No. 1.71) was dissolved. 0.2 g of 5% Pd/C was added, and catalytic reduction was carried out at the room temperature for 8 hours under atmospheric pressure. After finishing the reaction, the catalyst was filtered and washed with methanol. The filtrate was concentrated under reduced pressure. The resulting oily material was sludged with hexane to obtain 0.8 g of the desired product as a crystal. The yield was 79%.

Other compounds which are represented by the general formula (1) and were prepared by procedures similar to these examples are exemplified in Table 5 to Table 8 below.

TABLE 5

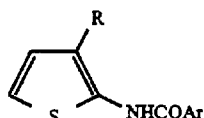
(2-substituted 3-acylamino-thiophene derivatives)



Compound No.	R	Ar (substituent)	m.p. (°C.)	¹ H-NMR (400MHz) (CDCl ₃ , δ-value)
1.1	isopropyl	A2(R ¹ = CF ₃)	109-110	1.31(6H, d, J=7.3, 3.20(1H, sept, J=7.3), 3.99(3H, s), 7.11(1H, d, J=5.1), 7.47(1H, d, J=5.1), 7.56(1H, bs), 8.06(1H, s)
1.2	(1S)-1-methylpropyl	A2(R ¹ = CF ₃)	139-140	0.89(3H, t, J=7.3), 1.30(3H, d, J=7.3), 1.59-1.69(2H, m), 2.85-2.93(1H, m), 3.99(3H, s), 7.13(1H, d, J=5.1), 7.46(1H, d, J=5.1), 7.54(1H, bs), 8.05(1H, s)
1.3	1-methylpropyl	A1(R ¹ = CF ₃ , R ² = Me)	112-114	0.89(3H, t, J=7.3), 1.30(3H, d, J=7.3), 1.59-1.69(2H, m), 2.85-2.93(1H, m), 3.99(3H, s), 7.13(1H, d, J=5.1), 7.46(1H, d, J=5.1), 7.54(1H, bs), 8.05(1H, s)
1.4	1-methylpropyl	A2(R ¹ = CF ₃)		
1.5	(1S)-1-methylpropyl	A6	96-100	0.92(3H, t, J=7.3), 1.33(3H, t, J=7.3), 1.61-1.73(2H, m), 3.30(1H, sext, J=7.3), 7.17(1H, d, J=5.9), 7.42(1H, dd, J=8.1, 5.1), 7.50(1H, d, J=5.9), 8.14(1H, bs), 8.30(1H, dd, J=8.1, 1.5), 8.51(1H, dd, J=5.1, 1.5)
1.6	1-ethylpropyl	A2(R ¹ = CF ₃)	126-127	0.85(6H, t, J=7.3), 1.49-1.3(2H, m), 1.71-1.81(2H, m), 2.17-2.67(1H, m), 3.99(3H, s), 7.16(1H, d, J=5.9), 7.49(1H, d, J=5.9), 7.55(1H, bs), 8.05(1H, s)
1.7	1-methylbutyl	A1(R ¹ = CF ₃ , R ² = Me)	79-80	0.88(3H, t, J=7.3), 1.23-1.8(5H, m), 1.55-1.63(2H, m), 2.98(1H, sext, J=7.3), 3.99(3H, s), 7.13(1H, d, J=5.9), 7.45(1H, d, J=5.9), 7.55(1H, bs), 8.05(1H, s)
1.8	1-methylbutyl	A2(R ¹ = CF ₃)		
1.9	1-methylbutyl	A7	oil	0.88(6H, d, J=6.6), 1.27(3H, d, J=6.6), 1.43-1.58(3H, m), 2.77(3H, s), 3.06(1H, m), 7.15(1H, d, J=5.9), 7.41(1H, d, J=5.1), 7.58(1H, bs)
1.10	1,3-dimethylbutyl	A1(R ¹ = CF ₃ , R ² = Me)		
1.11	1,3-dimethylbutyl	A1(R ¹ = CF ₃ , R ² = H)	103-105	0.86(6H, d, J=6.8), 1.25(3H, d, J=6.8), 1.43-1.64(3H, m), 3.08(1H, sext, J=6.8), 3.99(3H, s), 7.12(1H, d, J=5.1), 7.43(1H, d, J=5.1), 7.53(1H, bs), 8.05(1H, s)
1.12	1,3-dimethylbutyl	A1(R ¹ = R ² = Me)		
1.13	1,3-dimethylbutyl	A2(R ¹ = CF ₃)		
1.14	1,3-dimethylbutyl	A2(R ¹ = Me)		
1.15	1,3-dimethylbutyl	A2(R ¹ = CHF ₂)		

TABLE 7

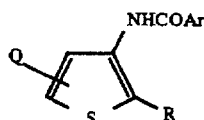
(3-substituted 2-acylaminothiophene derivatives)



Compound No.	R	Ar (substituent)	m.p. (°C.)	¹ H-NMR (400MHz) (CDCl ₃ , δ-value)
3.1	phenyl	A2(R ¹ = CF ₃)	141-142.5	3.97(3H, s), 6.97(1H, d, J=5.1), 7.00(1H, d, J=5.1), 7.36-7.52(5H, m), 8.03(1H, s), 8.56(1H, brs)
3.2	4-chlorophenyl	A2(R ¹ = CF ₃)	166-167	3.98(3H, s), 6.93(1H, d, J=5.9), 7.01(1H, d, J=5.9), 7.34(2H, d, J=8.1), 7.45(2H, d, J=8.1), 8.04(1H, s), 8.46(1H, brs)
3.3	phenyl	A1(R ¹ = CF ₃ , R ² = Me)	oil	2.74(3H, s), 6.99(1H, d, J=5.1), 7.06(1H, d, J=5.1), 7.36-7.41(3H, m), 7.45-7.52(2H, m), 8.64(1H, brs)
3.4	3-chlorophenyl	A3		
3.5	4-chlorophenyl	A4(R ¹ = Me, n = 0)		
3.6	2-chlorophenyl	A5		
3.7	3-chlorophenyl	A6		
3.8	4-chlorophenyl	A7		
3.9	4-tolyl	A2(R ¹ = CF ₃)	153-155	2.41(3H, s), 3.96(3H, s), 6.94(1H, d, J=5.9), 6.99(1H, d, J=5.9), 7.29(4H, s), 8.02(1H, s), 8.67(1H, brs)
3.10	4-methoxyphenyl	A2(R ¹ = CF ₃)	148-151	3.87(3H, s), 4.02(3H, s), 6.93(1H, d, J=5.1), 6.98-7.04(3H, m), 7.32(2H, d, J=8.1), 8.02(1H, s), 8.51(1H, brs)
3.11	4-tolyl	A1(R ¹ = CF ₃ , R ² = H)		
3.12	4-methoxyphenyl	A1(R ¹ = CF ₃ , R ² = Me)	147-148	2.74(3H, s), 3.86(3H, s), 9.65(1H, d, J=5.1), 7.00-7.05(3H, m), 7.32(2H, d, J=8.1), 8.58(1H, brs)
3.13	phenyl	A6	147-151	
3.14	phenyl	A5(R ¹ = Cl)	95-99	

TABLE 8

(2-substituted 3-acylaminothiophene derivatives)



Compound No.	Q	R	Ar (substituent)	m.p. (°C.)	¹ H-NMR (400MHz) (CDCl ₃ , δ-value)
4.1	5-methyl	phenyl	A2(R ¹ = CF ₃)	151-152	
4.2	5-methyl	1,3-dimethylberyl	A6		
4.3	5-methoxy	1,3-dimethylbutyl	A2(R ¹ = CF ₃)		
4.4	5-methyl	3-chlorophenyl	A1(R ¹ = CF ₃ , R ² = H)		
4.5	4-chloro	4-tolyl	A2(R ¹ = CF ₃)		
4.6	5-methyl	4-chlorophenyl	A2(R ¹ = CF ₃)		

Next, formulation examples and test examples will be illustrated on the agricultural and horticultural fungicide of the invention.

Formulation Example 1 (Dust Formulation)

100 Parts of dust formulation was prepared by uniformly grinding and mixing 3 parts of the compound having Compound No. 1.2, 20 parts of diatomaceous earth, 77 parts of clay.

Formulation Example 2 (Wettable Powder)

100 Parts of wettable powder was prepared by uniformly grinding and mixing 25 parts of the compound having Compound No. 1.13, 72 parts of diatomaceous earth, 1 part of sodium ligninsulfonate and 2 parts of sodium alkylbenzenesulfonate.

Formulation Example 3 (Wettable Powder)

100 Parts of wettable powder was prepared by uniformly grinding and mixing 50 parts of the compound having

Compound No. 1.24, 30 parts of clay, 10 parts of white carbon, 5 parts of sodium laurylphosphate, and 5 parts of sodium alkyl naphthalenesulfonate.

Formulation Example 4 (Wettable Powder)

100 Parts of wettable powder was prepared by uniformly grinding and mixing 50 parts of the compound having Compound No. 1.61, 10 parts of sodium ligninsulfonate, 5 parts of sodium alkyl naphthalenesulfonate, 10 parts of white carbon and 25 parts of diatomaceous earth.

Formulation Example 5 (Emulsifiable Concentrate)

100 Parts of emulsifiable concentrate was prepared by uniformly dissolving and mixing 10 parts of the compound having Compound No. 1.77, 10 parts of cyclohexane, 60 parts of xylene and 20 parts of SORPOL (surface active agent manufactured by Toho Chemical Co.).

Formulation Example 6 (Flowable Formulation)

100 Parts of flowable formulation was prepared by wet-grinding with a sand grinder 40 parts of the compound having Compound No. 1.13, 3 parts of carboxymethylcellulose, 2 parts of sodium ligninsulfonate, 1 part of sodium dioctylsulfosuccinate, and 54 parts of water.

The compounds of the invention will hereinafter be illustrated the activity as an agricultural and horticultural fungicide by way of test examples.

Test Example 1

Control Test (1) Against Gray Mold of Kidney Beans

In a green house, two seedlings of kidney beans (cultivar: Top Crop) were grown in each plastic pot having a diameter of 7.5 cm until development of cotyledon.

A wettable powder which was prepared according to Formulation Example 3 was diluted, to the prescribed concentration (active ingredient concentration of 200 ppm) and air dried after spraying on the seedlings with 50 ml portions per four pots.

A conidiospore suspension (1×10^5 spores/ml) was prepared from gray mold fungus (*Botrytis cinerea*, MBC resistant, RS strain) which was cultured on a PDA medium, and spray-inoculated on the cotyledon, and allowed to stay in a greenhouse at 20°–23° C. for 7 days under relative humidity of 95% or more.

After 7 days from the inoculation, the lesion area of gray mold per leaf of kidney beans was examined on the basis of the following index. Results are illustrated in Table 9. The numerical value in the Table shows a preventive value, and "-" means untested.

