

PATENT SPECIFICATION

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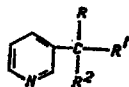
COMPLETE SPECIFICATION

Method for Protecting Plants from Fungi and Compositions therefor

We, ELI LILLY AND COMPANY, a Corporation organised and existing under the laws of the State of Indiana, United States of America, of 740 South Alabama Street, City of Indianapolis, State of Indiana, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

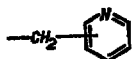
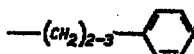
The present invention relates to a method for protecting plant foliage from fungi with pyridine derivatives and compositions containing the pyridine derivatives.

The present invention provides a method for protecting plants from attack by fungi which comprises contacting a fungus-susceptible plant with a fungicidal amount of a pyridine derivative having the following formula:



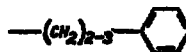
Formula I

wherein R is a hydrogen or halogen atom, or a hydroxyl, amino, cyano, acetoxy, carboxy, carbo(C₂—C₈) alkoxy, C₁—C₈ alkoxy, C₁—C₄ alkyl mercapto, C₁—C₄ alkyl, benzyl or phenyl radical; R¹ is a



naphthylmethyl, C₈—C₈ cycloalkyl, C₈—C₈

cycloalkenyl, pyridyl, thienyl, benzyl or phenyl radical; R² is a



naphthylmethyl, C₈—C₈ cycloalkyl, C₈—C₈ cycloalkenyl, C₁—C₈ alkyl, C₂—C₄ alkynyl, C₂—C₄ alkenyl, trifluoromethyl, pyridyl, thienyl, benzyl or phenyl radical; and wherein the pyridine ring of the formula, the benzyl, phenyl, pyridyl or thienyl radicals of R₁R¹ or R² may be substituted with one or more halogen atoms, or nitro, C₁—C₄ alkyl, methoxy, ethoxy, methylmercapto, ethylmercapto, trifluoromethyl, C₁—C₄ alkyl —SO₂—, C₁—C₄ alkyl —SO radicals; or an acid addition salt or N-oxide thereof. The pyridine ring of the above formula, phenyl, benzyl, pyridyl or thienyl radical may be substituted for example with a halogen atom, or nitro, C₁—C₄ alkyl, methoxy, ethoxy, methylmercapto, ethylmercapto, trifluoromethyl, C₁—C₄ alkyl—SO₂— or C₁—C₄ alkyl—SO-radical.

As used therein:

C₁—C₄ alkyl is illustrated by methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, *sec*-butyl, and *tert*-butyl;

C₂—C₄ alkynyl is illustrated by ethynyl, propynyl, and butynyl;

C₂—C₄ alkenyl is illustrated by vinyl, allyl, and butenyl;

Naphthylmethyl is illustrated by 1-naphthylmethyl and 2-naphthylmethyl.

C₈—C₈ cycloalkyl is illustrated by cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl.

Compounds coming within the scope of the generic formula, *supra*, include:

αα - Bis - (4 - iodophenyl) - 3 - pyridine-methanol

α - (2 - Fluorophenyl) - α - phenyl - 3 - pyridinemethanol

- α - Vinyl - α - phenyl - 3 - pyridinemethanol N - oxide
 α - (4 - Bromophenyl) - α - phenyl - 3 - pyridinemethanol N - oxide
 5 α, α - Bis - (4 - chlorophenyl) - 3 - pyridyl-methyl acetate
 α - Phenyl - β - (2 - pyridyl) - α - (3 - pyridyl)ethyl acetate N - oxide
 10 α - (4 - Chlorobenzyl) - α - allyl - 3 - pyridinemethanol N - oxide
 α - (4 - Methyl - 3 - chlorophenyl) - α - (2 - thienyl) - 3 - pyridinemethanol
 α - (2 - Butenyl) - α - (4 - methoxybenzyl) - 3 - pyridinemethanol
 15 α - (4 - Iodobenzyl) - α - (4 - pyridyl) - 3 - pyridinemethanol
 α, α - Bis - (2 - phenylethyl) - 3 - pyridine-methanol N - oxide
 α - (3,4 - Dichlorobenzyl) - α - (3 - chloro-phenyl - 3 - pyridyl methane N - oxide.
 20 α - (4 - Methylthiophenyl) - α - phenyl - 3 - pyridyl methane
 3 - (α - *n* - Butylbenzyl)pyridine
 α - (4 - Ethoxyphenyl) - α - phenyl - 3 - pyridyl methane hydrobromide.
 25 α, α - Bis(4 - ethylphenyl) - 3 - pyridyl methane oxalate
 α, α - Bis(4 - nitrophenyl) - 3 - pyridyl methane N - oxide
 30 α - (3 - Bromophenyl) - α - phenyl - 3 - pyridyl methane sulfate.
 α, α - Bis (3 - bromophenyl) - 3 - pyridyl methane nitrate
 α - Cyclopentyl - α - (4 - chlorophenyl) - 3 - pyridyl methane
 35 α - Cyclohexyl α - (3 - bromophenyl) - 3 - pyridyl methane
 α - (2 - Chlorobenzyl) - α - cyclooctyl - 3 - pyridyl methane
 40 α - Phenyl - α - (3 - thienyl) - 3 - pyridyl methane N - oxide
 α - (4 - Chlorophenyl) - α - (2 - pyridyl) - 3 - pyridyl methane
 α - Cyano - α - phenyl - α - (3 - thienyl) - 3 - pyridyl methane
 45 Tri - (3 - pyridyl)methane N - oxide
 α - Carboxy - α, α bis(phenyl) - 3 - pyridyl methane
 α - (Carboethoxy) - α - phenyl - α - (4 - chlorophenyl) - 3 - pyridyl methane N - oxide
 50 α, α - Bis(4 - iodophenyl) - 3 - pyridyl - methane *p* - toluene - sulfonate
 α - Phenyl - α - (4 - chlorobenzyl) - 3 - pyridyl methane
 55 α - Phenyl - α - (2 - thienyl) - 3 - pyridyl methane
 α - (4 - Chlorophenyl) - α - (2 - thienyl) - 3 - pyridyl methane maleate.
 60 The acid addition salts of the pyridine bases and their N-oxides can be prepared employing, for example, the following acids: hydrochloric, hydrobromic, sulfuric, phosphoric, nitric, oxalic, methanesulfonic, *p*-toluenesulfonic, and maleic acids.
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The pyridine derivatives have been found to be useful in controlling many fungi which attack food crops and ornamental plants. Susceptible fungi which attack food crops include *Erysiphe polygoni*, the causative organism of bean powdery mildew; and *Erysiphe cichoracearum*, the causative organism of squash powdery mildew; as well as *Phytophthora infestans*, the causative organism of tomato and potato late blight; *Coletotrichum lagenarium*, the causative organism of cucumber anthracnose; and *Uromyces phaseoli*, the causative organism of bean rust. Among susceptible fungi which affect ornamental plants is *Sphaerotheca pannosa* var. *rosae*, the causative organism of powdery mildew of rose, and *Erysiphe graminis*, the causative organism of powdery mildew of grass.

