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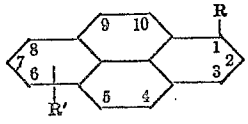
1-SUBSTITUTED PYRENES AS FUNGICIDES

Dewayne C. Torgeson, Dobbs Ferry, N.Y., Erich Marcus and Joseph A. Lambrech, Charleston, W. Va., assignors to Union Carbide Corporation, a corporation of New York

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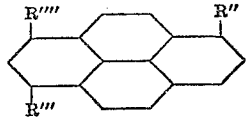
This invention relates to methods and compositions for the control of fungi. More particularly, the present invention relates to methods and compositions employing 1-substituted pyrenes for the control of fungi, particularly the powdery mildews that attack vegetable, fruit, and ornamental plants.

The 1-substituted pyrenes to which the present invention relates are substituted in the one position by an organic radical. The term "organic radical," as used throughout this specification, includes any group of atoms, either organic or inorganic, that normally passes unchanged from one molecule of a carbon compound to another (see Hackh's Chemical Dictionary, Third Edition, McGraw-Hill Co., New York, page 714 (1944)). The 1-substituted pyrenes of the present invention may also be substituted in the six or eight position by an organic radical of the same or of a different kind than the orangic radical at the one position. Such pyrenes may be illustrated by the structural formula:



wherein R is an organic radical and R' is either hydrogen or an organic radical attached at either the six or eight position.

Preferred for use as fungicides are the compounds having the formula:



wherein R'' is an organic radical, and R''' and R'''' are selected from the group consisting of hydrogen and organic radicals, at least one of said R''' and R'''' being hydrogen. Particularly preferred are such compounds having a molecular weight of up to about 700. Illustrative of such 1-substituted pyrenes are:

Compound No. 1—1,6-dinitropyrene
Compound No. 2—1,8-dinitropyrene
Compound No. 3—Ethyle 1-pyrenalmalonate
Compound No. 4—1-nitropyrene
Compound No. 5—1-benzoylpyrene
Compound No. 6—1-aminopyrene
Compound No. 7—1-acetylpyrene
Compound No. 8—1-phthalimidopyrene
Compound No. 9—N-acetylaminopyrene
Compound No. 10—1,6-dibenzoylpyrene
Compound No. 11—1,8-dibenzoylpyrene
Compound No. 12—X-nitro-1-acetylpyrene
Compound No. 13—3-(1-pyrenyl)acrylic acid
Compound No. 14—1-thiocyanopyrene
Compound No. 15—1-pyrenecarboxaldehyde
Compound No. 16—1-acetylpyrene oxime
Compound No. 17—1-(omega-nitrovinyl)pyrene

Compound No. 18—1-(ortho-carboxybenzoyl)pyrene
Compound No. 19—1-(1-pyrenalamino)pyrene
Compound No. 20—1-(alpha-hydroxyethyl)pyrene
Compound No. 21—1-ethylpyrene
Compound No. 22—1,1'-dipyrenylthiourea
Compound No. 23—1-benzalaminopyrene
Compound No. 24—1-cynnamoylpyrene
Compound No. 25—1-(1-naphthoyl)pyrene
Compound No. 26—1-(para-toluyl)pyrene
Compound No. 27—1-(2,4-dichlorobenzoyl)pyrene
Compound No. 28—1-(para-chlorobenzoyl)pyrene
Compound No. 29—1-(para-nitrobenzoyl)pyrene
Compound No. 30—Dimethylpyrene-1,6-dicarbamate
Compound No. 31—Dimethyl pyrene-1,8-dicarbamate
Compound No. 32—1-butyrylpyrene
Compound No. 33—N-(1pyrenyl)benzamide
Compound No. 34—N,N'-diacetoacetyl-1,6-diaminopyrene
Compound No. 35—1-pyrenylacetothiomorpholide
Compound No. 36—1-pyrenecarboxaldoxime
Compound No. 37—1-acetylpyrene semicarbazone
Compound No. 38—1-(N-morpholinomethyl)pyrene hydrochloride
Compound No. 39—1-(N,N-diethylaminomethyl)pyrene hydrochloride
Compound No. 40—1,1'-dipyrenyl disulfide
Compound No. 41—1-(N-piperidinomethyl)pyrene hydrochloride
Compound No. 42—1-(N-pyrrolidinomethyl)pyrene hydrochloride
Compound No. 43—1-(N,N-dimethylaminomethyl) pyrene hydrochloride
Compound No. 44—1-(N,N-dibutylaminomethyl)pyrene hydrochloride
Compound No. 45—1-(para-nitrobenzalamino)pyrene
Compound No. 46—1-pyrenalaniline
Compound No. 47—1-(N,N-dihexylaminomethyl)pyrene hydrochloride
Compound No. 48—1-[N-(N'methyl)piperazinomethyl] pyrene dihydrochloride
Compound No. 49—1-cinnamalaminopyrene
Compound No. 50—1-(N-anilinomethyl)pyrene
Compound No. 51—1-(alpha-N-methylaminoethyl) pyrene hydrochloride
Compound No. 52—n-Butyl-1-pyrenecarboxylate
Compound No. 53—1-thiopyrenol
Compound No. 54—X-nitro-1-ethylpyrene
Compound No. 55—1-pyrenylmercaptoacetic acid
Compound No. 56—N-(1-pyrenyl)maleimide
Compound No. 57—N-(1-pyrenyl)maleamic acid
Compound No. 58—1-nicotinylpyrene
Compound No. 59—1-(N,N-di-(2-ethylhexyl)aminomethyl)pyrene hydrochloride
Compound No. 60—1-(anthralamino)pyrene
Compound No. 61—1-(1-pyrenalamino)pyridine
Compound No. 62—1-(hydroxymethyl)pyrene
Compound No. 63—1-(N,N-diallylaminomethyl)pyrene hydrochloride
Compound No. 64—1-(1-naphthalamino)pyrene
Compound No. 65—1-(N-(2-pyridyl)aminomethyl) pyrene
Compound No. 66—N-methyl-N,N-bis(1-pyrenylmethyl) amine hydrochloride
Compound No. 67—1-pyrenalbutylamine
Compound No. 68—1-(N-butylaminomethyl)pyrene
Compound No. 69—1-(alpha-N-hexylaminoethyl)pyrene hydrochloride
Compound No. 70—1-(N-butylaminomethyl)pyrene hydrochloride
Compound No. 71—1-(alpha-aminoethyl)pyrene hydrochloride