Severity

0: no lesion

1: lesion area is 5% or less

2: lesion area is 5–25%

3: lesion area is 25–50%

4: lesion area is 50% or more

The mean value of each treated area and untreated area is defined as severity.

Preventive value (%) = $(1 - \text{severity in the treated area} / \text{severity in the untreated area}) \times 100$

Test Example 2

Control Test 2) Against Gray Mold of Kidney Beans

In a green house, two seedlings of kidney beans (cultivar: Top Crop) were grown in each plastic pot having a diameter of 7.5 cm until development of cotyledon.

A wettable powder which was prepared according to Formulation Example 3 was diluted to the prescribed concentration (active ingredient concentration of 200 ppm) and air dried after spraying on the seedlings with 50 ml portions per four pots.

A conidiospore suspension (1×10^5 spores/ml) was prepared from gray mold (*Botrytis cinerea*, MBC resistant, dicarboximide resistant, RR strain) which was cultured on a PDA medium, and spray-inoculated on the cotyledon, and allowed to stay in a greenhouse at 20°–23° C. for 7 days under relative humidity of 95% or more.

After 7 days from the inoculation, the lesion area of gray mold per leaf of kidney beans was examined on the basis of the following index. Results are illustrated in Table 9.

Severity

0: no lesion

1: lesion area is 5% or less

2: lesion area is 5–25%

3: lesion area is 25–50%

4: lesion area is 50% or more

The mean value of each treated area and untreated area is defined as severity.

Preventive value (%) = $(1 - \text{severity in the treated area} / \text{severity in the untreated area}) \times 100$

Test Example 3

Control Test Against Cucumber Powdery Mildew

In a green house, two seedlings of cucumber (cultivar: Sagami Hanjiro) were grown in each plastic pot having a diameter of 7.5 cm until the 1.5 leaf stage.

A wettable powder which was prepared according to Formulation Example 3 was diluted to the prescribed concentration (active ingredient concentration of 200 ppm) and air dried after spraying on the seedlings with 50 ml portions per three pots.

A conidiospore suspension (1×10^6 spores/ml) was prepared by suspending conidiospore of cucumber powdery mildew fungus in water which contains a small amount of spreader, and spray inoculated on the leaf, and allowed to stay in a greenhouse for 7 days.

After 7 days from the inoculation, the lesion area of powdery mildew per leaf of cucumber was examined on the basis of the following index. Results are illustrated in Table 9.

Severity

0: no lesion

1: lesion area is 5% or less

2: lesion area is 5–25%

3: lesion area is 25–50%

4: lesion area is 50% or more

The mean value of each treated area and untreated area is defined as severity.

Preventive value (%) = $(1 - \text{severity in the treated area} / \text{severity in the untreated area}) \times 100$

Test Example 4

Control Test Against Wheat Powdery Mildew (EBI Resistant Strain)

In a green house, 15–20 seedlings of wheat (cultivar: Chihoku) were grown in each plastic pot having a diameter of 6 cm until the 1.5 leaf stage.

A wettable powder which was prepared according to Formulation Example 3 was diluted to the prescribed concentration (active ingredient concentration of 200 ppm) and air dried after spraying on the seedlings with 50 ml portions per three pots.

Thus treated seedlings were successively sprayed with conidiospore of wheat powdery mildew fungus (*Erysiphe graminis* f. sp. *tritici*, EBI resistant strain) and allowed to stand in a room at 18° C.

After 7 days from the inoculation, the lesion area of powdery mildew on the primary leaf of wheat was examined on the basis of the following index. Results are illustrated in Table 9.

Severity

0: no lesion

1: lesion area is 5% or less

2: lesion area is 5–25%

3: lesion area is 25–50%

4: lesion area is 50% or more

The mean value of each treated area and untreated area is defined as severity.

Preventive value (%) = $(1 - \text{severity in the treated area} / \text{severity in the untreated area}) \times 100$

Test Example 5

Control Test Against Wheat Brown Rust

In a green house, 15-20 seedlings of wheat (cultivar: Norin NO. 64) were grown in each plastic pot having a diameter of 6 cm until the 1.5 leaf stage.

A wettable powder which was prepared according to Formulation Example 4 was diluted to the prescribed concentration (active ingredient concentration of 200 ppm) and air dried after spraying on the seedlings with 50 ml portions per three pots.

Thus treated seedlings were successively sprayed with summer spore of wheat brown rust fungus (*Puccinia recondita*), allowed to stand in a moist condition for 2 days and transferred to a room which was maintained at 18° C.

After 10 days from the inoculation, the lesion area of red rust on the primary leaf of wheat was examined on the basis of the following index. Results are illustrated in Table 9.

Severity

0: no lesion

1: lesion area is 5% or less

2: lesion area is 5-25%

3: lesion area is 25-50%

4: lesion area is 50% or more

The mean value of each treated area and untreated area is defined as severity.

Preventive value (%)=(1-severity in the treated area/severity in the untreated area)×100

TABLE 9

Compound No.	Example 1 Gray mold (RS strain)	Example 2 Gray mold (RR strain)	Example 3 Powdery mildew (EBI sensitive)	Example 4 Powdery mildew (EBI resistant)	Example 5 Rust (EBI sensitive)
1.1	100	100	100	100	100
1.2	100	100	100	100	100
1.4	100	100	100	100	100
1.5	100	100	100	30	50
1.6	100	100	100	100	100
1.7	100	100	100	100	100
1.8	100	100	100	100	100
1.10	100	100	100	100	100
1.13	100	100	100	100	100
1.21	80	100	100	100	—
1.23	100	100	100	100	100
1.24	100	100	100	100	100
1.33	50	45	100	100	100
1.36	100	100	100	100	100
1.41	100	100	100	100	100
1.60	100	100	100	100	83
1.61	100	100	100	100	100
1.62	100	100	100	100	83
1.64	100	100	43	33	45
1.65	100	100	90	83	83
1.67	100	100	100	100	100
1.68	100	100	100	100	47
1.69	100	100	90	90	33
1.71	100	100	40	33	100
1.75	100	100	100	100	100
1.76	90	90	100	100	83
1.77	100	100	100	100	100
1.78	100	100	100	100	90
1.79	100	100	100	100	30
1.80	100	100	100	100	100
1.81	100	100	100	100	100
1.82	100	100	100	100	33
1.83	100	100	30	30	90
1.87	90	90	30	30	33
1.96	80	70	40	40	90
1.97	100	100	40	40	100
1.98	100	100	95	90	100

TABLE 9-continued

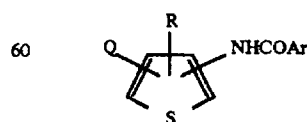
Compound No.	Example 1 Gray mold (RS strain)	Example 2 Gray mold (RR strain)	Example 3 Powdery mildew (EBI sensitive)	Example 4 Powdery mildew (EBI resistant)	Example 5 Rust (EBI sensitive)
1.106	100	100	100	100	100
1.113	100	100	100	100	100
1.118	100	100	100	100	100
1.120	100	100	100	100	100
1.121	100	100	100	100	100
1.125	100	100	100	100	100
1.127	100	100	100	100	100
1.128	30	25	100	100	80
1.132	30	30	100	100	90
1.138	25	30	100	100	90
1.142	100	100	90	80	100
1.143	100	100	100	100	100
1.144	100	100	100	100	100
1.145	100	100	100	100	100
1.146	100	100	100	100	100
1.147	100	100	100	100	100
1.148	100	100	100	100	100
1.149	100	100	100	100	100
1.150	100	100	100	100	40
1.151	100	100	90	90	100
1.152	100	100	80	80	30
1.153	30	20	100	100	100
1.156	60	70	0	0	0
1.157	70	70	100	100	30
1.158	100	100	100	100	100
1.159	70	60	0	0	0
1.160	100	100	100	100	80
1.161	100	100	100	100	100
1.162	80	70	100	100	100
1.163	80	80	100	100	100
1.164	100	100	100	100	100
1.165	100	100	80	85	100
1.166	80	70	100	100	—
1.167	80	75	100	100	—
3.1	100	100	70	70	30
3.2	90	90	100	100	90
3.3	100	100	80	70	30
3.9	70	60	0	0	0
3.12	30	20	100	100	90
3.13	100	80	0	0	100
3.14	100	90	0	0	100
4.1	90	80	0	0	0
Ref. Comp No. 1	100	0	—	—	—
Ref. Comp No. 2	—	—	100	0	87
Ref. Comp No. 3	10	20	0	0	0
Ref. Comp No. 4	30	20	0	0	0

Reference Compound

- 50 No. 1: procymidone; N-(3,5-dichlorophenyl)-1,2-dimethylcyclopropane-1,2-dicarboxamide
 No. 2: triadimefon; 1-(4-chlorophenoxy)-3,3-dimethyl-1-(1,2,4-triazol-1-yl)-2-butanone
 No. 3: N-(2-isopropylphenyl)-5-chloro-1,3-dimethylpyrazole-4-carboxamide
 No. 4: N-(2-propylphenyl)-2-methyl-4-trifluoromethylthiazole-5-carboxamide

What is claimed is:

1. A substituted thiophene compound of the formula (1)



wherein Q is a hydrogen atom, fluorine atom, chlorine atom, bromine atom, iodine atom, methyl group, trifluoromethyl group, methoxy group, methylthio group, methylsulfonyl group, methylsulfoxy group, nitro group or amino group; R

113



US005238956A

United States Patent [19]
Clough et al.

[11] **Patent Number:** **5,238,956**
 [45] **Date of Patent:** **Aug. 24, 1993**

[54] **FUNGICIDAL AROMATIC DIOXIME**

[75] **Inventors:** John M. Clough, Marlow;
 Christopher R. A. Godfrey,
 Bracknell; Paul J. de Fraine,
 Wokingham, all of England

[73] **Assignee:** Imperial Chemical Industries plc,
 London, Great Britain

[21] **Appl. No.:** 745,820

[22] **Filed:** Aug. 16, 1991

[30] **Foreign Application Priority Data**

Aug. 22, 1990 [GB] United Kingdom 9018408

[51] **Int. Cl.⁵** A61K 31/235; C07C 229/06

[52] **U.S. Cl.** 514/506; 514/508;
 560/19; 560/21; 560/22; 560/23

[58] **Field of Search** 560/16, 19, 21, 22,
 560/23; 514/506, 508

[56] **References Cited**

U.S. PATENT DOCUMENTS

5,051,447 9/1991 Wenderoth et al. 450/22
 5,055,471 10/1991 de Fraine et al. 514/255

FOREIGN PATENT DOCUMENTS

463488 2/1992 European Pat. Off. .