Those pyridine compounds in which, referring to the formula given above, R is hydrogen and R¹ and R² are phenyl or cycloalkyl, or cycloalkenyl, are preferred for treating turf since they are most effective in combatting *Sclerotinia homeocarpa*, the causative agent of the fungal disease known as turf dollar spot.

In carrying out the method of the present invention, compositions containing the active ingredient are applied to the infected or susceptible plant surfaces. A convenient and preferred method is to spray the plant surfaces with a liquid dispersion or emulsion of the toxicant.

The compositions of the present invention desirably contain in addition to the substituted pyridine toxicant one or more additives selected from water, polyhydroxy compounds, petroleum distillates, and other dispersion media, surface-active dispersing agents, emulsifiers, and finely divided inert solids. The concentration of the substituted pyridine compound in these compositions may vary depending on whether the composition is intended for dried application as a dust to plants or is intended as an emulsifiable concentrate or a wettable powder designed to be subsequently diluted with additional inert carrier such as water to produce the ultimate treating composition.

The active compounds are applied to plants in effective amounts, varying somewhat with the severity of the fungus infection and with other factors such as the environment in which treatment is conducted. In general, it will be found that an aqueous spray containing from $\frac{1}{2}$ to 400 ppm. of active material is satisfactory when treatment is to be carried out in the greenhouse.

As is well understood in the art, a somewhat higher concentration of the fungicide is desirable when treatment is to be carried out in the field. In that case, the preferred range is from 1 to 600 ppm. of active ingredient. Thus the preferred concentration range of the fungicide is from $\frac{1}{2}$ to 600 ppm. of fungicidally active material.

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Treating compositions are most conveniently formulated by preparing liquid or solid concentrates which are subsequently diluted to the desired level for use. Emulsifiable liquid concentrates can be prepared by incorporating from 0.05 to 5 percent of the active ingredient and an emulsifying agent in a suitable water-immiscible organic liquid. Such concentrates may be further diluted with water to form spray mixtures in the form of oil-in-water emulsions. Such spray compositions then comprise active toxicant, water-immiscible solvent, emulsifying agent, and water. Suitable emulsifying agents can be of the non-ionic or ionic types or blends thereof, and include condensation products of alkylene oxides with phenols and organic acids, polyoxyethylene derivatives of sorbitan esters, complex ether-alcohols, and anionics of the aralkyl sulfonate type. Suitable organic liquids which may be employed include aromatic hydrocarbons, aliphatic hydrocarbons, cycloaliphatic hydrocarbons, and mixtures thereof such as petroleum distillates.

Solid concentrate mixtures can be prepared by incorporating from 10 to 25 percent of the substituted pyridine compound in finely divided solid carriers such as bentonite, fuller's earth, diatomaceous earth, hydrated silica, diatomaceous silica, expanded mica, talc and chalk. Such concentrates can be formulated, if desired, for direct use as dust treating compositions, or can be diluted, if desired, with additional inert solid carriers to produce dusting powders containing 0.05 to 1 percent by weight of the substituted pyridine toxicant. Alternatively, dispersing and/or wetting agents can be incorporated along with the substituted pyridine in the solid carrier to form wettable powder concentrates ranging from 10 to 25 percent concentration which subsequently can be dispersed in water or other aqueous carrier to form spray compositions. Suitable wetting and emulsifying agents include sodium lignosulfate, sulfonate-oxide condensate blends, sulfonate non-ionic blends and anionic wetting agents.

Further, the substituted pyridine toxicant can be incorporated in solutions, simple dispersions, aerosol formulations, and other media adaptable to be employed for treating vegetation.