Compound No. 72—1-(alpha-aminobenzyl)pyrene hydrochloride
Compound No. 73—1-(aminomethyl)pyrene hydrochloride
Compound No. 74—Tris(1-pyrenylmethyl)amine hydrochloride
Compound No. 75—1-pyrenylidenebismorpholine
Compound No. 76—1-aminopyrene hydrochloride
Compound No. 77—1-(N-methylaminomethyl)pyrene
Compound No. 78—1-pyrenalmethylamine
Compound No. 79—2-(1-(1-pyrenyl)ethylmercapto)-2-imidazoline hydrochloride
Compound No. 80—1-(chloromethyl)pyrene
Compound No. 81—2-(1-pyrenylmethylmercapto)-2-imidazoline hydrochloride
Compound No. 82—1-pyrenol

Growers of fruits, vegetables, grain, and forage crops are faced with many plant disease problems. One group of diseases, caused by the powdery mildews, are particularly troublesome. The powdery mildews are obligate parasites; that is, they can grow and multiply only on a living host plant. Any plant which is forced to feed the fungus suffers a reduction in actively functioning leaf area and partial or complete destruction of leaves, stems, fruits, and other plant parts. The affected plant parts may be disfigured, stunted, or killed.

The first visible sign of a powdery mildew infection is a gray to white felt-like growth on the leaves. As the disease progresses, the leaves curl and fold, and may die and drop off prematurely. The infection may spread to any succulent plant part such as the stems, fruits, and the like.

The powdery mildews are found in most of the world's agricultural areas. They attack and damage a wide range of plants. Among those attacked are cereal grains, forage, and fruit crops such as clover, apples, cherries, peaches, grapes, cantaloupes, beans, and ornamentals such as roses, lilacs, and the like.

The fungicides in common use today are not generally effective against the powdery mildews.

Sulfur has been used to control powdery mildew on some crops. However, control with sulfur has never been too satisfactory because it frequently injures the fruit, buds, blossoms, or foliage of treated plants. This is particularly true in hot weather. On some crops such as grapes which are particularly sensitive to sulfur, it cannot be safely used.

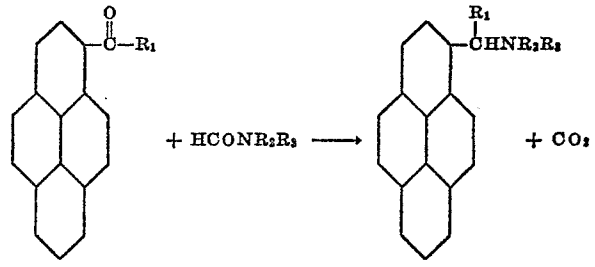
We have discovered that the 1-substituted pyrenes give excellent control of the powdery mildews. These materials, when properly used, are safe to both the plant and the operator applying them.