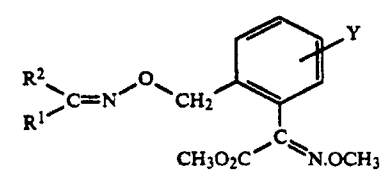
Primary Examiner—Mukund J. Shah

Assistant Examiner—Y. N. Gupta

Attorney, Agent, or Firm—Michael J. Bradley; William
 E. Dickheiser

[57] **ABSTRACT**

Fungicidal compounds of the formula (I):



and stereoisomers thereof, wherein Y is a specified small group or single atom and R¹ and R² are selected from a wide range of specified substituents.

5 Claims, No Drawings

FUNGICIDAL AROMATIC DIOXIME

This invention relates to derivatives of propenoic acid useful as fungicides, to processes for preparing them, to compositions containing them, and to methods of using them to combat fungi, especially fungal infections of plants.

According to the present invention there is provided a compound having the formula (I), and stereoisomers thereof, wherein Y is hydrogen, halo, hydroxy, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ haloalkyl, C₁₋₄ haloalkoxy, C₁₋₄ alkylcarbonyl, C₁₋₄ alkoxy carbonyl, phenoxy, nitro or cyano; R¹ and R², which may be the same or different, are hydrogen, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted heterocyclylalkyl, optionally substituted cycloalkylalkyl, optionally substituted aralkyl, optionally substituted heteroarylalkyl, optionally substituted aryloxyalkyl, optionally substituted heteroaryloxyalkyl, optionally substituted heteroarylthioalkyl, optionally substituted arylthioalkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aryloxy, optionally substituted heteroaryloxy, nitro, halo, cyano, —NR³R⁴, —CO₂R³, —CONR³R⁴, —COR³, —S(O)_nR³ wherein n is 0, 1 or 2, (CH₂)_mPO(OR³)₂ wherein m is 0 or 1, or R¹ and R² join to form a carbocyclic or heterocyclic ring system; and R³ and R⁴, which are the same or different, are hydrogen, optionally substituted alkyl, optionally substituted aralkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl or optionally substituted heteroaryl, or R³ and R⁴ join to form an optionally substituted heterocyclic ring.

The compounds of the invention contain at least two carbon-nitrogen double bonds and are sometimes obtained in the form of mixtures of geometric isomers. However these mixtures can be separated into individual isomers and this invention embraces such isomers and mixtures thereof in all proportions.

The individual isomers which result from the unsymmetrically substituted double bond of the oxime ether groups are identified by the commonly used terms "E" and "Z". These terms are defined according to the Cahn-Ingold-Prelog system which is fully described in the literature (see, for example, J March, "Advanced Organic Chemistry", 3rd edition, Wiley-Interscience, page 109 et seq).

For the carbon-nitrogen double bond of the oximinoacetate group, usually one isomer is more active fungicidally than the other, the more active isomer usually being the one wherein the groups —CO₂CH₃ and —OCH₃ are on opposite sides of the carbon-nitrogen double bond (the (E)-isomer). These (E)-isomers form a preferred embodiment of this invention.

The use hereinafter of the formula (A) signifies a separable mixture of both geometric isomers about the carbon-nitrogen double bond of the oxime ether, i.e. the isomers containing the groups of formulae (B) and (C).

Geometric pairs of isomers about the carbon-nitrogen bond of the oximino-acetate group of the compounds listed later in Table I are identified by the letters A and B. In many instances, using solvent systems such as ether or ethyl acetate, or mixtures of one of these with hexane, the isomers termed A and B of a compound have significantly different R_f values when analysed by thin-layer chromatography on silica gel. Of each pair of

isomers the isomer which is the less polar on silica gel is termed the Isomer A and the more polar one, Isomer B. Halo includes fluoro, chloro, bromo and iodo.

Alkyl and the alkyl moieties of alkoxy, aralkyl, aryloxyalkyl, heteroarylalkyl, heteroaryloxyalkyl, arylthioalkyl, heteroarylthioalkyl, can be in the form of straight or branched chains and, unless otherwise stated, suitably contain from 1 to 6 carbon atoms. Examples are methyl, ethyl, iso-propyl and tert-butyl. Optional substituents include halo (especially chloro and fluoro), hydroxy and C₁₋₄ alkoxy. Examples of substituted alkyl and substituted alkoxy are trifluoromethyl and trifluoromethoxy.

Cycloalkyl is suitably C₃₋₆ cycloalkyl, for example cyclopropyl or cyclohexyl, and cycloalkylalkyl is suitably C₃₋₆ cycloalkyl(C₁₋₄)alkyl, for example 1- or 2-cyclopropylethyl.

Alkenyl and alkynyl suitably contain from 2 to 6 carbon atoms, typically 2 to 4 carbon atoms, in the form of straight or branched chains. Examples are ethenyl, allyl and propargyl. Substituted alkenyl and alkynyl groups include optionally substituted aryl- and heteroarylalkenyl (especially optionally substituted aryl- and heteroaryl(C₂₋₄)alkenyl and, particularly, optionally substituted phenylethenyl) and aryl- and heteroarylalkynyl.

Aryl and the aryl moieties of aralkyl, arylalkenyl, arylalkynyl, aryloxy and aryloxyalkyl include phenyl and naphthyl.

The carbocyclic or heterocyclic ring system which R¹ and R² may form together is suitably a C₄₋₁₀ (typically C₅₋₁₀) aliphatic, aromatic or mixed aliphatic/aromatic carbocyclic ring system, for example cyclopentyl, cyclohexyl, cyclohexadienonyl and such groups carrying one or two optionally substituted fused benzene rings and/or substituents such as methyl; or it may be a 4- to 10-membered heterocyclic ring system, for example tetrahydropyranyl.

the term heteroaryl is used to described aromatic heterocyclic groups. Heteroaryl and heterocyclyl and the heteroaryl and heterocyclyl moieties of other groups, such as heteroaryloxyalkyl and heterocyclalkyl, are typically 5- or 6-membered rings containing one or more O, N or S heteroatoms which may be fused to one or more other aromatic, heteroaromatic or heterocyclic rings such as a benzene ring. Examples are thieryl, furyl, pyrrolyl, isoxazolyl, oxazolyl, pyrazolyl, imidazolyl, triazolyl, thiazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazinyl, benzofuryl, benzothienyl, dibenzofuryl, indolyl, quinolinyl and quinoxalinyl groups and, where appropriate, N-oxides and N-alkyl salts thereof.

The optionally substituted heterocyclic ring which R³ and R⁴ may join together to form is suitably a 5 to 7 membered hetero ring having 1 to 3 heteroatoms which are independently selected from O, S or N, and having 1 to 3 substituents which are, for example, halogen, cyano, nitro, C₁₋₆ alkyl, C₁₋₆ alkoxy, group, C₁₋₆ alkylthio, or a heterocyclic ring such as described in the previous paragraph. Examples are pyrrolidine, piperidine, morpholine, thiomorpholine, piperazine, hexamethyleneimine, tetrahydroquinoline, tetrahydroisoquinoline and 2,3-dihydro-1,4-benzoxazine.

Substituents which may be present in optionally substituted aryl and heteroaryl moieties include one or more of the following: halo, hydroxy, mercapto, C₁₋₄ alkyl (especially methyl and ethyl), C₂₋₄ alkenyl (especially allyl), C₂₋₄ alkynyl (especially propargyl), C₁₋₄

TABLE I-continued

COM- POUND NO.	R ¹	R ²	Y
52	cyano	cyano	H
53	Ø	Ø	H
54	Ø	Ø	H
55	Ø	Ø	H
56	tert-C ₄ H ₉	H	H
57	C ₆ H ₅ CH ₂	H	H
58	2,4-di-Cl-C ₆ H ₃	H	H
59	2,4-di-F-C ₆ H ₃	H	H
60	3,5-di-CH ₃ -C ₆ H ₃	H	H
61	3,5-di-CH ₃ O-C ₆ H ₃	H	H
62A*	pyrazin-2-yl	CH ₃	H
62B*	pyrazin-2-yl	CH ₃	H
63	6-CH ₃ -pyrid-3-yl	CH ₃	H
64	pyrid-2-yl	C ₂ H ₅	H
65	pyrid-3-yl	CH ₃	H
66	pyrimidin-5-yl	iso-C ₃ H ₇	H
67	iso-C ₃ H ₇	pyrimidin-5-yl	H
68	pyrid-4-yl	CH ₃	H
69	6-Cl-pyrid-2-yl	CH ₃	H
70	5-Cl-pyrid-2-yl	CH ₃	H
71	4-Cl-pyrid-2-yl	CH ₃	H
72	3-Cl-pyrid-2-yl	CH ₃	H
73	6-cyano-pyrid-2-yl	CH ₃	H
74	5-cyano-pyrid-2-yl	CH ₃	H
75	4-cyano-pyrid-2-yl	CH ₃	H
76	3-cyano-pyrid-2-yl	CH ₃	H
77	6-Br-pyrid-2-yl	CH ₃	H
78	5-Br-pyrid-2-yl	CH ₃	H
79	4-Br-pyrid-2-yl	CH ₃	H
80	3-Br-pyrid-2-yl	CH ₃	H
81	6-CH ₃ -pyrid-2-yl	CH ₃	H
82	5-CH ₃ -pyrid-2-yl	CH ₃	H
83	4-CH ₃ -pyrid-2-yl	CH ₃	H
84	3-CH ₃ -pyrid-2-yl	CH ₃	H
85	6-F-pyrid-2-yl	CH ₃	H
86	5-F-pyrid-2-yl	CH ₃	H
87	4-F-pyrid-2-yl	CH ₃	H
88	3-F-pyrid-2-yl	CH ₃	H
89	3-CH ₃ -pyrazin-2-yl	CH ₃	H
90	3-C ₂ H ₅ -pyrazin-2-yl	CH ₃	H
91	3-Cl-pyrazin-2-yl	CH ₃	H
92	3-CH ₃ O-pyrazin-2-yl	CH ₃	H
93	5-CO ₂ CH ₃ -pyrazin-2-yl	CH ₃	H
94	5-CO ₂ C ₂ H ₅ -pyrazin-2-yl	CH ₃	H
95	3-cyano-pyrazin-2-yl	CH ₃	H
96	pyrimidin-4-yl	CH ₃	H
97	2-Cl-pyrimidin-4-yl	CH ₃	H
98	2-CH ₃ O-pyrimidin-4-yl	CH ₃	H
99	2-CH ₃ -pyrimidin-4-yl	CH ₃	H
100	2-cyano-pyrimidin-4-yl	CH ₃	H
101	thiazol-2-yl	CH ₃	H
102	thien-3-yl	CH ₃	H
103	5-Cl-thien-2-yl	CH ₃	H
104	5-CH ₃ -thien-2-yl	CH ₃	H
105	5-Br-thien-2-yl	CH ₃	H
106	5-cyano-thien-2-yl	CH ₃	H
107	3-CH ₃ -thien-2-yl	CH ₃	H
108	2-CH ₃ O-C ₆ H ₄	CH ₃	H
109	3-CH ₃ O-C ₆ H ₄	CH ₃	H
110	4-CH ₃ O-C ₆ H ₄	CH ₃	H
111	2-CH ₃ -C ₆ H ₄	CH ₃	H
112	3-CH ₃ -C ₆ H ₄	CH ₃	H
113	4-CH ₃ -C ₆ H ₄	CH ₃	H
114	2-F-C ₆ H ₄	CH ₃	H
115	3-F-C ₆ H ₄	CH ₃	H
116	4-F-C ₆ H ₄	CH ₃	H
117	2-Cl-C ₆ H ₄	CH ₃	H
118	3-Cl-C ₆ H ₄	CH ₃	H
119	4-Cl-C ₆ H ₄	CH ₃	H
120	2-Br-C ₆ H ₄	CH ₃	H
121	3-Br-C ₆ H ₄	CH ₃	H
122	4-Br-C ₆ H ₄	CH ₃	H
123	2-NO ₂ -C ₆ H ₄	CH ₃	H
124	3-NO ₂ -C ₆ H ₄	CH ₃	H
125	4-NO ₂ -C ₆ H ₄	CH ₃	H
126	2-CF ₃ -C ₆ H ₄	CH ₃	H
127A*	3-CF ₃ -C ₆ H ₄	CH ₃	H
127B*	3-CF ₃ -C ₆ H ₄	CH ₃	H
128	4-CF ₃ -C ₆ H ₄	CH ₃	H