According to the method of the present invention, the toxicant composition is applied to infected or susceptible plant surfaces in any convenient fashion such as spraying, dusting, dipping, or drenching. A spray method is considered preferable, especially when large numbers of plants are involved, because of the rapidity and uniformity of treatment possible. In spraying, it is usually sufficient for the infected or susceptible surfaces to be thoroughly

wet with the liquid dispersion employed. Good results have been obtained by employing spray compositions whether they be emulsions or aqueous dispersions of solid concentrates.

The following examples illustrate the invention but are not to be construed as limiting.

EXAMPLE 1

The evaluation of the effectiveness of compounds of the above formula against *Erysiphe polygoni*, the causative organism of bean powdery mildew, was accomplished in the greenhouse in the following manner.

Fungicidal compositions were prepared by dissolving 40 mg. of the compound to be tested in 1 ml. of a solution of cyclohexanone containing 55 mg. of sulfonate non-ionic blend (Toximul R and S, Stepan Chemical Company, Northfield, Illinois; "Toximul" is a Trade Mark) and diluting to a volume of 100 ml. with water. This composition then contained 400 ppm. of fungicide. To prepare a composition containing 1000 ppm., 100 mg. of the compound to be tested was dissolved in 1 ml. of the cyclohexanone-sulfonate non-ionic blend solution and then diluted to a volume of 100 ml. with water.

Three bean seeds (Kentucky Wonder variety) were planted in 4-inch clay pots and allowed to germinate, and the plants were thinned to two plants per pot. Ten days from the day of planting, the test chemicals, compounded as described above, were sprayed on all leaf surfaces of the bean plants and allowed to dry. The plants were then placed in the greenhouse and Kentucky Wonder beans heavily infested with powdery mildew were placed above them for about five days, after which they were removed. At the end of five additional days the plants were observed for development of the disease. The appearance of the treated plants was compared with that of untreated plants and ratings of the control of the fungus were recorded. The control rating scale used was as follows:

- 0 — no control
- 1 — slight control
- 2 — moderate control
- 3 — good control
- 4 — complete control, no fungus

Chart 1 which follows sets forth the results of the testing of several substituted pyridines against *Erysiphe polygoni*. In the chart, column 1 gives the name of the compound; columns 2, 3, 4 and 5 give the protection rating of the compound at various rates in terms of p.p.m. at which the compound was applied to the test plants.

CHART 1

Compound	Protection 400 ppm.	Rating for an 80 ppm.	Application Rate of 16 ppm.	Rate of 3.2 ppm.
α,α -Bis-(3-chlorophenyl)-3-pyridine-methanol	4	4	3.5	2
α,α -Bis-(4-chlorophenyl)-3-pyridine-methanol	4	4	4	3
α -(4-Chlorophenyl)- α -(3-trifluoromethylphenyl)-3-pyridinemethanol	4	4	3.5	3+
α,α -Bis-(3-chlorophenyl)-3-pyridine-methanol hydrochloride	4	4	4	4
α,α -Bis-(m-tolyl)-3-pyridinemethanol hydrochloride	4	4	2	
α -(4-Chlorophenyl)- α -(3-trifluoromethylphenyl)-3-pyridinemethanol hydrochloride	4	4	4	3+
α,α -Bis-(3-bromophenyl)-3-pyridine-methanol	3.5	3	2	
α,α -Bis-(3,4-dichlorophenyl)-3-pyridinemethanol	3.5	2.5		
α -(4-Chlorophenyl)- α -phenyl-3-pyridinemethanol hydrochloride	4	4	4	
α,α -Bis-(p-tolyl)-3-pyridinemethanol	4	3.75	2.5	
α -Phenyl- α -(2-thienyl)-3-pyridine-methanol	4	4	2-	
α,α -Bis-(3-pyridyl)-benzyl alcohol	4	4	2	
α,α -Bis-(2-chlorophenyl)-3-pyridine-methanol hydrochloride	4	4	4	3.5
α -(4-Chlorophenyl)- α -phenyl-3-pyridinemethanol	4	4	4	
α -Chloro- α,α -bis-(4-chlorophenyl)-3-pyridylmethane hydrochloride	4	4	3+	
α,α -Bis-(4-chlorophenyl)-3-pyridine-methylamine dihydrochloride	4	4	4	
α -(4-Chlorobenzyl)- α -(4-chlorophenyl)-3-pyridinemethanol	4	4	4	
α -(3,4-Dichlorobenzyl)- α -(4-chlorophenyl)-3-pyridinemethanol	4	4	3	
α -(4-Chlorobenzyl)- α -phenyl-3-pyridine-methanol	4	4	4	1.5
α -(2,4-Dichlorobenzyl)- α -(4-chlorophenyl)-3-pyridinemethanol	4	4	4	2

CHART 1 (Continued)