The 1-substituted pyrenes of the present invention can be prepared by a number of methods. For example, nitropyrene can be prepared by the mild nitration of pyrene with nitric acid. The acetyl and benzoylpyrenes can be prepared by the reaction of the corresponding acid chloride with pyrene in the presence of aluminum chloride as a catalyst. The novel 1-aminoalkyl pyrenes may be prepared or described in copending application, Serial No. 782,624, filed December 24, 1958, to Marcus et al., by the reaction of a carbonyl compound selected from the group consisting of 1-pyrenecarboxaldehyde and a 1-acylpyrene, such as 1-acetylpyrene and 1-benzoylpyrene, with an amide having the formula $HCONR_2R_3$, wherein NR_2R_3 is selected from the group consisting of heterocyclic radicals containing from 5 to 6 atoms in the ring and radicals of the formula



wherein R_2 and R_3 are selected from the group consisting of hydrogen, alkyl, aryl, and pyridyl.

The reaction is illustrated by the following equation:



The carbonyl compound and the amide may generally be present in widely varying proportions, but are preferably present in a molar ratio of from about 1:1 to about 1:10, respectively. Formic acid, in an amount corresponding to 0.01 to 5 mols of formic acid per mol of carbonyl compound, is preferably present during the reaction.

The reaction may be conducted by heating a solution of the carbonyl compound in the amide at a temperature of from about 100 to about 250° C. for a period of from about 1 to about 100 hours, preferably at a temperature of from about 150 to about 200° C. for a period of about 2 to 10 hours.

When neither R_2 nor R_3 is hydrogen, the product may be recovered as a residue by distillation of any unreacted amide and formic acid, if present. The distillation is preferably conducted under vacuum. The residue product is, in many cases, pure enough for use without further treatment. However, the products may conveniently be isolated in the pure state, as the hydrochloride salts, by dissolving the crude product in a solvent such as ethyl ether, dioxane, or benzene and introducing dry hydrogen chloride gas into the solution (in an amount corresponding to at least one mole equivalent) to precipitate the 1-(aminoalkyl)pyrene hydrochloride. Similar salts of other anhydrous acids may also be prepared in a similar fashion.

The free amine can be obtained from the hydrochloride by treating it with an aqueous base, such as ammonia, and a water-immiscible solvent, such as ether or benzene. Separation of the organic layer, followed by removal of the solvent leaves the free amine as residue.

When R_2 or R_3 or both are hydrogen, the crude reaction mixture, after removal of excess amide and formic acid, if present, contains a mixture of the desired amine and its corresponding N-formyl derivative. The formyl derivative can be hydrolyzed by heating the crude reaction mixture with aqueous or alcoholic acid or base. A convenient method comprises refluxing the crude mixture with an excess of concentrated hydrochloric acid and butanol for 2 to 100 hours, preferably from 4 to 24 hours. The crude amine hydrochloride is obtained by distilling off hydrochloric acid, butanol, and formic acid. The crude amine hydrochloride can then be treated with an aqueous base, such as ammonia, and a water-immiscible solvent, such as benzene, to give a solution of the free amine in the nonaqueous layer. The free amine can then be recovered by distilling off the solvent, or the amine hydrochloride can be obtained by treating the solution with gaseous hydrogen chloride.

The monoalkylaminomethylpyrenes and monoarylaminomethylpyrenes are also prepared in two steps by catalytic reduction of the imines derived from 1-pyrenecarboxaldehyde and the corresponding amine. On the other hand (aminoalkyl), pyrenes in which R_2 and R_3 are both hydrogen are prepared most readily by hydrogenation of the oximes of the corresponding carbonyl compounds.

The following examples are illustrative of the preparation of the 1-substituted pyrenes of the present invention.

1-thiopyrenol has been prepared by reduction of 1-thiocyanopyrene with zinc and acetic acid. Oxidation of thiopyrenol with iodine gave the disulfide. Reaction of

thiopyrenol with chloroacetic acid gave the mercaptoacetic acid derivative.

N-(1-pyrenyl)maleamic acid was obtained by reaction of the amine with maleic anhydride. Cyclization of the maleamic acid with acetic anhydride afforded the maleimide. N,N'-diacetoacetyl-1,6(or8)-diaminopyrene was synthesized by the reaction of diketene with 1-aminopyrene.

The 1-substituted pyrenes of the present invention may be applied at the rate of 0.2 to 25 pounds per acre. We have found, however, that good control of fungi is obtained when the 1-substituted pyrenes are applied at the rate of 0.5 to 6 pounds per acre. They may be used alone, but are preferably employed with a carrier or diluent in the form of a solution or dispersion which can be sprayed on the plants or as a wettable powder which can be dusted on the plants.

Suitable solutions or dispersions for use in accordance with the present invention comprise from 1 to 95 parts by weight of a 1-substituted pyrene or mixture of 1-substituted pyrenes, as the active fungicidal ingredient, and from 5 to 99 parts by weight of a liquid carrier, such as water, alcohols, ether alcohols, ketones, petroleum distillates, vegetable oils, and the like and mixtures thereof.

Suitable wettable powders or dusts for use in accordance with the present invention comprise from 1 to 90 parts by weight of a 1-substituted pyrene or mixture of 1-substituted pyrene, as the active fungicidal ingredient, and from 10 to 99 parts by weight of a solid carrier, such as clay, talc, chalk, magnesium carbonate, diatomaceous earth, pyrophyllite, and mixtures of such materials.

The above compositions may also contain dispersing or emulsifying agents, such as the condensation products of alkylene oxides with phenols and organic acids, aryl alkyl sulfonates, complex ether alcohols, mahogany soaps, and quaternary ammonium compounds.

The compositions may also contain other toxicants, such as arsenates, rotenone, pyrethrum, imidazolines, dithiocarbamates, and mixtures of such materials.

The effectiveness of the 1-substituted pyrenes of the present invention as fungicides is demonstrated by the following experiments. The methods by which the experiments were carried out are described below and the results of the experiments are given in Table I below.

BEAN MILDEW TEST

Greenhouse tests were conducted with these materials for the control of powdery mildew of beans caused by the fungus *Erysiphe polygoni*.

For the tests against bean mildew, aqueous suspensions were prepared containing 0.04 part (all parts by weight), 0.008 part, and 0.0016 part of the chemicals to be tested. The suspensions also contained .05 part of dispersing agent, an alkyl phenyl polyethylene glycol ether, marketed under the proprietary mark "Tergitol" dispersant NPX, per 100 parts of water. Individual bean plants of about 10 days of age that had been inoculated two to four days previously by dusting with spores of the test organism were sprayed for 30 seconds with one or another of the suspensions. Check or control plants received no fungicidal spray. The plants were then placed in the greenhouse and after 10 days to two weeks the primary leaves were examined for mildew and scored as follows:

1=leaf over-run with mildew, equal to check plants.
2=many but distinctly separate spots on each leaf.
3=4–10 spots per leaf.
4=1–3 mildew spots per leaf.
5=no mildew infection.

EARLY BLIGHT TOMATO FOLIAGE DISEASE TEST

Test organism.—Early blight fungus *Alternaria solani* is the organism used in this test procedure. The organism is reared on potato dextrose agar in Petri dishes at a temperature of 20° C. Organisms used are transferred 10 days prior to testing; scraped and irradiated with ultraviolet light for 2 minutes on the seventh day following transfer.

Application of toxicant.—One tomato plant variety, Bonny Best, of a standard age and height per concentration is sprayed on a revolving turntable. One hundred to one hundred and ten ml. of the formulated water mixture of the chemical is applied to each plant by use of a Devilbis spray gun with air pressure set at 40 pounds. Application of this volume of spray takes 30 seconds. An equal volume of a water solution containing acetone and emulsifier in the same concentrations as in the fungicidal mixture but without the candidate fungicide, is also sprayed on six tomato plants and held as check or control plants. As soon as the spray has dried the plants are inoculated by again placing them on the turntable and spraying with a spore suspension of early blight, containing 25,000 to 30,000 per ml. of water, for 30 seconds at 20 pounds pressure.

Concentration of toxicant.—The test compounds are formulated by a standard procedure of solution in acetone, addition of an emulsifier and dilution with water. The compounds are evaluated at concentrations of 2000 and 80 p.p.m.

Holding conditions.—Following inoculation the plants are incubated for 24 hours at 72° F. and 100 percent relative humidity. The plants are then removed from the incubation chamber and held for an additional 24 hours at room temperature.

Record of results.—The total number of lesions per 11 15×magnification fields on 11 leaflets on the three top leaves of each plant are counted. A similar count is made on the control plants and the average number of lesions per plant is calculated. Control is based on a comparison of the number of lesions on the treated versus the untreated plants. Compounds are rated according to the following designations.

5=90–100% control
4=70–89% control
3=50–69% control
2=25–49% control
1=0–24% control

Table I

Compound Number	Early Blight (p.p.m.)		Bean Mildew (p.p.m.)		
	2,000	80	400	80	16
Misture of 1 and 2	4		5		3
3			4		3
4			5	5	4
5	5	3	5	5	4
6	4			2	3
7	2	3	5	5	4
8	2	4	2		
9	4	1	4	2	2
10		3	5	4	3
11	4	3	5	4	3
12			5	4	2
13	1	3	4	4	
14			5	4	3
15	4	4	5	4	3
16		3	5	3	2
17	5	4	5	3	2
18	5	4	5	5	2
19			3	3	2
20	3	2		5	5
21					5
22			5	2	2
23			5	5	4
24			5	5	3
25			5	5	4
26			4	3	3
27			5	4	2
28			5	4	3
29			4	4	2
Mixture of 30 and 31			3		2
32	5	4	4	4	3
33	3	3	2		
34	5	1	3	2	2
35			4	3	2
36			5	4	3
37	3	1	5	3	2
38	4	1	5	4	4
39	5	5	5	5	4
40			3	2	2
41	5	3	5	4	4
42	4	4	5	5	4

Table I—Continued

Compound Number	Early Blight (p.p.m.)		Bean Mildew (p.p.m.)		
	2,000	80	400	80	16
43	4	3	5	5	4
44		3	5	5	4
45			4	4	3
46			5	5	3
47	3	2	5	4	4
48	4	4	5	4	4
49			5		2
50	3	1	5	5	3
51	4	4		5	4
52					2
53			3		2
54	3	1	5	4	3
55			5	4	2
56			5	2	2
57			4	3	4
58			5	4	3

As used herein, unless otherwise indicated, all parts and percentages are by weight.

The term "p.p.m." means parts per million.

Similar tests were made against early blight employing toxicant concentrations of 1000 and 100 parts per million and against bean mildew employing toxicant concentrations of 500, 100 and 20 parts per million.

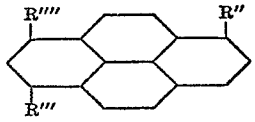
Table II

Compound Number	Early Blight (p.p.m.)		Bean Mildew (p.p.m.)		
	1,000	100	500	100	20
59				5	4
60			5	2	2
61			5	4	3
62	3	2	5	4	4
63	4	2	5	4	3
64			5	3	2
65			5	3	2
66	5	2	5	4	2
67			5	4	3
68	4	3		5	3
69	4	2	5	5	
70	5	3	5	5	4
71	5	2	5	5	4
72	4	2	5	5	5
73	4	1	5	5	5
74			5	5	3
75			5	4	3
76	3	1	5	4	1
77		4	5	4	4
78	4	2	5	5	4
79	4	3		5	3
80	4	3	5	5	2
81	4	3	5	5	2
82	4	4	5	4	

This application is a continuation-in-part of co-pending application, Serial No. 782,638, filed December 24, 1958, now abandoned.

We claim:

1. A method which comprises applying to fungi a fungicidal amount of a compound having the structural formula:



wherein R'' is an organic radical, R''' and R'''' are selected from the group consisting of hydrogen and organic radicals, at least one of said R''' and R'''' being hydrogen, said compound having a molecular weight of up to about 700.

2. A method which comprises applying to fungi a fungicidal amount of pyrene substituted in the 1-position by an organic radical, said substituted pyrene having a molecular weight of up to about 700.

3. A method which comprises applying to fungi a fungicidal amount of pyrene substituted in the 1- and 6-positions by an organic radical, said substituted pyrene having a molecular weight of up to about 700.

4. A method which comprises applying to fungi a fungicidal amount of pyrene substituted in the 1- and 8-positions by an organic radical, said substituted pyrene having a molecular weight of up to about 700.

5. A method which comprises applying to fungi a fungicidal amount of 1-nitropyrene.

6. A method which comprises applying to fungi a fungicidal amount of 1,6-dinitropyrene.

7. A method which comprises applying to fungi a fungicidal amount of 1,8-dinitropyrene.

8. A method which comprises applying to fungi a fungicidal amount of 1-acetylpyrene.

9. A method which comprises applying to fungi a fungicidal amount of 1-benzoylpyrene.

10. A method which comprises applying to fungi a fungicidal amount of 1,6-dibenzoylpyrene.

11. A method which comprises applying to fungi a fungicidal amount of 1,8-dibenzoylpyrene.

12. A method which comprises applying to fungi a fungicidal amount of 1-(hydroxymethyl)pyrene.

13. A method which comprises applying to fungi a fungicidal amount of 1-(N,N-dimethylaminomethyl)pyrene hydrochloride.

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