TABLE I-continued

COM- POUND NO.	R ¹	R ²	Y
129	2-cyano-C ₆ H ₄	CH ₃	H
130	3-cyano-C ₆ H ₄	CH ₃	H
131	4-cyano-C ₆ H ₄	CH ₃	H
132	3,4,5-(CH ₃ O) ₃ -C ₆ H ₂	CH ₃	H
133	3,5-di-F-pyrid-2-yl	CH ₃	H
134	3,4,5,6-F ₄ -pyrid-3-yl	CH ₃	H
135	2,6-di-Cl-pyrid-3-yl	CH ₃	H
136	pyridazin-3-yl	CH ₃	H
137	pyridazin-4-yl	CH ₃	H
138	6-CH ₃ -pyridazin-3-yl	CH ₃	H
139	4-cyano-quinolin-2-yl	CH ₃	H
140	quinoxalin-2-yl	CH ₃	H
141	C ₆ H ₅	CH ₃	6-F
142	C ₆ H ₅	CH ₃	6-Cl
143	6-CH ₃ -pyrimidin-4-yl	CH ₃	H
144	4-CH ₃ -pyrimidin-5-yl	CH ₃	H
145	4-CH ₃ -pyrimidin-2-yl	CH ₃	H
146	4,6-di-CH ₃ -pyrimidin-2-yl	CH ₃	H
147	2,6-di-CH ₃ -pyrimidin-4-yl	CH ₃	H
148	2,4-di-CH ₃ -pyrimidin-5-yl	CH ₃	H
149	6-Cl-pyrimidin-4-yl	CH ₃	H
150	6-CH ₃ O-pyrimidin-4-yl	CH ₃	H
151	4,6-di-CH ₃ O-pyrimidin-2-yl	CH ₃	H
152	Ø	Ø	H
153	Ø	Ø	H
154	pyrid-2-yl, N-oxide	CH ₃	H
155	5-C ₂ H ₅ -pyrid-2-yl	CH ₃	H
156	CH ₃ CO	CH ₃	H
157	C ₆ H ₅ CO	CH ₃	H
158	N-CH ₃ -pyrrol-2-yl	CH ₃	H
159	4-Cl-quinolin-2-yl	CH ₃	H
160	2,4-di-Cl-C ₆ H ₃	1,2,4-tri- azol-1-yl-CH ₂	H
161	2,4-di-Cl-C ₆ H ₃	pyrid-3- yl-CH ₂	H
162	2,4-di-CH ₃ -thiazol-5-yl	CH ₃	H
163	furan-2-yl	CH ₃	H
164	2,4-di-CH ₃ -furan-3-yl	CH ₃	H
165	pyrid-2-yl	pyrid-2-yl	H
166	6-C ₆ H ₅ -pyrimidin-4-yl	CH ₃	H
167	4-cyano-pyrid-3-yl	CH ₃	H
168	1,2,4-triazin-5-yl	CH ₃	H
169	3-CH ₃ -1,2,4-triazin-5-yl	CH ₃	H
170	3-C ₆ H ₅ -1,2,4-triazin-5-yl	CH ₃	H
171	3-SCH ₃ -1,2,4-triazin-5-yl	CH ₃	H
172	3-CH ₃ O-1,2,4-triazin-5-yl	CH ₃	H
173	5-CONH ₂ -pyrazin-2-yl	CH ₃	H
174	5-cyano-pyrazin-2-yl	CH ₃	H
175	5,6-di-CH ₃ -pyrazin-2-yl	CH ₃	H
176	3,5-di-CH ₃ -pyrazin-2-yl	CH ₃	H
177	3,6-di-CH ₃ -pyrazin-2-yl	CH ₃	H
178	5-CH ₃ -pyrazin-2-yl	CH ₃	H
179	6-CH ₃ -pyrazin-2-yl	CH ₃	H
180	5-Cl-pyrazin-2-yl	CH ₃	H
181	6-Cl-pyrazin-2-yl	CH ₃	H
182	5,6-dicyano-pyrazin-2-yl	CH ₃	H
183	4-SO ₂ CH ₃ -C ₆ H ₄	CH ₃	H
184	4-NH ₂ -C ₆ H ₄	CH ₃	H
185	2,4-di-Cl-C ₆ H ₃	CH ₃	H
186	2,4-di-CH ₃ -C ₆ H ₃	CH ₃	H
187	4-NHCONH ₂ -C ₆ H ₄	CH ₃	H
188	C ₆ H ₅	cyclopropyl	H
189	C ₆ H ₅	Cl	H
190	4-C ₂ H ₅ O-C ₆ H ₄	CF ₃	H
191	C ₆ H ₅	SCH ₃	H
192	C ₆ H ₅	F	H
193	C ₆ H ₅	OC ₂ H ₅	H
194	C(CH ₃) ₃	CH ₃	H
195	cyclohexyl-CH ₂	CH ₃	H
196	C ₆ H ₅ -CH ₂	CH ₃	H
197	pyrazin-2-yl-CH ₂	CH ₃	H
198	(E)-C ₆ H ₅ -CH=CH	CH ₃	H
199	C ₆ H ₅ -OCH ₂	CH ₃	H
200	C ₆ H ₅	CH ₂ Cl	H
201	benzthiazol-2-yl	CH ₃	H
202	benzoxazol-2-yl	CH ₃	H
203	pyrazin-2-yl	C ₂ H ₅	H

TABLE I-continued

COM- POUND NO.	R ¹	R ²	Y
204	5-CH ₃ O-pyrazin-2-yl	CH ₃	H
205	6-CH ₃ O-pyrazin-2-yl	CH ₃	H
206	6-cyano-pyrazin-2-yl	CH ₃	H
207	5-cyano-pyrid-3-yl	CH ₃	H
208	6-cyano-pyrid-4-yl	CH ₃	H
209	3-cyano-pyrid-4-yl	CH ₃	H
210	2-cyano-pyrid-4-yl	CH ₃	H
211	pyrimidin-5-yl	CH ₃	H
212	2-CH ₃ -pyrimidin-5-yl	CH ₃	H
213	3-CH ₃ O-isoxazol-5-yl	CH ₃	H
214	3-Br-isoxazol-5-yl	CH ₃	H
215	5-NO ₂ -thiazol-2-yl	CH ₃	H
216	5-CH ₃ -thiazol-2-yl	CH ₃	H
217	4-CH ₃ -thiazol-5-yl	CH ₃	H
218	2-Cl,4-CH ₃ -thiazol-5-yl	CH ₃	H
219	3,5-di-CH ₃ O-1,2,4-triazin-6-yl	CH ₃	H
220	3,6-di-CH ₃ -pyridazin-4-yl	CH ₃	H
221	2-(C ₆ H ₅ O)-C ₆ H ₄	CH ₃	H
222	3-(C ₆ H ₅ O)-C ₆ H ₄	CH ₃	H
223	4-(C ₆ H ₅ O)-C ₆ H ₄	CH ₃	H
224	1,2,4-triazol-1-yl-CH ₂	CH ₃	H
225	C ₆ H ₅	OCH ₃	H
226	OCH ₃	C ₆ H ₅	H
227	C ₆ H ₅	CH ₃ S(O)	H
228	C ₆ H ₅	CH ₃ S(O) ₂	H
229	C ₆ H ₅	N(CH ₃) ₂	H
230	C ₆ H ₅ O	CH ₃	H
231	C ₆ H ₅	Br	H
232	C ₆ H ₅	I	H
233	C ₆ H ₅	(CH ₃) ₂ CHS	H
234	pyrimidin-2-yl	CH ₃ O	H
235	pyrazin-2-yl	Cl	H
236	3-OC ₂ H ₅ -pyrazin-2-yl	CH ₃	H
237	pyrid-2-yl	SCH ₃	H
238	pyrid-2-yl	SO ₂ CH ₃	H
239	Pyrid-2-yl	SOCH ₃	H
240	3,5-di-CH ₃ -oxazol-4-yl	CH ₃	H
241	pyrid-2-yl	OCH ₃	H
242	pyrid-2-yl	SC ₂ H ₅	H
243	pyrid-2-yl	OC ₆ H ₅	H
244	pyrid-2-yl	OCH ₂ -C ₆ H ₅	H
245	6-OC ₂ H ₅ -pyrimidin-4-yl	CH ₃	H
246	pyrid-2-yl	NH ₂	H
247	SCH ₃	pyrid-2-yl	H
248	2,4-di-F-C ₆ H ₃	CH ₃	H
249	2,4-di-OCH ₃ -C ₆ H ₃	CH ₃	H
250	5-CH ₃ -pyrimidin-2-yl	CH ₃	H
251	SO ₂ CH ₃	pyrid-2-yl	H
252	pyrid-3-yl	SCH ₃	H
253	pyrid-3-yl	OCH ₃	H
254	6-CF ₃ -pyrid-2-yl	CH ₃	H
255	3-CF ₃ ,4-F-C ₆ H ₃	CH ₃	H
256	6-CF ₃ -pyrimidin-4-yl	CH ₃	H
257	3,5-di-F-C ₆ H ₃	CH ₃	H
258	2-CH ₃ S-pyrimidin-4-yl	CH ₃	H
259	2-CF ₃ -pyrimidin-4-yl	CH ₃	H
260	4-CF ₃ -pyrid-2-yl	CH ₃	H
261	2-phenyl-thiazol-4-yl	CH ₃	H
262	3-NH ₂ C(O)-C ₆ H ₄	CH ₃	H
263	4-CF ₃ -pyrimidin-2-yl	CH ₃	H
264	3,5-di-CF ₃ -C ₆ H ₃	CH ₃	H
265	2-(2-CN-C ₆ H ₄ -O-)-pyrimidin-4-yl	CH ₃	H
266	3-n-C ₃ H ₇ O-C ₆ H ₄	CH ₃	H
267	2-CH(CH ₃) ₂ -O-pyrimidin-4-yl	CH ₃	H
268	6-CF ₃ -pyrazin-2-yl	CH ₃	H
269	4-C ₂ H ₅ O-pyrimidin-2-yl	CH ₃	H
270	6-C ₂ F ₅ -pyrimidin-4-yl	CH ₃	H
271	3-CF ₃ O-C ₆ H ₄	CH ₃	H
272	4-CH ₃ O-pyrid-2-yl	CH ₃	H
273	2-propargyloxy-pyrimidin-4-yl	CH ₃	H
274	2-C ₂ H ₅ O-pyrimidin-4-yl	CH ₃	H
275	2-allyloxy-pyrimidin-4-yl	CH ₃	H
276	3-CH ₃ O-pyridazin-6-yl	CH ₃	H
277	3-C ₂ H ₅ O-pyridazin-6-yl	CH ₃	H
278	3-allyloxy-C ₆ H ₄	CH ₃	H
279	4-CH ₃ S-pyrimidin-2-yl	CH ₃	H
280	4-CH ₃ O-pyrimidin-2-yl	CH ₃	H
281	3-CF ₃ -C ₆ H ₄	SCH ₃	H