Compound	Protection 400 ppm.	Rating for an 80 ppm.	Application 16 ppm.	Rate of 3.2 ppm.
α -(1-Naphthylmethyl)- α -phenyl-3-pyridinemethanol	3.5	2.6	2.3	
α -(<i>o</i> -Bromophenyl)- α -(2,4-dichlorobenzyl)-3-pyridinemethanol	4	4	4	3
α -(4-Chlorobenzyl)- α -(<i>p</i> -tolyl)-3-pyridinemethanol	4	4	4	2.5
α -(4-Chlorophenyl)- α -(4-methoxybenzyl)-3-pyridinemethanol	4	4	2.3	
α -Phenyl- β -(2-pyridyl)- α -(3-pyridyl)-ethanol	2		2	
α -(4-Chlorophenyl)- β -(2-pyridyl)- α -3-(5-methylpyridyl)ethanol	4	3.3	1.3	
α -(2,4-Dichlorobenzyl)- α -pyridine-methanol hydrochloride	4	4	4	4
α -(2,4-Dichlorobenzyl)- α -(4-chlorophenyl)-3-pyridinemethanol methane-sulfonate	4	4	3+	
α -(4-Chlorophenyl)- α -phenethyl-3-pyridinemethanol	3	3.3	2	
The Nitration product of α -(3-pyridyl)- α , β -diphenyl-ethanol	3.5	4	2	
α -(2,4-Dichlorobenzyl)- α -(4-chlorophenyl)-3-pyridinemethanol N-oxide	3.5	4	4	
α , α -Bis-(4-chlorobenzyl)-3-pyridine-methanol	4	3	2—	
α , α -Bis-(2,4-dichlorobenzyl)-3-pyridine-methanol	3.5	4	3.5	
α -(4-Chlorobenzyl)- α -(2,4-dichlorobenzyl)-3-pyridinemethanol	4	4	4	
α -Benzyl- α -(2,4-dichlorobenzyl)-3-pyridinemethanol	4	4	3	2.5
α , α -Dibenzyl-3-pyridinemethanol	3+			
α -(4-Chlorophenyl)- α -ethynyl-3-pyridine-methanol	3.5			
α -(4-Chlorophenyl)- α -phenyl-3-(5-methylpyridine)-methanol	4	2.5	1.5	
α -(2,4-Dichlorobenzyl)- α -(4-chlorophenyl)-3-pyridinemethanol hemioxalate	4	4	4	

CHART 1 (Continued)

Compound	Protection Rating for an Application Rate of			
	400 ppm.	80 ppm.	16 ppm.	3.2 ppm.
α,α -Bis-(4-chlorophenyl)-3-pyridylmethyl methyl ether	4	4	4	
α,α -Bis-(4-chlorophenyl)-3-pyridylmethyl methyl ether hydrochloride	4	4	4	
α,α -Bis-(4-chlorophenyl)-3-pyridine-methanol phosphate	4	4	4	
α -(4-Methylthiophenyl)- α -phenyl-3-pyridinemethanol hydrochloride	4	4	4	
α -(n-Propyl)- α -(2-thienyl)-3-pyridine-methanol	4	3+	1	
α -Trifluoromethyl- α -phenyl-3-pyridine-methanol	3.5	2		
α -Ethyl- α -phenyl-3-pyridinemethanol	2			
α -Methyl- α -phenyl-3-pyridinemethanol	2			

EXAMPLE 2

5 A field trial was run to determine the efficacy of α,α -bis-(4-chlorophenyl)-3-pyridine-methanol and α,α -bis-(4-chlorophenyl)-3-pyridylmethane against *Erysiphe cichoracearum*, the casual organism of powdery mildew on squash.

10 The fungicidal compound was formulated as a 25 percent wettable powder and used at that rate as indicated in Chart 2 which follows.

In addition, α,α -bis-(4-chlorophenyl)-3-pyridine-methanol was formulated as a 0.5% and 2.0% dust, respectively and applied to the

15 growing squash.
Squash, Early Yellow Crookneck variety,

were planted in rows 30 feet long. Treatments were applied to alternate rows with the untreated rows acting as guard rows. The spray was applied using a 3-gallon compression 20 sprayers. Dusts were applied using a Hudson crank duster.

The liquid treatments were properly measured and brought up to a volume of one gallon and applied to 30 feet of row. 25

Evaluation of the incidence of the disease was made by two observers.

Results are shown in Chart 2. Column 1 gives the name of the compound; column 2, the rate of application; and columns 3 and 4, 30 the percent of powdery mildew observed.

CHART 2

Compound	Application Rate	Incidence of Powdery Mildew	
		Rep. I	Rep II
Control	—	81.25%	71.87%
α,α -Bis-(4-chlorophenyl)-3-pyridinemethanol	10 ppm. 25% WP	2.34	2.34
"	50 ppm. "	0.0	0.0
"	600 ppm. "	0.0	0.0
"	Dust 0.5%	0.0	0.0
"	Dust 2.0%	0.0	0.0
α,α -Bis(4-chlorophenyl)-3-pyridylmethane	Dust 0.5%	0.0	0.0

EXAMPLE 3

- 5 In a field trial, the ability of α,α -bis-(4-chlorophenyl)-3-pyridyl methane to combat *Sclerotinia homeocarpa*, the causative organism of Turf Dollar Spot, was tested. The two compositions tested were: (1) a 25 percent wettable powder composition of α,α -bis(4-chlorophenyl)-3-pyridyl methane at rates of 0.8, 2.0, and 3.4 pounds per acre, and (2) a 2 pound-per-gallon emulsifiable concentrate diluted to give a treatment rate of 1.0 pound per acre. Five gallons of liquid per 1,000 square feet were used.
- 10 Twelve plots of ground, each having an area of 13.5 square feet, were used, comprising three plots each of Astoria variety of bent-

grass, Highland variety of bentgrass, Seaside variety of bentgrass, and Penncross variety of bentgrass. A CO₂ pressure tank on a hand-pushed sully rig forces spray through two Tee Jet nozzles designed to spray a band 18 inches in width.

Each plot was observed for evidence of areas diseased with the Dollar Spot organism.

