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[54] Title: CYANOACETAMIDE DERIVATIVE, PLANT DISEASE PROTECTANT COMPRISING THE SAME AS AN ACTIVE INGREDIENT

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Attorney / Agent: Messrs. Romulo et al.

CYANOACETAMIDE DERIVATIVE, METHOD FOR PRODUCING THE SAME AND PLANT DISEASE PROTECTANT COMPRISING THE SAME AS AN ACTIVE INGREDIENT

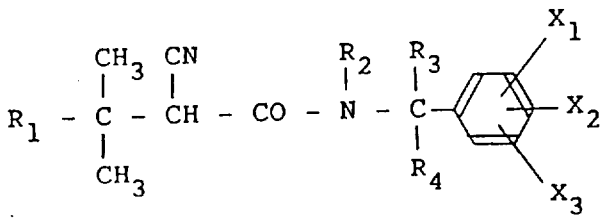
ABSTRACT OF THE DISCLOSURE

A cyanoacetamide derivative, a method for producing the same and a plant disease protectant comprising the same are disclosed. The cyanoacetamide derivative provided according to the present invention has an extremely high controlling activity against various plant diseases, particularly against rice blast (Pyricularia oryzae).

The present invention relates to a novel cyanoacetamide derivative, a method for producing the same and a plant disease protectant comprising the same as an active ingredient.

Various plant disease protectants have been developed till now, but they are not always said to be satisfactory in terms of efficiency, etc.

Many cyanoacetamide derivatives have been synthesized till now. For instance, JP-A-63-72663 describes a cyanoacetamide derivative represented by the formula (I) below as a compound having a high controlling activity against weeds together with the formulation examples and test examples.

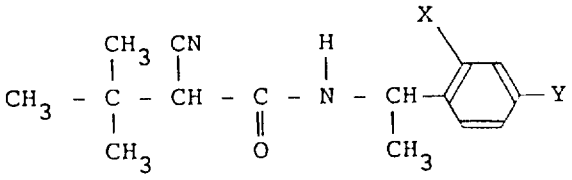


(I)

wherein R_1 is an alkyl group; R_2, R_3 and R_4 are, same or different, a hydrogen atom or an alkyl group; X_1, X_2 and X_3 are, same or different, a hydrogen or halogen atom or an

alkyl, halogenoalkyl, alkoxy, alkylthio, alkoxyalkyl, nitro or cyano group.

The present inventors have extensitvely studied to develop a compound having a high controlling activity against plant diseases, and as a result, have found that a cyanoacetamide derivative represented by the formula (II) (hereinafter referred to as the present compound),



(II)

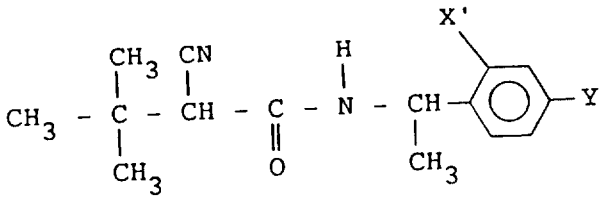
wherein X is a fluorine, chlorine atom or a lower alkoxy (C_1-C_2) group, and Y is a chlorine or bromine atom or a trifluoromethyl or lower fluoroalkoxy (C_1-C_2) group, has high foliage protecting and disease controlling activities and systemic disease controlling activity particularly against rice blast (Pyricularia oryzae). At the same time, we have found that the present compound has an extremely low phytotoxicity against rice even when it is applied in high dosage rates.

The present inventors thus attained to the present invention.

The present compounds have an extremely high controlling activity particularly against rice blast (Pyricularia oryzae). Specific examples of plant diseases

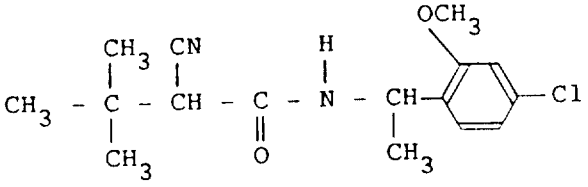
which can be controlled by the present compounds other than rice blast are helminthosporium leaf spot of rice (Cochliobolus miyabeanus), scab of apple (Venturia inaequalis), scan of pear (Venturia nashicola), anthracnose of Japanese persimmon (Gloeosporium kaki), anthracnose of melons (Colletotrichum lagenarium), anthracnose of kidney bean (Collectotrichum lindemuthianum), leaf spot of peanut (Mycosphaerella personatum), brown leaf spot of peanut (Cercospora arachidicola), anthracnose of tobacco (Colletotrichum tabacum), cercospora leaf spot of beet (Cercospora beticola), etc.