TABLE I-continued

COM- POUND NO.	R ¹	R ²	Y
282	3-CF ₃ -C ₆ H ₄	CF ₃	H
283	3-CF ₃ -C ₆ H ₄	C ₂ H ₅	H
284	3-CF ₃ -C ₆ H ₄	NH ₂	H
285	3-CF ₃ -C ₆ H ₄	Imidazolyl	H
286	3-CF ₃ -C ₆ H ₄	N(CH ₃) ₂	H
287	3-CF ₃ -C ₆ H ₄	NHCH ₃	H
288	PO(OC ₂ H ₅) ₂	CH ₃	H
289	PO(OC ₂ H ₅) ₂	C ₆ H ₅	H
290	4-CH ₃ O-6-(CO ₂ CH ₃)-pyrimidin-2-yl	CH ₃	H
291	pyrrol-2-yl	CH ₃	H
292	CH ₃	pyrrol-2-yl	H
293	5-CF ₃ -pyrid-3-yl	CH ₃	H
294	3-(pyrimidin-2-yl)-C ₆ H ₄	CH ₃	H
295	3-propargyloxy-C ₆ H ₄	CH ₃	H
296	CH ₃	H	H
297	5-(2,4-difluorophenyl)-furan-2-yl	CH ₃	H
298	CH ₃	5-(2,4-difluoro-phenyl)-furan-2-yl	H
299	C ₂ H ₅ O	CH ₃	H
300	4-tert-butyl-C ₆ H ₄	CH ₃	H
301	4-propargyloxy-pyrimidin-2-yl	CH ₃	H
302	2-C ₂ H ₅ O-C ₆ H ₄	CH ₃	H
303	4-C ₂ H ₅ -C ₆ H ₄	CH ₃	H
304	3-C ₂ H ₅ O-C ₆ H ₄	CH ₃	H
305	CH ₃ S	CH ₃	H
306	CH ₃ SO ₂	CH ₃	H
307	Ø	Ø	H
308	4-n-C ₃ H ₇ O-pyrimidin-2-yl	CH ₃	H
309	3-n-hexyloxy-C ₆ H ₄	CH ₃	H
310	4-n-butyloxy-pyrimidin-2-yl	CH ₃	H
311	benzothiophen-3-yl	CH ₃	H
312	3-[(CH ₃) ₂ C=CHCH ₂ O]-C ₆ H ₄	CH ₃	H
313	2,4-di-CH ₃ O-pyrimidin-6-yl	CH ₃	H
314	3-CF ₃ -C ₆ H ₄	1,2,4-triazol-1-yl	H
315	3-CH ₃ S-pyrazin-2-yl	CH ₃	H
316	3-N(CH ₃) ₂ -C ₆ H ₄	CH ₃	H
317	3-CF ₃ -C ₆ H ₄	Cl	H
318	Ø	Ø	H
319	benzofuran-2-yl	CH ₃	H
320	2-CH ₃ S(O)-pyrimidin-4-yl	CH ₃	H
321	3-NH ₂ C(S)-C ₆ H ₄	CH ₃	H
322	4-NH ₂ C(S)-pyrid-2-yl	CH ₃	H
323	3-(CH ₃ OCH ₂ CH ₂ OCH ₂ O)-C ₆ H ₄	CH ₃	H
324	3-(cyanomethoxy)-C ₆ H ₄	CH ₃	H
325	Ø	Ø	H
326	3-(F ₂ HC-O-)-C ₆ H ₄	CH ₃	H
327	6-C ₂ H ₅ O-pyrazin-2-yl	CH ₃	H

Key

*Compounds 62A, 62B, 127A and 127B are the isomers identified in Table II below.

Ø Groups R¹ and R² join to form a ring as shown under "Chemical Formulas" later.

TABLE II

MELTING POINTS AND OXIMINO-ACETATE ISOMER

Table II shows melting points for certain compounds described in Table I and whether the oximino-acetate group has the (E)- or (Z)-configuration

Compound No.	Isomer (E) or (Z)	Melting Point °C.
62A	Z	Oil
62B	E	117-120
127A	Z	Oil
127B	E	Oil
130	E	97
260	E	94.4-96.6
269	E	105
321	E	126-8

FUNGICIDAL AROMATIC DIOXIME

This invention relates to derivatives of propenoic acid useful as fungicides, to processes for preparing them, to compositions containing them, and to methods of using them to combat fungi, especially fungal infections of plants.

According to the present invention there is provided a compound having the formula (I), and stereoisomers thereof, wherein Y is hydrogen, halo, hydroxy, C₁₋₄ alkyl, C₁₋₄ alkoxy, C₁₋₄ haloalkyl, C₁₋₄ haloalkoxy, C₁₋₄ alkylcarbonyl, C₁₋₄ alkoxy carbonyl, phenoxy, nitro or cyano; R¹ and R², which may be the same or different, are hydrogen, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted heterocyclylalkyl, optionally substituted cycloalkylalkyl, optionally substituted aralkyl, optionally substituted heteroarylalkyl, optionally substituted aryloxyalkyl, optionally substituted heteroaryloxyalkyl, optionally substituted heteroarylthioalkyl, optionally substituted arylthioalkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted aryloxy, optionally substituted heteroaryloxy, nitro, halo, cyano, —NR³R⁴, —CO₂R³, —CONR³R⁴, —COR³, —S(O)_nR³ wherein n is 0, 1 or 2, (CH₂)_mPO(OR³)₂ wherein m is 0 or 1, or R¹ and R² join to form a carbocyclic or heterocyclic ring system; and R³ and R⁴, which are the same or different, are hydrogen, optionally substituted alkyl, optionally substituted aralkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl or optionally substituted heteroaryl, or R³ and R⁴ join to form an optionally substituted heterocyclic ring.

The compounds of the invention contain at least two carbon-nitrogen double bonds and are sometimes obtained in the form of mixtures of geometric isomers. However these mixtures can be separated into individual isomers and this invention embraces such isomers and mixtures thereof in all proportions.

The individual isomers which result from the unsymmetrically substituted double bond of the oxime ether groups are identified by the commonly used terms "E" and "Z". These terms are defined according to the Cahn-Ingold-Prelog system which is fully described in the literature (see, for example, J March, "Advanced Organic Chemistry", 3rd edition, Wiley-Interscience, page 109 et seq).

For the carbon-nitrogen double bond of the oximinoacetate group, usually one isomer is more active fungicidally than the other, the more active isomer usually being the one wherein the groups —CO₂CH₃ and —OCH₃ are on opposite sides of the carbon-nitrogen double bond (the (E)-isomer). These (E)-isomers form a preferred embodiment of this invention.

The use hereinafter of the formula (A) signifies a separable mixture of both geometric isomers about the carbon-nitrogen double bond of the oxime ether, i.e. the isomers containing the groups of formulae (B) and (C).

Geometric pairs of isomers about the carbon-nitrogen bond of the oximinoacetate group of the compounds listed later in Table I are identified by the letters A and B. In many instances, using solvent systems such as ether or ethyl acetate, or mixtures of one of these with hexane, the isomers termed A and B of a compound have significantly different R_f values when analysed by thin-layer chromatography on silica gel. Of each pair of

isomers the isomer which is the less polar on silica gel is termed the Isomer A and the more polar one, Isomer B. Halo includes fluoro, chloro, bromo and iodo.

Alkyl and the alkyl moieties of alkoxy, aralkyl, aryloxyalkyl, heteroarylalkyl, heteroaryloxyalkyl, arylthioalkyl, heteroarylthioalkyl, can be in the form of straight or branched chains and, unless otherwise stated, suitably contain from 1 to 6 carbon atoms. Examples are methyl, ethyl, iso-propyl and tert-butyl. Optional substituents include halo (especially chloro and fluoro), hydroxy and C₁₋₄ alkoxy. Examples of substituted alkyl and substituted alkoxy are trifluoromethyl and trifluoromethoxy.

Cycloalkyl is suitably C₃₋₆ cycloalkyl, for example cyclopropyl or cyclohexyl, and cycloalkylalkyl is suitably C₃₋₆ cycloalkyl(C₁₋₄)alkyl, for example 1- or 2-cyclopropylethyl.

Alkenyl and alkynyl suitably contain from 2 to 6 carbon atoms, typically 2 to 4 carbon atoms, in the form of straight or branched chains. Examples are ethenyl, allyl and propargyl. Substituted alkenyl and alkynyl groups include optionally substituted aryl- and heteroarylalkenyl (especially optionally substituted aryl- and heteroaryl(C₂₋₄)alkenyl and, particularly, optionally substituted phenylethenyl) and aryl- and heteroarylalkynyl.

Aryl and the aryl moieties of aralkyl, arylalkenyl, arylalkynyl, aryloxy and aryloxyalkyl include phenyl and naphthyl.

The carbocyclic or heterocyclic ring system which R¹ and R² may form together is suitably a C₄₋₁₀ (typically C₅₋₁₀) aliphatic, aromatic or mixed aliphatic/aromatic carbocyclic ring system, for example cyclopentyl, cyclohexyl, cyclohexadienonyl and such groups carrying one or two optionally substituted fused benzene rings and/or substituents such as methyl; or it may be a 4- to 10-membered heterocyclic ring system, for example tetrahydropyran.