Results of the treatment are shown in Chart 3. Column 1 identifies the compound under test, referred to as EL—237; column 2 the number of the treatment; column 3, the type of formulation; column 4, the rate of application in terms of pounds of active ingredient per acre; columns 5, 6, 7, and 8, the percent of Dollar Spot disease observed.

CHART 3

Compound	Treat. No.	Formulation	Rate Pounds/Acre	% Dollar Spot Disease in Varieties of Bentgrass			
				Astoria	Highland	Seaside	Penncross
Control	1	—	—	13	37	81	40
EL—237	2	25% WP	0.8	0	0	0	0
EL—237	3	"	2.0	1	1	2	1
EL—237	4	"	3.4	0	0	0	0
EL—237	5	2 pounds/gallon EC	1.0	0	5	6	1

WP = wettable powder.

EC = emulsifiable concentrate

The compounds useful in the fungicidal processes of this invention can readily be prepared by one of the following procedures:

- 5 One method for synthesis of the tri-substituted methanols is to add a solution of a Grignard reagent to a solution of a suitable organic ketone such as diphenyl ketone, 3-pyridyl phenyl ketone, 2-thienyl phenyl ketone, at a suitable temperature for a time sufficient to bring about substantial reaction thereof.

- 10 For example, the Grignard reagent prepared from *p*-bromochlorobenzene and magnesium turnings in ether is added to an ether solution of *p*-chlorophenyl 3-pyridyl ketone and the reaction product mixture is stirred at room temperature for about 18 hours. The time of reaction can be varied without adversely affecting the yield of the desired product. The reaction product mixture is hydrolyzed in the usual manner with aqueous ammonium chloride. The mixture is extracted with ether, and the ether evaporated *in vacuo*, leaving a residue which is recrystallized to yield α,α -bis-(4-chlorophenyl)-3-pyridinemethanol.

- 25 Alternatively, a solution of the ketone can be added to the Grignard reagent in ether or other suitable solvent. The reaction product mixture is then worked up as described above.

- 30 Another preparative method used for the synthesis of the tri-substituted methanols is that using 3-pyridyl lithium. According to this method, 3-pyridyl lithium, prepared by the reaction in ether of butyl lithium with a 3-halopyridine, is allowed to react in a nitrogen atmosphere with a suitable diaryl ketone or alkyl aryl ketone in ether solution at a temperature of -50° to -60°C. , to yield a pyridyl diaryl methanol.

- 40 For example, to 3-pyridyl lithium in ether, maintained in a nitrogen atmosphere at a temperature of -50° to -60°C. , is added an ether solution of phenyl 2-thienyl ketone, and the temperature of the reaction mixture held at -50° to -60°C. while stirring for about two hours. The reaction product mixture is warmed to room temperature and an aqueous solution of ammonium chloride added. The mixture is extracted with ether to obtain an ether solution of the product, which is purified by the acid-base treatment well-known to the art. The desired product, α -(2-thienyl)- α -phenyl-3-pyridinemethanol is obtained as a solid. The hydrochloride salt is conveniently prepared by saturating an ether solution of the free base with anhydrous hydrogen chloride, a method well-known to the art.

- 55 Compounds in which R in the above formula is other than hydroxyl, such as amino, halogen, alkoxy, or alkylmercapto, are prepared by standard metathetic reactions with the hydroxyl derivatives. For example, a pyridyl diphenylmethyl chloride can be prepared by treatment of the corresponding methanol with concentrated hydrochloric acid. A pyridyl

65 diphenyl methylamino compound can in turn be prepared from this methyl chloride derivative by reaction with ammonia or an amine. Similarly, the alkoxy and alkylmercapto compounds are readily prepared from the corresponding chloride or bromide.

70 The pyridine-N-oxides falling within the scope of the generic formula, *supra*, are conveniently prepared by oxidation of the corresponding free base with hydrogen peroxide in glacial acetic acid solution.

75 For example, a mixture of α,α -bis-(4-chlorophenyl)-3-pyridinemethanol, glacial acetic acid, and 30 percent hydrogen peroxide is warmed for a couple of hours on the steam bath and allowed to remain overnight at room temperature. The reaction product mixture is concentrated to dryness *in vacuo* and the residue recrystallized from boiling benzene to yield α,α -bis-(4-chlorophenyl)-3-pyridine methanol-N-oxide.

85 Compounds of the type represented by α,α -bis-(2,4-dichlorobenzyl)-3-pyridinemethanol are conveniently prepared by reaction of a Grignard reagent with a $\text{C}_1\text{--C}_4$ alkyl nicotinate or a benzyl pyridyl ketone, the reaction product mixture being worked up in the customary manner with the product being obtained in the form of the free base or in the form of one of the desired acid addition salts.

90 Compounds such as α -(4-chlorophenyl)- α -ethynyl-3-pyridinemethanol are prepared by reaction of sodium acetylide with a suitable ketone, in this case, 3-pyridyl-4-chlorophenyl ketone in liquid ammonia with stirring for a couple of hours or so. The excess liquid ammonia is allowed to evaporate and the residue is recrystallized from a suitable solvent to yield the desired product.

105 Compounds containing the $\text{C}_2\text{--C}_4$ alkenyl grouping can be obtained by partial reduction of compounds containing the $\text{C}_2\text{--C}_4$ alkynyl grouping, such partial reduction being carried out by methods well-known to the art.

110 The following compounds are prepared by the above described processes and are further examples of compounds useful in the present invention.