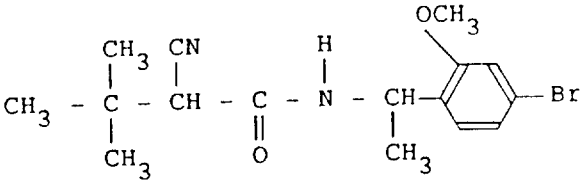
Of the present compounds, those which are more preferred in terms of the controlling activity are compounds represented by the formula (III),

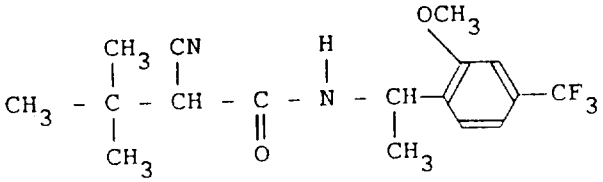


(III)

wherein X' is a lower alkoxy (C_1-C_2) group, and Y is a chlorine or bromine atom or a trifluoromethyl or lower fluoroalkoxy (C_1-C_2) group; and those which are most preferred are compounds represented by the following formulae:



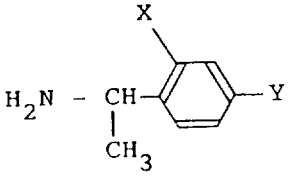




A method for producing the present compounds is explained in detail below.

Method A:

The present compounds can be obtained by reacting an α-methylbenzylamine derivative represetned by the formula (IV)



(IV)

wherein X and Y are the same meaning as described above, with an α-cyano-tert-butylacetic acid or its reactive derivative in the presence of one or more reaction assistants if necessary.

Specific examples of the α-cyano-tert-butylacetic acid or its reactive derivative used in the above reaction are the corresponding carboxylic acid, acid anhydride, acid chloride, acid bromide and carboxylic acid esters (e.g. methyl ester, ethyl ester), etc. As examples of the reaction assistant, there are mentioned the following compounds depending on the type of the α-cyano-tert-butylacetic acid or its reactive derivative : Dicyclohexylcarbodiimide, 1-ethyl-3-(3-dimethylamino-propyl)carbodiimide hydrochloride, 1,1'-carbonyldi-imidazole, phosphorus pentachloride, phosphorus trichloride, phosphorus oxychloride, thionyl chloride, phosgene, sodium hydroxide, potassium hydroxide, sodium methylate, sodium ethylate, triethylamine, pyridine, quinoline, N,N-dimethylaniline, N,N-diethylaniline, N-methylmorpholine, etc.

In the above reaction, normally, the reaction temperature is from 0° to 200°C; the reaction time is from 0.1 to 24 hours. As to the amount of the reagents used for the reaction, the amount of the α-methylbenzylamine derivative represented by the formula (IV) is usually from 1 to 1.2 moles based on 1 mole of the α-cyano-tert-butyl-acetic acid or its reactive derivative, and that of the reaction assistant is usually from 1 mmole to 5 moles

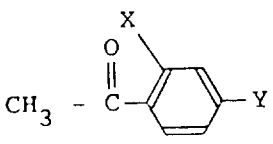
based on the same.

In the above reaction, a reaction solvent is not always necessary, but generally, the reaction is carried out in the presence of a solvent.

Specific examples of the usable solvent are solvents such as aliphatic hydrocarbons (e.g. hexane, heptane, ligroin), aromatic hydrocarbons (e.g. benzene, toluene, xylene), ethers (e.g. diethyl ether, diisopropyl ether, tetrahydrofuran (THF), dioxane, diethylene glycol dimethyl ether), halogen-containing solvents (e.g. dichloromethane, chloroform, carbon tetrachloride, 1,2-dichloroethane, chlorobenzene), N,N-dimethylforammide (DMF), dimethyl sulfoxide, acetonitrile, water, etc. and mixtures thereof.

After the completion of the reaction, the intended present compounds can be obtained by carrying out the usual workup such as extraction, concentration, filtration, etc. and additionally, if necessary, column chromatography, recrystallization, etc.