The term heteroaryl is used to described aromatic heterocyclic groups. Heteroaryl and heterocyclyl and the heteroaryl and heterocyclyl moieties of other groups, such as heteroaryloxyalkyl and heterocyclalkyl, are typically 5- or 6-membered rings containing one or more O, N or S heteroatoms which may be fused to one or more other aromatic, heteroaromatic or heterocyclic rings such as a benzene ring. Examples are thienyl, furyl, pyrrolyl, isoxazolyl, oxazolyl, pyrazolyl, imidazolyl, triazolyl, thiazolyl, pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, triazinyl, benzofuryl, benzothienyl, dibenzofuryl, indolyl, quinolinyl and quinoxalinyl groups and, where appropriate, N-oxides and N-alkyl salts thereof.

The optionally substituted heterocyclic ring which R³ and R⁴ may join together to form is suitably a 5 to 7 membered hetero ring having 1 to 3 heteroatoms which are independently selected from O, S or N, and having 1 to 3 substituents which are, for example, halogen, cyano, nitro, C₁₋₆ alkyl, C₁₋₆ alkoxy, group, C₁₋₆ alkylthio, or a heterocyclic ring such as described in the previous paragraph. Examples are pyrrolidine, piperidine, morpholine, thiomorpholine, piperazine, hexamethyleneimine, tetrahydroquinoline, tetrahydroisoquinoline, 2,3-dihydro-1,4-benzoxazine.

Substituents which may be present in optionally substituted aryl and heteroaryl moieties include one or more of the following: halo, hydroxy, mercapto, C₁₋₄ alkyl (especially methyl and ethyl), C₂₋₄ alkenyl (especially allyl), C₂₋₄ alkynyl (especially propargyl), C₁₋₄

TABLE III

SELECTED PROTON NMR DATA

Table III shows selected proton NMR data for certain compounds described in Table I. Chemical shifts are measured in ppm from tetramethylsilane, and deuteriochloroform was used as solvent throughout. The operating frequency of the NMR spectrometer was 270 MHz unless otherwise specified. The following abbreviations are used:

br = broad
s = singlet
d = doublet
t = triplet
q = quartet
m = multiplet

Compound No	NMR Data
62A	2.39(3H, s), 3.91(3H, s), 4.06(3H, s), 5.56(2H, s), 7.3-7.6(4H, m), 8.51(2H, m), 9.15(1H, m) ppm.
62B	2.28(3H, s), 3.86(3H, s), 4.05(3H, s), 5.19(2H, s), 7.1-7.6(4H, m), 8.50(2H, m), 9.10(1H, m) ppm.
127A	2.33(3H, s), 3.88(3H, s), 4.02(3H, s), 5.50(2H, s), 7.3-7.9(8H, m) ppm.
127B	2.21(3H, s), 3.82(3H, s), 4.03(3H, s), 5.15(2H, s), 7.1-7.9(8H, m) ppm.

The compounds of the invention having the formula (I) can be prepared by the routes shown in Scheme I. Throughout Scheme I the terms Y, R¹ and R² are as defined above, L is a leaving group such as halogen (chlorine, bromine or iodine), and Q is a halogen (chlorine, bromine or iodine). Each reaction is performed in a suitable solvent or without a solvent and at a suitable temperature.

Thus compounds of the invention having the formula (I) can be prepared by treating ketoesters of formula (II) with methoxylamine (or a salt of methoxylamine).

Alternatively, compounds of the invention having the formula (I) can be prepared by methylation of oximes of formula (VII) using a methylating agent such as a methyl halide (methyl iodide, methyl bromide or methyl chloride) or dimethylsulphate, usually in the presence of a base such as sodium methoxide or potassium carbonate (see, for example, H. S. Anker and H. T. Clarke, *Organic Synthesis*, Collective Vol. 3, 172). Diazomethane may also be used for this O-methylation.

Alternatively, compounds of the invention of formula (I) may be prepared by reaction between oximes of formula (XIII) and oxime ethers of formula (VIII), generally in the presence of a base. One way of performing this reaction is to treat the oxime (XIII) with the base (such as sodium hydride or sodium methoxide) in a solvent (such as N,N-dimethylformamide or tetrahydrofuran) and then to add the oxime ether (VIII) to the resulting oxime anion.

Ketoesters of the formula (II) may be prepared by treating methyl 3-methoxypropenoates of the formula (III) with an oxidising agent such as potassium permanganate or ozone. Methyl 3-methoxypropenoates of the formula (III) can be prepared using the methods described in EP-A-0370629. Alternatively ketoesters of the formula (II) may be prepared by treating a ketoester of formula (IV) with an oxime of formula (XIII) and a suitable base such as silver carbonate in a suitable solvent such as hexane or toluene.

Other methods for the preparation of the ketoester of formula (II) include the oxidation of phenylacetates of formula (V) with a suitable oxidising agent such as selenium dioxide; and treatment of a phenyl halide of formula (VI) with a metalating species (for example butyl-lithium or magnesium) and reacting the product with an oxalate species of formula GCOCO₂CH₃, wherein G is a methoxy group, a chlorine atom or an imidazole ring (see, for example, J. S. Nimitz and H. S.

Mosher, *Journal of Organic Chemistry* 1981, 46, 211-213).

Ketoesters of formula (IV) are described in EP-A-0363818 and can be prepared by the halogenation (especially chlorination or bromination) of ketoesters of formula (X).

Oximes of formula (VII) can be prepared by nitrosation of phenylacetates of formula (V) using either nitrous acid or an ester of nitrous acid in the presence of a base such as sodium methoxide (see, for example, O. Touster, *Organic Reactions*, 1953, 7, 327, particularly page 342 and S. Kukolja, S. E. Draheim, B. J. Graves, D. C. Hunden, J. L. Pfeil, R. D. G. Cooper, J. L. Ott, and F. T. Counter, *J. Med. Chem.*, 1985, 28, 1896). Alternatively, oximes of formula (VII) can be prepared by treating ketoesters of formula (II) with hydroxylamine (or salt of hydroxylamine).

Other methods for the preparation of oximes (VII) have been reported in the chemical literature (see, for example, T. Shimizu, Y. Hayashi and K. Teramura, *Bull. Chem. Soc. Jpn.*, 1985, 58, 2519; G. W. Shaffer, *Can. J. Chem.*, 1970, 48, 1958).

Phenylacetates of formula (V), oxime ethers of formula (VI) and oximes of formula (XIII) can be prepared by standard procedures described in the chemical literature.

Oxime ethers of the formula (VIII) are described in EP-A-0254426. They are prepared by halogenation (especially chlorination or bromination) of oxime ethers of formula (IX). Oxime ethers of formula (IX) can be prepared from ketoesters of formula (X) by treatment with methoxylamine (or a salt of methoxylamine). Oxime ethers of formula (IX) can be prepared by methylation of oximes of formula (XI) using methods described previously. Oximes of formula (XI) may be prepared either by treatment ketoesters of formula (X) with hydroxylamine (or a salt of hydroxylamine) or by nitrosation of a phenylacetate of formula (XII) using methods described for the preparation of oximes of formula (VII) from phenylacetates of formula (V).

The compounds are active fungicides and may be used to control one or more of the following pathogens: *Pyricularia oryzae* on rice; *Puccinia recondite*, *Puccinia striiformis* and other on wheat, *Puccinia hordei*, *Puccinia striiformis* and other rusts on barley, and rusts on other hosts e.g. coffee, pears, apples, peanuts, vegetables and ornamental plants; *Erysiphe graminis* (powdery mildew) on barley and wheat and other powdery mildews on various hosts such as *Sphaerotheca macularis* on hops, *Sphaerotheca fulginea* on cucurbits (e.g. cucumber), *Podospaera leucotricha* on apple and *Uniclinula necator* on vines; *Helminthosporium* spp., *Rhynchosporium* spp., *Septoria* spp., *Pynrenophora* spp., *Pseudocercospora herpotrichoides* and *Gaeumannomyces graminis* on cereals; *Cercospora arachidicola* and *Cercosporidium personata* on peanuts and other *Cercospora* species on other hosts, for example, sugar beet, bananas, soya beans and rice; *Botrytis cinerea* (grey mould) on tomatoes, strawberries, vegetables, vines and other hosts; *Alternaria* spp. on vegetables (e.g. cucumber), oil-seed rape, apples, tomatoes and other hosts; *Venturia inaequalis* (scab) on apples; *Plasmopara viticola* on vines; other downy mildews such as *Bremia lactucae* on lettuce, *Pernospora* spp. on soybeans, tobacco, onions and other hosts, *Pseudoperonospora humuli* on hops and *Pseudoperonospora cubensis* on cucurbits; *Phytophthora infestans* on potatoes and tomatoes and other *Phytophthora* spp. on vegetables, strawberries, avocado, pepper, ornamentals, tobacco,

cocoa and other hosts; *Thanatephorus cucumeris* on rice and other *Rhizoctonia* species on various hosts such as wheat and barley, vegetables, cotton and turf.

Some of the compounds show a broad range of activities against fungi in vitro. They may also have activity against various post-harvest diseases of fruit (e.g. *Penicillium digitatum* and *italicum* and *Trichoderma viride* on oranges, *Gloeosporium musarum* on bananas and *Botrytis cinerea* on grapes).

Further, some of the compounds may be active as seed dressings against pathogens including *Fusarium* spp., *Septoria* spp., *Tilletia* spp., (bunt, a seed-borne disease of wheat), *Ustilago* spp. and *Helminthosporium* spp. on cereals, *Rhizoctonia solani* on cotton and *Pyricularia oryzae* on rice.

The compounds may move acropetally/locally in plant tissue. Moreover, the compounds may be volatile enough to be active in the vapour phase against fungi on the plant.

The invention therefore provides a method of combating fungi which comprises applying to a plant, to a seed of a plant or to the locus of the plant or seed a fungicidally effective amount of a compound as hereinbefore defined, or a composition containing the same.

The compounds may be used directly for agricultural purposes but are more conveniently formulated into compositions using a carrier or diluent. The invention thus provides fungicidal compositions comprising a compound as hereinbefore defined and an acceptable carrier or diluent therefor.

The compounds can be applied in a number of ways. For example, they can be applied, formulated or unformulated, directly to the foliage of a plant, to seeds or to other medium in which plants are growing or are to be planted, or they can be sprayed on, dusted on or applied as a cream or paste formulation, or they can be applied as a vapour or as slow release granules.

Application can be to any part of the plant including the foliage, stems, branches or roots, or to soil surrounding the roots, or to the seed before it is planted, or to the soil generally, to paddy water or to hydroponic culture systems. The invention compounds may also be injected into plants or sprayed onto vegetation using electrodynamic spraying techniques or other low volume methods.

The term "plant" as used herein includes seedlings, bushes and trees. Furthermore, the fungicidal method of the invention includes preventative, protectant, prophylactic and eradicant treatments.