α,α -bis-(4-chlorophenyl)-3-pyridinemethanol hydrochloride having a melting point of about $165\text{--}175^{\circ}\text{C.}$

115 α,α -Bis-(4-chlorophenyl)-3-pyridinemethanol *p*-toluene-sulfonate. Melting point: $147\text{--}148^{\circ}\text{C.}$

α,α -Bis-(4-chlorophenyl)-3-pyridinemethanol methane sulfonate. Melting point: $104\text{--}108^{\circ}\text{C.}$

α,α -Bis-(4-chlorophenyl)-3-pyridinemethanol sulfate. Melting point: $186\text{--}188^{\circ}\text{C.}$

Diphenyl 3-pyridinemethanol. Melting point: $117\text{--}118^{\circ}\text{C.}$

125 α -Benzyl- α -(4-chlorobenzyl)-3-pyridinemethanol. Melting point: $121\text{--}123^{\circ}\text{C.}$

- α - Benzyl - α - (4 - chlorobenzyl) - 3 - pyridinemethanol hydrochloride. Melting point: 180—183°C.
- 5 α - (3 - Chlorophenyl) - α - (4 - chlorobenzyl) - 3 - pyridinemethanol. Melting point: 132—133°C.
- α - (3 - Chlorophenyl) - α - (2,4 - dichlorobenzyl) - 3 - pyridinemethanol. Melting point: 145—148°C.
- 10 α - (2 - Chlorophenyl) - α - (2,4 - dichlorobenzyl) - 3 - pyridinemethanol. Melting point: 160—161°C.
- α - (4 - Chlorobenzyl) - α - (2,4 - dichlorobenzyl) - 3 - pyridinemethanol hydrochloride. Melting point: 198—200°C.
- 15 α - (2,4 - Dichlorobenzyl) - α - phenyl - 3 - pyridinemethanol. Melting point: 134°C.
- α,α - Bis - (4 - chlorobenzyl) - 3 - pyridinemethanol hydrochloride. Melting point: 215—218°C.
- 20 α - (x - Bromophenyl) - α - (2,4 - dichlorobenzyl) - 3 - pyridinemethanol. Melting point: 177—178°C.
- α - (3 - Bromobenzyl) - α - (4 - chlorophenyl) - 3 - pyridinemethanol. Melting point: 133.5—135°C.
- 25 α - (x - Bromophenyl) - α - (4 - chlorobenzyl) - 3 - pyridinemethanol. Melting point: 170—172°C.
- 30 α - (4 - Methoxyphenyl) - α - phenyl - 3 - pyridinemethanol. Melting point: 117.5—119°C.
- α - (4 - Chlorophenyl) - α - 3,4 - dichlorobenzyl) - 3 - pyridinemethanol. Melting point: 149—150.5°C.
- 35 α - Benzyl - α - (4 - chlorophenyl) - 3 - pyridinemethanol. Melting point: 130—131.5°C.
- α - (2,4 - Dichlorobenzyl) - α - (4 - chlorophenyl) - 3 - pyridinemethanol phosphate. Melting point: 188—189°C.
- 40 α - (2,4 - Dichlorobenzyl) - α - (4 - chlorophenyl) - 3 - pyridinemethanol sulfate. Melting point: 151—152°C.
- 45 α - (2,4 - Dichlorobenzyl) - α - (4 - chlorophenyl) - 3 - pyridinemethanol nitrate. Melting point: 172—174°C. (d).
- α - (2,4 - Dichlorobenzyl) - α - (4 - chlorophenyl) - 3 - pyridinemethanol *p* - toluenesulfonate. Melting point: 215—217°C.
- 50 α - (2 - Thienyl) - α - phenyl - 3 - pyridinemethanol. Melting point: about 117°C.
- α - (2 - Thienyl) - α - phenyl - 3 - pyridinemethanol hydrochloride having a melting point of about 172°C.
- 55 α - Isopropyl - α - phenyl - 3 - pyridinemethanol. Melting point: 128—129°C.
- α,α - Bis - (cyclopropyl) - 3 - pyridinemethanol hydrochloride. Melting point: 149°C.
- 60 α - (4 - Methylthiophenyl) - α - 3 - pyridinemethanol. Melting point: 151—153°C.
- α - (4 - Chlorophenyl) - α - cyclopropyl - 3 - pyridinemethanol. Melting point: 83—85°C.
- α - (4 - Chlorophenyl) - α - cyclopropyl - 3 - pyridinemethanol hydrochloride. Melting point: 146°C.
- α - Cyclobutyl - α - phenyl - 3 - pyridinemethanol. Melting point: 125—126°C.
- 70 α - (4 - Chlorophenyl) - α - phenyl - 3 - pyridinemethanol phosphate. Melting point: 183—185°C.
- α - (4 - Chlorophenyl) - α - phenyl - 3 - pyridinemethanol oxalate. Melting point: 137—140°C. (dec.).
- α,α - Bis - (4 - chlorophenyl) - 3 - pyridinemethanol N-oxide. Melting point of about 140°C.
- 80 α - Phenyl - α - (3 - pyridyl) - β - (4 - pyridyl)ethanol. Melting point: 132°C.
- α - (4 - Chlorophenyl) - α - (3 - pyridyl) - β - (2 - pyridyl)ethanol. Melting point: 101°C.
- α - (4 - Chlorophenyl) - α - (5 - methyl - 3 - pyridyl) - β - (2 - pyridyl)ethanol. Melting point: 131°C.
- 85 α,α - Bis - (2,4 - dichlorobenzyl) - 3 - pyridinemethanol hydrochloride. Melting point of about 200 to 205°C.
- 90 The nitration product of 1-(3-pyridyl)-1,2-diphenylethanol.
- The 3-pyridyl methane derivatives useful in this invention can be prepared by any one of several methods.
- 95 Condensing two moles of benzene or a substituted benzene with pyridyl-3-carboxaldehyde in the presence of concentrated sulfuric acid yields 3-pyridyl diphenylmethane or 3-pyridyl di(substituted-phenyl)methane, respectively. The product is readily isolated from the reaction mixture by a conventional extraction procedure.
- Alternatively, a diaryl 3-pyridine methanol is heated in a mixture of glacial acetic acid, concentrated hydrochloric acid, and 47 percent aqueous hydriodic acid to reduce the hydroxyl group, as taught by Sperber et al., U.S. Patent 2,727,895 (December 20, 1955).
- 100 When the methane carbon atom is tetra-substituted, the compounds are prepared by alkylating the diaryl 3-pyridyl methanes in the presence of sodium or potassium amide in liquid ammonia.
- The following compounds were prepared according to these methods:
- 105 3-pyridyl diphenylmethane having a boiling point of 155°C. at 0.7 mm. It crystallized on standing and had a melting point of about 70—71.5°C.
- 120 3-Pyridyl diphenylmethane hydrochloride having a melting point of about 169—170°C.
- α,α - Bis - (4 - fluorophenyl) - 3 - pyridyl methane. Boiling point: 170—173°C./1.25 mm.
- 125 α,α - Bis - (4 - methyl - 3 - chlorophenyl) - 3 - pyridyl methane. Boiling point: 205°C./0.2 mm.