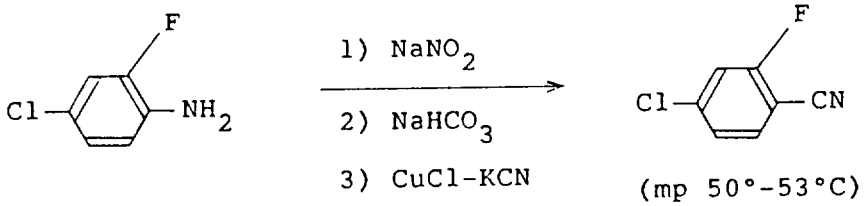
In Method A, the α-methylbenzylamine derivative represented by the formula (IV), one of the starting materials for producing the present compounds, can be synthesized, for example, from a compound represented by the formula,



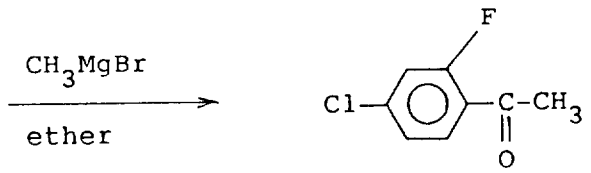
(V)

wherein X and Y are the same meaning as defined above, according to the Leuckart's reaction described in Organic Reactions, Vol. 5, 301-330 (1949).

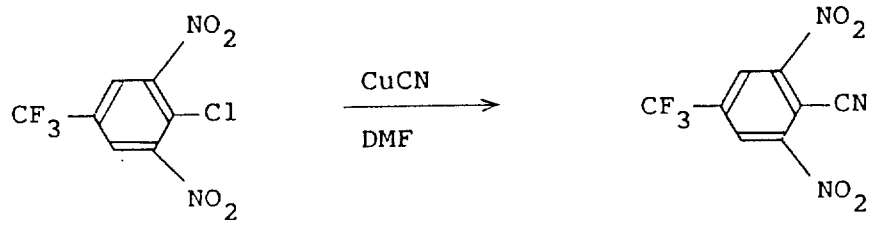
For producing the compound represented by the formula (V), a commercially available product may be used, or it can be synthesized by the following method shown below.

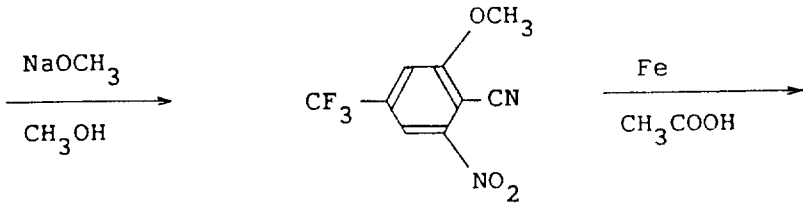


(mp 50°-53°C)

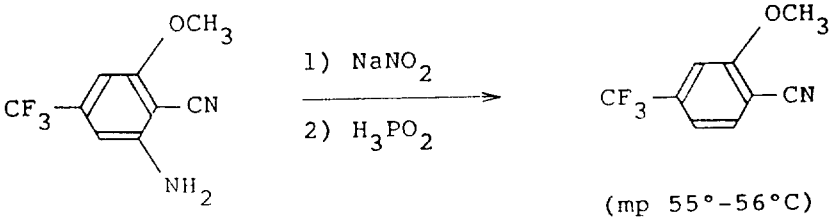


(bp 56°-58°C/
0.5 mmHg)



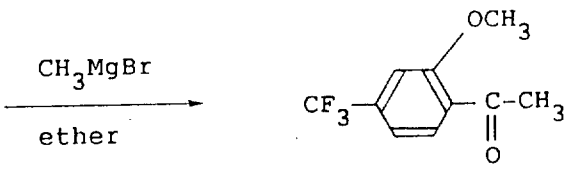


[J. Org. Chem., 39, 1939 (1974)]