The compounds are preferably used for agricultural and horticultural purposes in the form of a composition. The type of composition used in any instance will depend upon the particular purpose envisaged.

The compositions may be in the form of dustable powders or granules comprising the active ingredient (invention compound) and a solid diluent or carrier, for example, fillers such as kaolin, bentonite, kieselguhr, dolomite, calcium carbonate, talc, powdered magnesite, fuller's earth, gypsum, diatomaceous earth and china clay. Such granules can be preformed granules suitable for application to the soil without further treatment. These granules can be made either by impregnating pellets of filler with the active ingredient or by pelleting a mixture of the active ingredient and powdered filler. Compositions for dressing seed may include an agent (for example, a mineral oil) for assisting the adhesion of the composition to the seed; alternatively the active ingredient can be formulated for seed dressing purposes

using an organic solvent (for example, N-methylpyrrolidone, propylene glycol or N,N-dimethylformamide). The compositions may also be in the form of wettable powders or water dispersible granules comprising wetting or dispersing agents to facilitate the dispersion in liquids. The powders and granules may also contain fillers and suspending agents.

Emulsifiable concentrates or emulsions may be prepared by dissolving the active ingredient in an organic solvent optionally containing a wetting or emulsifying agent and then adding the mixture to water which may also contain a wetting or emulsifying agent. Suitable organic solvents are aromatic solvents such as alkylbenzenes and alkylnaphthalenes, ketones such as cyclohexanone and methylcyclohexanone, chlorinated hydrocarbons such as chlorobenzene and trichlorethane, and alcohols such as benzyl alcohol, furfuryl alcohol, butanol and glycol ethers.

Suspension concentrates of largely insoluble solids may be prepared by ball or bead milling with a dispersing agent with a suspending agent included to stop the solid settling.

Compositions to be used as sprays may be in the form of aerosols wherein the formulation is held in a container under pressure of a propellant, e.g. fluorotrichloromethane or dichlorodifluoromethane.

The invention compounds can be mixed in the dry state with a pyrotechnic mixture to form a composition suitable for generating in enclosed spaces a smoke containing the compounds.

Alternatively, the compounds may be used in microencapsulated form. They may also be formulated in biodegradable polymeric formulations to obtain a slow, controlled release of the active substance.

By including suitable additives, for example additives for improving the distribution, adhesive power and resistance to rain on treated surfaces, the different compositions can be better adapted for various utilities.

The invention compounds can be used as mixtures with fertilisers (e.g. nitrogen-, potassium- or phosphorus-containing fertilisers). Compositions comprising only granules of fertiliser incorporating, for example coated with, the compound are preferred. Such granules suitably contain up to 25% by weight of the compound. The invention therefore also provides a fertiliser composition comprising a fertiliser and the compound of general formula (I) or a salt or metal complex thereof.

Wettable powders, emulsifiable concentrates and suspension concentrates will normally contain surfactants, e.g. a wetting agent, dispersing agent, emulsifying agent or suspending agent. These agents can be cationic, anionic or non-ionic agents.

Suitable cationic agents are quaternary ammonium compounds, for example, cetyltrimethylammonium bromide. Suitable anionic agents are soaps, salts of aliphatic monoesters of sulphuric acid (for example, sodium lauryl sulphate), and salts of sulphonated aromatic compounds (for example, sodium dodecylbenzenesulphonate, sodium, calcium or ammonium lignosulphonate, butylnaphthalene sulphonate, and a mixture of sodium diisopropyl- and triisopropyl-naphthalene sulphonates).

Suitable non-ionic agents are the condensation products of ethylene oxide with fatty alcohols such as oleyl or cetyl alcohol, or with alkyl phenols such as octyl- or nonylphenol and octylcresol. Other non-ionic agents are the partial esters derived from long chain fatty acids

TABLE I-continued

COM- POUND NO.	R ¹	R ²	Y
52	cyano	cyano	H
53	Ø	Ø	H
54	Ø	Ø	H
55	Ø	Ø	H
56	tert-C ₄ H ₉	H	H
57	C ₆ H ₅ CH ₂	H	H
58	2,4-di-Cl-C ₆ H ₃	H	H
59	2,4-di-F-C ₆ H ₃	H	H
60	3,5-di-CH ₃ -C ₆ H ₃	H	H
61	3,5-di-CH ₃ O-C ₆ H ₃	H	H
62A*	pyrazin-2-yl	CH ₃	H
62B*	pyrazin-2-yl	CH ₃	H
63	6-CH ₃ -pyrid-3-yl	CH ₃	H
64	pyrid-2-yl	C ₂ H ₅	H
65	pyrid-3-yl	CH ₃	H
66	pyrimidin-5-yl	iso-C ₃ H ₇	H
67	iso-C ₃ H ₇	pyrimidin-5-yl	H
68	pyrid-4-yl	CH ₃	H
69	6-Cl-pyrid-2-yl	CH ₃	H
70	5-Cl-pyrid-2-yl	CH ₃	H
71	4-Cl-pyrid-2-yl	CH ₃	H
72	3-Cl-pyrid-2-yl	CH ₃	H
73	6-cyano-pyrid-2-yl	CH ₃	H
74	5-cyano-pyrid-2-yl	CH ₃	H
75	4-cyano-pyrid-2-yl	CH ₃	H
76	3-cyano-pyrid-2-yl	CH ₃	H
77	6-Br-pyrid-2-yl	CH ₃	H
78	5-Br-pyrid-2-yl	CH ₃	H
79	4-Br-pyrid-2-yl	CH ₃	H
80	3-Br-pyrid-2-yl	CH ₃	H
81	6-CH ₃ -pyrid-2-yl	CH ₃	H
82	5-CH ₃ -pyrid-2-yl	CH ₃	H
83	4-CH ₃ -pyrid-2-yl	CH ₃	H
84	3-CH ₃ -pyrid-2-yl	CH ₃	H
85	6-F-pyrid-2-yl	CH ₃	H
86	5-F-pyrid-2-yl	CH ₃	H
87	4-F-pyrid-2-yl	CH ₃	H
88	3-F-pyrid-2-yl	CH ₃	H
89	3-CH ₃ -pyrazin-2-yl	CH ₃	H
90	3-C ₂ H ₅ -pyrazin-2-yl	CH ₃	H
91	3-Cl-pyrazin-2-yl	CH ₃	H
92	3-CH ₃ O-pyrazin-2-yl	CH ₃	H
93	5-CO ₂ CH ₃ -pyrazin-2-yl	CH ₃	H
94	5-CO ₂ C ₂ H ₅ -pyrazin-2-yl	CH ₃	H
95	3-cyano-pyrazin-2-yl	CH ₃	H
96	pyrimidin-4-yl	CH ₃	H
97	2-Cl-pyrimidin-4-yl	CH ₃	H
98	2-CH ₃ O-pyrimidin-4-yl	CH ₃	H
99	2-CH ₃ -pyrimidin-4-yl	CH ₃	H
100	2-cyano-pyrimidin-4-yl	CH ₃	H
101	thiazol-2-yl	CH ₃	H
102	thien-3-yl	CH ₃	H
103	5-Cl-thien-2-yl	CH ₃	H
104	5-CH ₃ -thien-2-yl	CH ₃	H
105	5-Br-thien-2-yl	CH ₃	H
106	5-cyano-thien-2-yl	CH ₃	H
107	3-CH ₃ -thien-2-yl	CH ₃	H
108	2-CH ₃ O-C ₆ H ₄	CH ₃	H
109	3-CH ₃ O-C ₆ H ₄	CH ₃	H
110	4-CH ₃ O-C ₆ H ₄	CH ₃	H
111	2-CH ₃ -C ₆ H ₄	CH ₃	H
112	3-CH ₃ -C ₆ H ₄	CH ₃	H
113	4-CH ₃ -C ₆ H ₄	CH ₃	H
114	2-F-C ₆ H ₄	CH ₃	H
115	3-F-C ₆ H ₄	CH ₃	H
116	4-F-C ₆ H ₄	CH ₃	H
117	2-Cl-C ₆ H ₄	CH ₃	H
118	3-Cl-C ₆ H ₄	CH ₃	H
119	4-Cl-C ₆ H ₄	CH ₃	H
120	2-Br-C ₆ H ₄	CH ₃	H
121	3-Br-C ₆ H ₄	CH ₃	H
122	4-Br-C ₆ H ₄	CH ₃	H
123	2-NO ₂ -C ₆ H ₄	CH ₃	H
124	3-NO ₂ -C ₆ H ₄	CH ₃	H
125	4-NO ₂ -C ₆ H ₄	CH ₃	H
126	2-CF ₃ -C ₆ H ₄	CH ₃	H
127A*	3-CF ₃ -C ₆ H ₄	CH ₃	H
127B*	3-CF ₃ -C ₆ H ₄	CH ₃	H
128	4-CF ₃ -C ₆ H ₄	CH ₃	H