α,α - Bis(4 - methoxyphenyl) - 3 - pyridyl methane. Boiling point: 211—213°C./0.5 mm.

5 α,α - Bis - (p - tolyl) - 3 - pyridyl methane. Boiling point: 235°C./15 mm.

α,α - Bis(4 - chlorophenyl) - 3 - pyridyl methane having a boiling point of about 160°C./0.05 mm.

10 α,α - Bis - (4 - chlorophenyl) - 3 - pyridyl methane hydrochloride having a melting point of about 70°C.

α - (4 - Chlorophenyl) - α - phenyl - 3 - pyridyl methane. Boiling point: 157°C./0.05 mm.

15 1 - Phenyl - 1 - (3 - pyridyl) - 2 - (4 - pyridyl)ethane. Melting point: 75—76°C.

3 - Bis(2,4 - dichlorophenyl)methylpyridine hydrochloride. Melting point: 165°C.

20 3 - (a - n - Pentylbenzyl)pyridine. Boiling point: 131—135°C./0.05 mm. $n_D^{25} = 1.5443$.

3 - [α - methyl - α,α - bis(4 - chlorophenyl)-methyl]pyridine hydrochloride having a melting point of about 165°C.

25 3 - [α,α - Bis(4 - chlorophenyl)phenethyl]-pyridine. Melting point: 126—128°C.

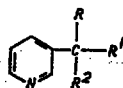
3 - [α,α - Bis(4 - chlorophenyl)phenethyl]-pyridine hydrochloride. Melting point: 204—206°C.

30 The N-oxides of the foregoing compounds are prepared by dissolving 10 parts by weight of the pyridine compound in 100 parts by weight of acetic acid containing 25 parts by weight of 30% hydrogen peroxide. The mixture is warmed to about 80°C. for about eight hours. The reaction mixture is evaporated to a small volume *in vacuo* and to the residue are added 10 parts of water. The aqueous mixture is extracted with ether, and the ether containing the N-oxide is evaporated to dryness, leaving a residue of the N-oxide.

40 The radical "x-bromophenyl" indicates that it is not known in what position the bromine atom is attached to the phenyl radical.

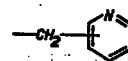
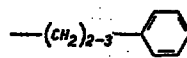
WHAT WE CLAIM IS:—

45 1. A method for protecting plants from attack by fungi which comprises contacting a fungus-susceptible plant with a fungicidal amount of a pyridine derivative having the following formula:

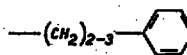


Formula I

50 wherein R is a hydrogen or halogen atom, or a hydroxyl, amino, cyano, acetoxy, carboxyl, carbo(C_1-C_3) alkoxy, C_1-C_3 alkoxy, C_1-C_4 alkyl mercapto, C_1-C_4 alkyl, benzyl or phenyl radical; R^1 is a



naphthylmethyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloalkenyl, pyridyl, thienyl, benzyl or phenyl radical; R^2 is a



65 naphthylmethyl, C_3-C_6 cycloalkyl, C_3-C_6 cycloalkenyl, C_1-C_6 alkyl, C_2-C_4 alkynyl, C_2-C_4 alkenyl, trifluoromethyl, pyridyl, thienyl, benzyl or phenyl radical; and wherein the pyridine ring of the formula, the benzyl, phenyl, pyridyl or thienyl radicals of R, R^1 or R^2 may be substituted with one or more halogen atoms, or nitro, C_1-C_4 alkyl, methoxy, ethoxy, methylmercapto, ethylmercapto, trifluoromethyl, C_1-C_4 alkyl $-SO_2-$, C_1-C_4 alkyl $-SO$ radicals; or an acid addition salt or N-oxide thereof.

2. The method of claim 1 wherein the pyridine derivative is a compound of the above formula wherein each of R^1 and R^2 is a phenyl, cycloalkyl, or cycloalkenyl radical and R is a hydrogen atom.

3. The method of claim 1 or claim 2 wherein said pyridine derivative is applied in combination with an inert diluent.

4. The method of claim 1, 2 or 3 wherein said pyridine derivative is applied in combination with an inert diluent and a wetting agent.

5. The method of claim 1, 2, 3 or 4 wherein said pyridine derivative is applied in the form of a composition containing within the range of $\frac{1}{2}$ to 600 p.p.m. thereof.

6. The method of any of claims 1, and 3 to 5 wherein the pyridine derivative is α -(2,4-dichlorobenzyl) - α - (4 - chlorophenyl) - 3 - pyridinemethanol, α - α - bis(3 - chlorophenyl)-3 - pyridine - methanol hydrochloride, α,α - bis(4 - chlorophenyl) - 3 - pyridinemethanol or α - (4 - chlorobenzyl) - α - (2,4 - dichlorobenzyl) - 3 - pyridinemethanol.

7. A liquid concentrate suitable for dilution with water to yield a fungicidal spray, said concentrate comprising an inert diluent and an emulsifying agent in admixture with an amount within the range of from 0.05 to 5 percent by weight of a fungicidal pyridine derivative as defined in claim 1, 2 or 6.

8. A fungicidal composition comprising an inert diluent, a wetting agent and a fungicidally effective amount of a pyridine derivative as defined in claim 1, 2 or 6.

9. A solid concentrate suitable for dilution with a finely divided solid carrier to yield a

α,α - Bis(4 - methoxyphenyl) - 3 - pyridyl methane. Boiling point: 211—213°C./0.5 mm.

5 α,α - Bis - (p - tolyl) - 3 - pyridyl methane. Boiling point: 235°C./15 mm.

α,α - Bis(4 - chlorophenyl) - 3 - pyridyl methane having a boiling point of about 160°C./0.05 mm.

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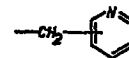
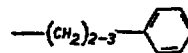
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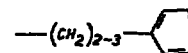


Formula I

55 wherein R is a hydrogen or halogen atom, or a hydroxyl, amino, cyano, acetoxy, carboxyl, carbo(C_1-C_3) alkoxy, C_1-C_3 alkoxy, C_1-C_4 alkyl mercapto, C_1-C_4 alkyl, benzyl or phenyl radical; R^1 is a



naphthylmethyl, C_3-C_8 cycloalkyl, C_3-C_8 cycloalkenyl, pyridyl, thienyl, benzyl or phenyl radical; R^2 is a



65 naphthylmethyl, C_3-C_8 cycloalkyl, C_4-C_8 cycloalkenyl, C_1-C_8 alkyl, C_2-C_4 alkynyl, C_2-C_4 alkenyl, trifluoromethyl, pyridyl, thienyl, benzyl or phenyl radical; and wherein the pyridine ring of the formula, the benzyl, phenyl, pyridyl or thienyl radicals of R, R^1 or R^2 may be substituted with one or more halogen atoms, or nitro, C_1-C_4 alkyl, methoxy, ethoxy, methylmercapto, ethylmercapto, trifluoromethyl, C_1-C_4 alkyl $-SO_2-$, C_1-C_4 alkyl $-SO$ radicals; or an acid addition salt or N-oxide thereof.

2. The method of claim 1 wherein the pyridine derivative is a compound of the above formula wherein each of R^1 and R^2 is a phenyl, cycloalkyl, or cycloalkenyl radical and R is a hydrogen atom.

3. The method of claim 1 or claim 2 wherein said pyridine derivative is applied in combination with an inert diluent.

4. The method of claim 1, 2 or 3 wherein said pyridine derivative is applied in combination with an inert diluent and a wetting agent.

5. The method of claim 1, 2, 3 or 4 wherein said pyridine derivative is applied in the form of a composition containing within the range of $\frac{1}{2}$ to 600 p.p.m. thereof.

6. The method of any of claims 1, and 3 to 5 wherein the pyridine derivative is α -(2,4-dichlorobenzyl) - α - (4 - chlorophenyl) - 3 - pyridinemethanol, α - α - bis(3 - chlorophenyl) - 3 - pyridine - methanol hydrochloride, α,α - bis(4 - chlorophenyl) - 3 - pyridinemethanol or α - (4 - chlorobenzyl) - α - (2,4 - dichlorobenzyl) - 3 - pyridinemethanol.

7. A liquid concentrate suitable for dilution with water to yield a fungicidal spray, said concentrate comprising an inert diluent and an emulsifying agent in admixture with an amount within the range of from 0.05 to 5 percent by weight of a fungicidal pyridine derivative as defined in claim 1, 2 or 6.

8. A fungicidal composition comprising an inert diluent, a wetting agent and a fungicidally effective amount of a pyridine derivative as defined in claim 1, 2 or 6.

9. A solid concentrate suitable for dilution with a finely divided solid carrier to yield a



- 5 fungicidal dusting powder, said powder comprising an inert solid diluent in admixture with an amount within the range from 10 to 25 percent by weight of the pyridine derivative as defined in claim 1, 2 or 6.
10. A fungicidal composition according to claim 8 substantially as herein described.
11. A fungicidal concentrate according to claim 7 or 9 substantially as herein described.
12. A method for protecting plants according to claim 1 substantially as herein described. 10

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