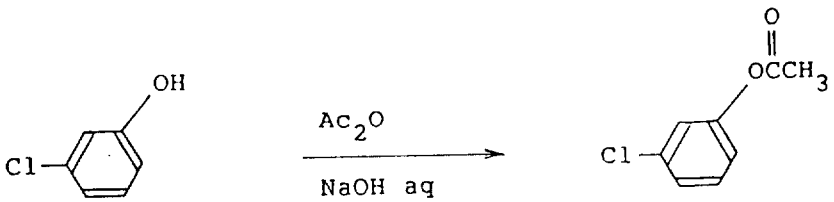


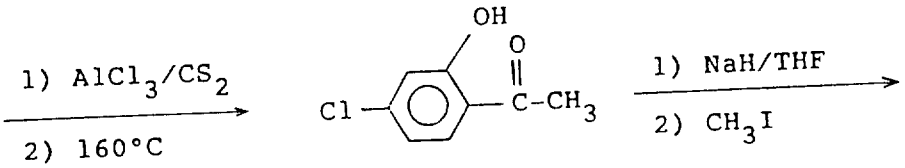
(mp 135°-137°C)

(mp 55°-56°C)

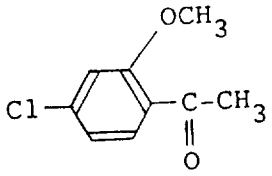


(mp 50°-53°C)



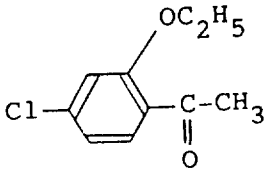


[J. Chem. Soc., 1960, 1279]

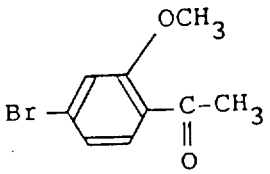


(mp 58°C)

The following compounds were obtained by the same method.



(mp 173°-175°C)



(mp 105°C)

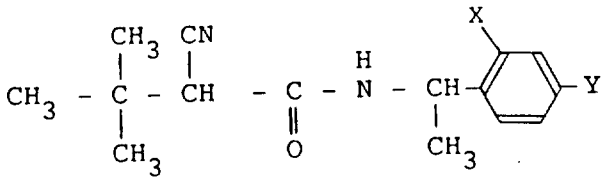
On the other hand, the α-cyano-tert-butylacetic acid or its reactive derivative, which is the other starting material for producing the present compounds, can be synthesized, for example, by the method described in J.

Am. Chem. Soc., 72, 4796 (1950) or Justus Liebigs Ann. Chem. 718, 101 (1968) and a usual method for converting the reaction product to its derivative, i.e. a method comprising producing a carboxylic acid by the hydrolysis of a carboxylic acid ester [e.g., Arkiv Kemi, 2, 321 (1950)] and producing a carboxylic acid halide by the acid-halogenation of the carboxylic acid [e.g., Tetrahedron, 35, 1965 (1979)].

The present compounds have at least two asymmetric carbon atoms and at least four stereoisomers. They also include the optical isomers in which the absolute configuration of the benzyl position is (R). In this case, optically active α-methylbenzylamine derivatives, one of the starting materials, represented by the formula (II) and having an absolute configuration of (R) in the benzyl position can be obtained, for examle, by the optical resolution of the corresponding racemates according to the method described in J. Chem. Soc. (B), 1971, 2418.

Some of the cyanoacetamide derivatives of the formula (II) which can be obtained by this method are shown below.

Table 1



X	Y	X	Y
F	Cl	F	OCH_3
Cl	Cl	Cl	OCF_3
OCH_3	Cl	OCH_3	OCF_3
OC_2H_5	Cl	OC_2H_5	OCF_3
F	Br	F	$OCHF_2$
Cl	Br	Cl	$OCHF_2$
OCH_3	Br	OCH_3	$OCHF_2$
OC_2H_5	Br	OC_2H_5	$OCHF_2$
F	CF_3	F	OCF_2CF_2H
Cl	CF_3	Cl	OCF_2CF_2H
OCH_3	CF_3	OCH_3	OCF_2CF_2H
OC_2H_5	CF_3	OC_2H_5	OCF_2CF_2H

When the present compounds may be used as an active ingredient for plant disease protectants, they may be used as they are without adding any other ingredients. Usually, however, they are formulated before use into emulsifiable concentrates, wettable powders, suspension formulations, granules, dusts, etc. by mixing with solid carriers, liquid carriers, surface active agents and other

auxiliaries for formulation.

These preparations usually contain from 0.1 to 99% by weight, preferably from 0.2 to 95% by weight of the present compounds as an active ingredient.

Specific examples of the solid carriers are fine powders or granules of kaolin clay, attapulgite clay, bentonite, terra abla, pyrophyllite, talc, diatomaceous earth, calcite, corn stalk powder, walnut shell powder, urea, ammonium sulfate, synthetic hydrated silicon dioxide, etc. Specific examples of the liquid carriers are aromatic hydrocarbons (e.g. xylene, methylnaphthalene), alcohols (e.g. isopropanol, ethylene glycol, cellosolve), ketones (e.g. acetone, cyclohexanone, isophorone), vegetable oils (e.g. soybean oil, cotton seed oil), dimethyl sulfoxide, acetonitrile, water, etc.

Specific examples of the surface active agents used for emulsification, dispersion, wetting, etc. are anionic surface active agents such as the salt of alkyl sulfates, alkyl(aryl)sulfonates, dialkyl sulfosuccinates, the salt of polyoxyethylene alkylaryl ether phosphoric acid esters, naphthalenesulfonic acid/formalin condensates, etc. and nonionic surface active agents such as polyoxyethylene alkyl ether, polyoxyethylene polyoxypropylene block copolymers, sorbitan fatty acid esters, polyoxyethylene sorbitan fatty acid esters, etc.

Specific examples of the auxiliaries for formulation are lignosulfonates, alginates, polyvinyl alcohol, gum arabic, CMC (carboxymethyl cellulose), PAP

(isopropyl acid phosphate), etc.

These preparations are used as they are, or used for foliage application in dilution with water, soil incorporation by dusting or granule application, soil application, etc. An increase in the controlling activity can be expected by using them in mixture with other plant disease controlling agents. These preparations can be used in mixture with insecticides, acaricides, nematocides, herbicides, plant growth regulators, fertilizers, soil improvers, etc.

When the present compounds are used as an active ingredient for plant disease controlling agents, their dosage rate varies with weather conditions, preparation forms, when, how and where they are applied, diseases to be controlled, crops to be protected, etc. However it is usually from 0.05 to 200 g/are, preferably from 0.1 to 100 g/are. When the emulsifiable concentrates, wettable powders, suspension formulations, etc. are applied in dilution with water, the application concentration of the present compounds is usually from 0.00005 to 0.5%, preferably from 0.0001 to 0.2%. The granules, dusts, etc. are usually applied as they are without dilution.

The present invention is illustrated in more detail with reference to the following production examples, formulation examples and test examples, but it should not be interpreted to be limited to these examples.

Production examples are shown below.

Production Example 1 (Compound No. 3)

0.58 Gram (3.6 mmoles) of 1,1'-carbonyldiimidazole was added in small portions to a solution of 0.42 g (3 mmoles) of α-cyano-tert-butylacetic acid in 5 ml of dry tetrahydrofuran. The mixture was stirred at room temperature for 1 hour. To this solution was added by drops 0.56 g (3 mmoles) of 1-(4-chloro-2-methoxyphenyl)ethylamine, and the resulting mixture was stirred at room temperature for 2 hours. After the reaction had been completed, the solvent was removed. Purifying the resulting crude product by column chromatography on silica gel (eluent, hexane : ethyl acetate = 2 : 1) gave 0.83 g of N-[1-(4-chloro-2-methyloxyphenyl)ethyl]-2-cyano-3,3-dimethylbutanamide.

m.p. 144°-147°C

^{1}H-NMR ($CDCl_3$/TMS, δ (ppm))

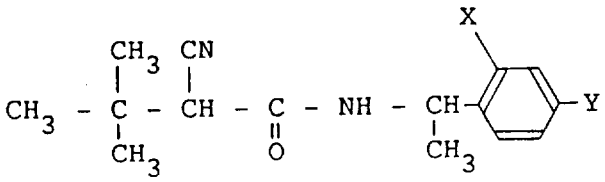
δ (ppm) 1.08 (s, 9H), 1.16 (s, 9H)
1.45 (d, J=7Hz, 3H),
3.05 (s, 1H), 3.09 (s, 1H),
3.85 (s, 3H), 4.85-5.4 (m, 1H),
6.7-7.4 (m, 4H)

Mass spectrum (m/e, 70 eV):

308 (M^+), 293, 251, 184, 169, 103

Table 2 shows some examples of the present compounds synthesized by the above method.

Table 2



Compound No.	X	Y	Melting point (°C)
(1)	F	Cl	110 - 114
(2)	Cl	Cl	186 - 188
(3)	OCH_3	Cl	144 - 147
(4)	OC_2H_5	Cl	122 - 124
(5)	OCH_3	Br	136 - 139
(6)	OCH_3	CF_3	119 - 122

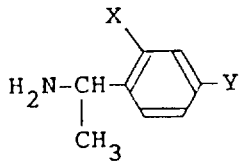
Referential Production Example

A mixture of 7.43 g (40.3 mmoles) of 4-chloro-2-methoxyacetophenone, 7.48 g (161.2 mmoles) of formamide and 1 ml of 90% aqueous formic acid was heated at 180°-190°C for 6 hours, and then cooled. After the reaction had been completed, water was added to the reaction mixture. Then, the mixture was extracted with chloroform, and concentrated. To the obtained oily residue (9.37 g) was added a conc. hydrochloric acid, and the residue was heated at 100°C for 1 hour. After the reaction had been completed, the reaction mixture was cooled with ice and then water was added to the mixture. After extracting

twice with chloroform in order to remove impurities, water was added to the extract. Then, after being alkalified by an aqueous solution of sodium hydroxide with ice-cooling, the aqueous layer was extracted twice with ether. Drying of the layer over anhydrous magnesium sulfate and removal of the solvent from the layer were carried out in this order to obtain 5.24 g of 1-(4-chloro-2-methoxyphenyl)ethylamine (yield, 70%).

Some of the α-methylbenzylamine derivatives of the formula (II) which were synthesized by the above method are shown in Table 3.

Table 3



X	Y	^{1}H-NMR ($CDCl_3$/TMS, δ (ppm))
OCH_3	Cl	1.31 (d, J=7Hz, 3H), 1.55 (s, 2H), 3.73 (s, 3H), 4.24 (q, J=7Hz, 1H), 6.5-7.35 (m, 3H)
OCH_3	Br	1.32 (d, J=7Hz, 3H), 1.58 (s, 2H), 3.76 (s, 3H), 4.25 (q, J=7Hz, 1H), 6.8-7.3 (m, 3H)
F	Cl	1.38 (d, J=7Hz, 3H), 1.61 (br s, 2H), 4.34 (q, J=7Hz, 1H), 6.85-7.6 (m, 3H)
OCH_3	CF_3	1.39 (d, J=7Hz, 3H), 1.66 (s, 2H), 3.90 (s, 3H), 4.43 (q, J=7Hz, 1H), 7.0-7.65 (m, 3H)

Formulation examples are shown below.

In the examples, the present compounds are identified by Compound No. in Table 2, and parts are by weight.

Formulation Example 1

Mixing and well pulverizing 50 parts of each of the present compounds (1) to (6), 3 parts of calcium lignosulfonate, 2 parts of sodium lauryl sulfate and 45 parts of synthetic hydrated silicon dioxide gives a wettable powder containing each compound.

Formulation Example 2

Mixing and wet-pulverizing 25 parts of each of the present compounds (1) to (6), 3 parts of polyoxyethylene sorbitan monooleate, 3 parts of CMC and 69 parts of water until the particle size of the active ingredient is reduced to 5 microns or less gives a suspension formulation containing each compound.

Formulation Example 3

Mixing and well pulverizing 2 parts of each of the present compounds (1) to (6), 88 parts of kaolin clay and 10 parts of talc gives a dust containing each compound.

Formulation Example 4

Well mixing 20 parts of each of the present compounds (1) to (6), 14 parts of polyoxyethylene

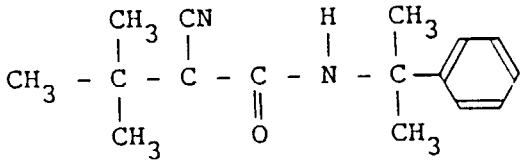
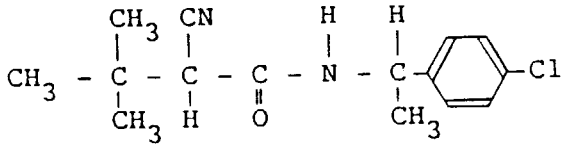
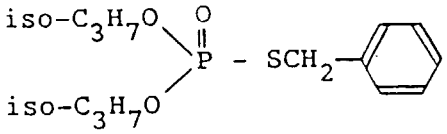
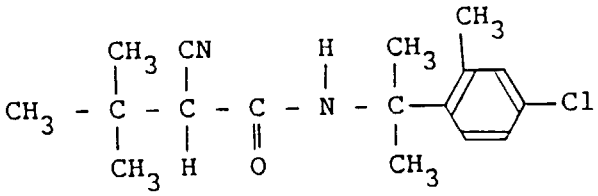
styrylphenyl ether, 6 parts of calcium dodecylbenzene-sulfonate and 60 parts of xylene gives an emulsifiable concentrate containing each compound.

Formulation Example 5

Mixing and well pulverizing 2 parts of each of the present compounds (1) to (6), 1 part of synthetic hydrated silicon dioxide, 2 parts of calcium ligno-sulfonate, 30 parts of bentonite and 65 parts of kaolin clay followed by well kneading with water, granulating and drying gives a granule containing each compound.

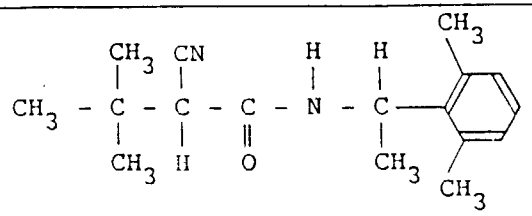
The following test examples demonstrate the usefulness of the present compounds as a plant disease protectant. In the test examples, the present compounds are identified by Compound No. in Table 2, and compounds used as a control are identified by Compound symbol in Table 4 below.

Table 4

Compound symbol	Structural formula	Remarks
A		Compound disclosed in JP-A-63-72663, Production Example No. 1
B		Compound disclosed in JP-A-01-156951, (Tokkai Hei) Production Example No. 1
C		Commercial product (IBP)
D		Compound disclosed in JP-A-63-72663, Compound No. 14

- cont'd -

Table 4 (cont'd)

E		Compound disclosed in JP-A-63-72663, Compound No. 43

The following six ratings, 5, 4, 3, 2, 1, 0, express the controlling activity according to the condition of disease of test plants at the time of examination, i.e. the macroscopically observed degrees of colony and infected area on the leaves, stems, etc.

5 No colony nor infected area is observed.

4 About 10% of colony or infected area is observed.

3 About 30% of colony or infected area is observed.

2 About 50% of colony or infected area is observed.

1 About 70% of colony or infected area is observed.

0 More than about 70% of colony or infected area is observed, there being no difference in the condition of disease between the treated and untreated plots.

Test Example 1 Controlling test on rice blast (Pyricularia oryzae) (preventive effect)

Sandy loam was filled in plastic pots, and rice (var., Kinki No. 33) was sowed and cultivated into seedlings for 20 days in a greenhouse. The wettable powder of each test compound prepared according to Formulation Example 1 was diluted with water to a prescribed concentration and foliar-applied onto the seedlings so that the spray liquor was thoroughly attached to the leaf surface. After the spraying, the seedlings were air-dried and inoculated by spraying the spore suspension of Pyricularia oryzae. After the inoculation, the seedlings were cultivated at 28°C under a dark and

highly humid condition for 4 days to examine the controlling activity. Table 5 shows the results.

Table 5

Test compound		Controlling activity
Compound No.	Application concentration of active ingredient (ppm)	
(1)	500	5
	50	5
(2)	500	5
	50	5
(3)	500	5
	50	5
(4)	500	5
	50	4
(5)	500	5
	50	5
(6)	500	5
	50	5
A	500	0
	50	0
C	500	4
	50	2
D	500	2
	50	0
E	500	2
	50	0

Test Example 2 Controlling test on rice blast (Pyricularia oryzae) (systemic effect)

Sandy loam was filled in plastic pots, and rice (var., Kinki No. 33) was sowed and cultivated into seedlings for 14 days in a greenhouse. The emulsifiable concentrate of each test compound prepared according to Formulation Example 4 was diluted with water, and the soil was drenched with a prescribed amount of this aqueous dilute solution. After the drenching, the seedlings were cultivated for 7 days in a greenhouse and inoculated by spraying the spore suspension of Pyricularia oryzae. After the inoculation, the seedlings were allowed to stand at 28°C under a dark and highly humid condition for 4 days to examine the controlling activity. Table 6 shows the results.

Table 6

Test compound		Controlling activity
Compound No.	Application rate of active ingredient (g/10 areas)	
(1)	500	5
	50	5
(2)	500	5
	50	5
(3)	500	5
	50	5
(4)	500	5
	50	4
(5)	500	5
	50	5
(6)	500	5
	50	5
A	500	0
	50	0
C	500	4
	50	1
D	500	2
	50	0
E	500	2
	50	0

Test Example 3 Test of phytotoxicity against rice

Sandy loam was filled in plastic pots, and rice (var., Kinki No. 33) was sowed and cultinated into seedlings for 14 days in a greenhouse. The emulsifiable concentrate of each test compound prepared according to Formulation Example 4 was diluted with water, and the soil

was drenched with a prescribed amount of this aqueous dilute solution. After the drenching, the seedlings were cultivated for 7 days in a greenhouse and then allowed to stand at 28°C under a dark and highly humid condition for 4 days to examine the phytotoxicity. Table 7 shows the results.

The following 4 ratings, -, ±, +, ++, express the severity of phytotoxicity to test plants at the time of examination, i.e. the visually observed condition of the leaves, stem, etc.

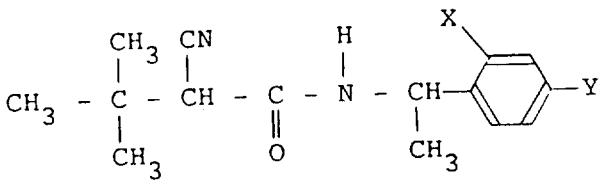
- \- No phytotoxicity is observed.
- ± Phytotoxicity is slightly observed.
- \+ Phytotoxicity is weakly observed.
- ++ Phytotoxicity is strongly observed.

Table 7

Test compound		Phytotoxicity
Compound No.	Application concentration of active ingredient (ppm)	
(2)	1000	-
(3)	"	-
(4)	"	-
(5)	"	-
(6)	"	-
A	"	++
B	"	++
D	"	++
E	"	++

WHAT IS CLAIMED IS:

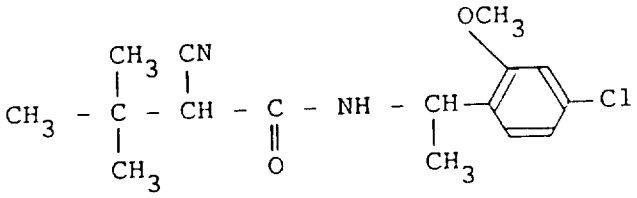
1. A cyanoacetamide derivative represented by the formula,



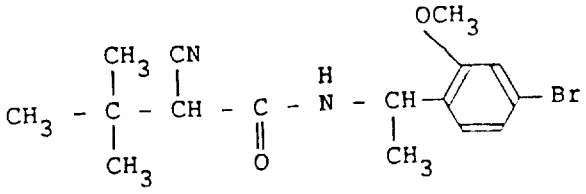
wherein X is a fluorine, chlorine atom or a lower alkoxy (C_1-C_2) group, and Y is a chlorine or bromine atom or a trifluoromethyl or lower fluoroalkoxy (C_1-C_2) group.

2. A cyanoacetamide derivative according to claim 1, wherein X is a lower alkoxy (C_1-C_2) group, and Y is a chlorine or bromine atom or a trifluoromethyl or lower fluoroalkoxy (C_1-C_2) group.

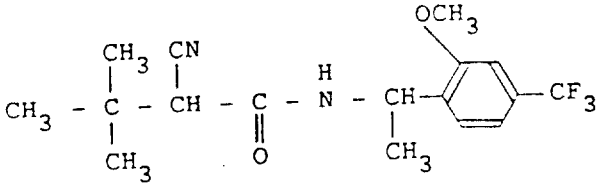
3. A cyanoacetamide derivative according to claim 1 having the formula,



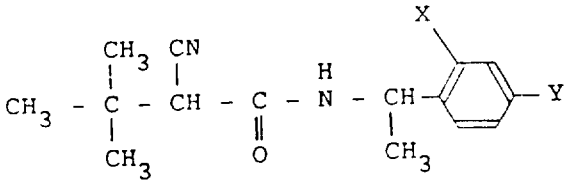
4. A cyanoacetamide derivative according to claim 1 having the formula,



5. A cyanoacetamide derivative according to claim 1 having the formula,



6. A plant disease protectant which comprises as an active ingredient an effective amount of a cyanoacetamide derivative represented by the formula,



wherein X is a fluorine, chlorine atom or a lower alkoxy (C_1-C_2) group, and Y is a chlorine or bromine atom or a trifluoromethyl or lower fluoroalkoxy (C_1-C_2) group.

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