TABLE I-continued

COM- POUND NO.	R ¹	R ²	Y
129	2-cyano-C ₆ H ₄	CH ₃	H
130	3-cyano-C ₆ H ₄	CH ₃	H
131	4-cyano-C ₆ H ₄	CH ₃	H
132	3,4,5-(CH ₃ O) ₃ -C ₆ H ₂	CH ₃	H
133	3,5-di-F-pyrid-2-yl	CH ₃	H
134	3,4,5,6-F ₄ -pyrid-3-yl	CH ₃	H
135	2,6-di-Cl-pyrid-3-yl	CH ₃	H
136	pyridazin-3-yl	CH ₃	H
137	pyridazin-4-yl	CH ₃	H
138	6-CH ₃ -pyridazin-3-yl	CH ₃	H
139	4-cyano-quinolin-2-yl	CH ₃	H
140	quinoxalin-2-yl	CH ₃	H
141	C ₆ H ₅	CH ₃	6-F
142	C ₆ H ₅	CH ₃	6-Cl
143	6-CH ₃ -pyrimidin-4-yl	CH ₃	H
144	4-CH ₃ -pyrimidin-5-yl	CH ₃	H
145	4-CH ₃ -pyrimidin-2-yl	CH ₃	H
146	4,6-di-CH ₃ -pyrimidin-2-yl	CH ₃	H
147	2,6-di-CH ₃ -pyrimidin-4-yl	CH ₃	H
148	2,4-di-CH ₃ -pyrimidin-5-yl	CH ₃	H
149	6-Cl-pyrimidin-4-yl	CH ₃	H
150	6-CH ₃ O-pyrimidin-4-yl	CH ₃	H
151	4,6-di-CH ₃ O-pyrimidin-2-yl	CH ₃	H
152	Ø	Ø	H
153	Ø	Ø	H
154	pyrid-2-yl, N-oxide	CH ₃	H
155	5-C ₂ H ₅ -pyrid-2-yl	CH ₃	H
156	CH ₃ CO	CH ₃	H
157	C ₆ H ₅ CO	CH ₃	H
158	N-CH ₃ -pyrrol-2-yl	CH ₃	H
159	4-Cl-quinolin-2-yl	CH ₃	H
160	2,4-di-Cl-C ₆ H ₃	1,2,4-tri- azol-1-yl-CH ₂	H
161	2,4-di-Cl-C ₆ H ₃	pyrid-3- yl-CH ₂	H
162	2,4-di-CH ₃ -thiazol-5-yl	CH ₃	H
163	furan-2-yl	CH ₃	H
164	2,4-di-CH ₃ -furan-3-yl	CH ₃	H
165	pyrid-2-yl	pyrid-2-yl	H
166	6-C ₆ H ₅ -pyrimidin-4-yl	CH ₃	H
167	4-cyano-pyrid-3-yl	CH ₃	H
168	1,2,4-triazin-5-yl	CH ₃	H
169	3-CH ₃ -1,2,4-triazin-5-yl	CH ₃	H
170	3-C ₆ H ₅ -1,2,4-triazin-5-yl	CH ₃	H
171	3-SCH ₃ -1,2,4-triazin-5-yl	CH ₃	H
172	3-CH ₃ O-1,2,4-triazin-5-yl	CH ₃	H
173	5-CONH ₂ -pyrazin-2-yl	CH ₃	H
174	5-cyano-pyrazin-2-yl	CH ₃	H
175	5,6-di-CH ₃ -pyrazin-2-yl	CH ₃	H
176	3,5-di-CH ₃ -pyrazin-2-yl	CH ₃	H
177	3,6-di-CH ₃ -pyrazin-2-yl	CH ₃	H
178	5-CH ₃ -pyrazin-2-yl	CH ₃	H
179	6-CH ₃ -pyrazin-2-yl	CH ₃	H
180	5-Cl-pyrazin-2-yl	CH ₃	H
181	6-Cl-pyrazin-2-yl	CH ₃	H
182	5,6-dicyano-pyrazin-2-yl	CH ₃	H
183	4-SO ₂ CH ₃ -C ₆ H ₄	CH ₃	H
184	4-NH ₂ -C ₆ H ₄	CH ₃	H
185	2,4-di-Cl-C ₆ H ₃	CH ₃	H
186	2,4-di-CH ₃ -C ₆ H ₃	CH ₃	H
187	4-NHCONH ₂ -C ₆ H ₄	CH ₃	H
188	C ₆ H ₅	cyclopropyl	H
189	C ₆ H ₅	Cl	H
190	4-C ₂ H ₅ O-C ₆ H ₄	CF ₃	H
191	C ₆ H ₅	SCH ₃	H
192	C ₆ H ₅	F	H
193	C ₆ H ₅	OC ₂ H ₅	H
194	C(CH ₃) ₃	CH ₃	H
195	cyclohexyl-CH ₂	CH ₃	H
196	C ₆ H ₅ -CH ₂	CH ₃	H
197	pyrazin-2-yl-CH ₂	CH ₃	H
198	(E)-C ₆ H ₅ -CH=CH	CH ₃	H
199	C ₆ H ₅ -OCH ₂	CH ₃	H
200	C ₆ H ₅	CH ₂ Cl	H
201	benzthiazol-2-yl	CH ₃	H
202	benzoxazol-2-yl	CH ₃	H
203	pyrazin-2-yl	C ₂ H ₅	H

and hexitol anhydrides, the condensation products of the said partial esters with ethylene oxide, and the lecithins. Suitable suspending agents are hydrophilic colloids (for example, polyvinylpyrrolidone and sodium carboxymethylcellulose), and swelling clays such as bentonite or attapulgite.

Compositions for use as aqueous dispersions or emulsions are generally supplied in the form of a concentrate containing a high proportion of the active ingredient, the concentrate being diluted with water before use. These concentrates should preferably be able to withstand storage for prolonged periods and after such storage be capable of dilution with water in order to form aqueous preparations which remain homogeneous for a sufficient time to enable them to be applied by conventional spray equipment. The concentrates may conveniently contain up to 95%, suitably 10-85%, for example 25-60%, by weight of the active ingredient. After dilution to form aqueous preparations, such preparations may contain varying amounts of the active ingredient depending upon the intended purpose, but an aqueous preparation containing 0.0005% or 0.01% to 10% by weight of active ingredient may be used.

The compositions of this invention may contain other compounds having biological activity, e.g. compounds having similar or complementary fungicidal activity or which possess plant growth regulating, herbicidal or insecticidal activity.

A fungicidal compound which may be present in the composition of the invention may be one which is capable of combating ear diseases of cereals (e.g. wheat) such as *Septoria*, *Gibberella* and *Helminthosporium* spp., seed and soil-borne diseases and downy and powdery mildews on grapes and powdery mildew and scab on apple, etc. By including another fungicide, the composition can have a broader spectrum of activity than the compound of general formula (I) alone. Further the other fungicide can have a synergistic effect on the fungicidal activity of the compound of general formula (I). Examples of fungicidal compounds which may be included in the composition of the invention are (RS)-1-aminopropylphosphonic acid, (RS)-4-(4-chlorophenyl)-2-phenyl-2-(1H-1,2,4-triazol-1-ylmethyl)butyronitrile, (Z)-N-but-2-enyloxymethyl-2-chloro-2',6'-diethylacetanilide, 1-(2-cyano-2-methoxyiminoacetyl)-3-ethyl urea, 3-(2,4-dichlorophenyl)-2-(1H-1,2,4-triazol-1-yl)quinazolin-4(3H)-one, 4-bromo-2-cyano-N,N-dimethyl-6-trifluoromethylbenzimidazole-1-sulphonamide, 5-ethyl-5,8-dihydro-8-oxo(1,3)-dioxol(4,5-g)quinoline-7-carboxylic acid α -[N-(3-chloro-2,6-xylyl)-2-methoxyacetamido]- γ -butyrolactone, aldimorph, anilazine, benalaxyl, benomyl, biloxazol, bina-pacryl, biteranol, blasticidin S, bromuconazole, bupirimate, buthiobate, captafol, captan, carbendazim, carboxin, chlorbenzthiazole, chloroneb, chlorothalonil, chlorozolinate, copper containing compounds such as copper oxychloride, copper sulphate and Bordeaux mixture, cycloheximide, cymoxanil, cyproconazole, cyprofuram, di-2-pyridyl disulphide 1,1'-dioxide, dichlofluanid, dichlone, diclobutrazol, diclomezine, dicloran, difenoconazole, dimethamorph, dimethirimol, diniconazole, dinocap, ditalimfos, dithianon, dode-morph, dodine, edifenphos, etaconazole, ethirimol, ethyl

(Z)-N-benzyl-N-([methyl(methylthioethylideneamino-oxycarbonyl)amino]thio)- β -alaninate, etridiazole, fenapanil, fenarimol, fenfuram, fencpiclonil, fenpropidin, fenpropimorph, fentin acetate, fentin hydroxide, flutolanil, flutriafol, flusilazole, folpet, fosetyl-

aluminium, fuberidazole, furalaxyl, furconazole-cis, guazatine, hexaconazole, hydroxyisoxazole, imazalil, imibenconazole, iprobenfos, iprodione, isoprothiolane, kasugamycin, mancozeb, maneb, mepanipyrim, mepronil, metalaxyl, methfuroxam, metsulfosax, myclobutanil, neoasozin, nickel dimethyldithiocarbamate, nitrothal-isopropyl, nuarimol, ofurace, organomercury compounds, oxadixyl, oxycarboxin, pefurazoate, penconazole, pencycuron, phenazin oxide, phthalide, polyoxin D, polyram, probenazole, prochloraz, procymidone, propamocarb, propiconazole, propineb, prothiocarb, pyrazophos, pyrifenoxy, pyroquilon, pyroxyfur, pyrrolnitrin, quinomethionate, quintozone, SSF-109, streptomycin, sulphur, tebuconazole, techlofthalam, tecnazene, tetraconazole, thiabendazole, thicyofen, thiophanate-methyl, thiram, tolclofos-methyl, triacetate salt of 1,1'-iminodi(octamethylene)diguandine, triadimefon, triadimenol, triazbutyl, tricyclazole, tridemorph, triforine, validamycin A, vinclozolin, zarilamid and zineb. The compounds of general formula (I) can be mixed with soil, peat or other rooting media for the protection of plants against seed-borne, soil-borne or foliar fungal diseases.

Suitable insecticides which may be incorporated in the composition of the invention include buprofezin, carbaryl, carbofuran, carbosulfan, chlorpyrifos, cycloprothrin, demeton-s-methyl, diazinon, dimethoate, ethofenprox, fenitrothion, fenobucarb, fenthion, formothion, isoprocab, isoxathion, monocrotophos, phenothoate, pirimicarb, propaphos and XMC.

Plant growth regulating compounds are compounds which control weeds or seedhead, formation, or selectively control the growth of less desirable plants (e.g. grasses).

Examples of suitable plant growth regulating compounds for use with the invention compounds are 3,6-dichloropicolinic acid, 1-(4-chlorophenyl)-4,6-dimethyl-2-oxo-1,2-dihydropyridine-3-carboxylic acid, methyl-3,6-dichloroanisate, abscisic acid, asulam, benzoyl-prop-ethyl, carbetamide, daminozide, difenzoquat, dikegulac, ethephon, fententezole, fluoridamid, glyphosate, glyphosine, hydroxybenzotriazoles (e.g. bromoxynil), inabenzofide, isopyrimol, long chain fatty alcohols and acids, maleic hydrazide, mefluidide, morphactins (e.g. chlorfluoroccol), paclobutrazol, phenoxyacetic acids (e.g. 2,4-D or MCPA), substituted benzoic acid (e.g. triiodobenzoic acid), substituted quaternary ammonium and phosphonium compounds (e.g. chloromequat, chlorphonium or mepiquatchloride), tecnazene, the auxins (e.g. indoleacetic acid, indolebutyric acid, naphthylacetic acid or naphthoxyacetic acid), the cytokinins (e.g. benzimidazole, benzyladenine, benzylaminopurine, diphenylurea or kinetin), the gibberellins (e.g. GA₃, GA₄ or GA₇) and triapenthenol.

The following Examples illustrate the invention. Throughout the Examples, the term 'ether' refers to diethyl ether, magnesium sulphate was used to dry solutions, and solutions were concentrated under reduced pressure. Reactions involving air- or water-sensitive intermediates were performed under an atmosphere of nitrogen and solvents were dried before use, where appropriate. Unless otherwise stated, chromatography was performed on a column of silica gel as the stationary phase. Where shown, infrared and NMR data are selective; no attempt is made to list every absorption in all cases. ¹H NMR spectra were recorded using CDCl₃ solutions unless otherwise stated. The following abbreviations are used throughout: