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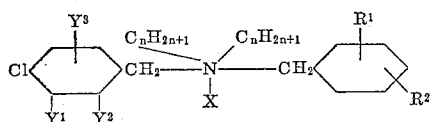
DIALKYLHALOBENZYLALKYL BENZYL NON-PHYTOTOXIC QUATERNARY AMMONIUM COMPOUNDS

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This invention concerns novel quaternary ammonium compounds which are particularly effective for controlling scab on apple trees with safety thereto even in seasons requiring repeated applications. These compounds have the formula

(I)



where R^1 is hydrogen or an alkyl group of one to four carbon atoms, R^2 is an alkyl group of 9 to 15 carbon atoms, the total number of carbon atoms in R^1 and R^2 being not over 16 carbon atoms, Y^1 and Y^2 are hydrogen or chlorine, at least one of these being chlorine, Y^3 is hydrogen or chlorine, the total number of chlorine atoms in the phenyl group carrying the Y substituents being not over three, n is an integer with a value of one to two, and X is an anion.

It will be seen that there are restrictions as to the position and the number of chlorine atoms in the benzyl group. These restrictions arise from the necessity of balancing fungicidal action against lack of phytotoxic action. Similar factors have to do with the alkylbenzyl group, wherein the size of R^2 is of importance although its position does not seem to be a determining factor. There may be one or more methyl or other small alkyl substituents. A class of preferred compounds has one methyl substituent and one long alkyl group on this benzyl group.

These restrictions are necessary to ensure the balance of fungitoxicity coupled with lack of phytotoxicity. A balance favorable to controlling fungus diseases without harm to the host plant is obviously desirable. It depends upon a combination of properties which are completely beyond prediction. There are difficulties in finding compounds or a small group of compounds which will be effective in controlling such a disease as apple scab and yet be safe on plants at all stages of development and under diverse and even extreme conditions of weather and climate.

Use of many quaternary ammonium compounds in conventional spray schedules has been found to cause difficulties from phytotoxicity. Often the fruit is marked or stained. A marked improvement resulted when it was proposed to apply some quaternary compounds at intervals only when lesions appear. Under favorable climatic conditions and in seasons when weather conditions are helpful, the modified schedule appears useful in some geographic areas. Further experience has, however, demonstrated that in cool seasons, in areas with high humidities, under conditions of considerable rain fall, or with combinations of unfavorable factors, the usual quaternary ammonium compounds are lacking in effectiveness or are phytotoxic, as shown by damage to leaves and/or fruit.

As a typical quaternary ammonium salt having fungicidal action, there may be considered the class of alkyl-dimethylbenzyl ammonium salts, wherein the alkyl group is long-chained, usually dodecyl. These give good fungicidal action under favorable conditions, but those with

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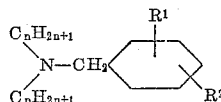
alkyl groups providing good solubility for proper application lack persistence and those with longer alkyl groups providing better persistence lack fungitoxicity. At the rates of application needed for good control of scab, these salts cannot be frequently applied without causing undesirable effects. Thus, under conditions of severe infection or under unfavorable weather conditions, such salts lack the required balance.

Ways have been sought to enhance the fungitoxicity and persistence of the well known alkyl-dimethylbenzyl ammonium salts. The introduction of chlorine into the benzyl group has been suggested to increase the killing power of alkyl-dimethylbenzyl salts. Unfortunately, the undesired effects increase more rapidly than the desirable actions. This same unfavorable turn is encountered with quaternaries depending for activity on an N-alkylphenoxyethoxyethyl group and like ether-containing groups.

It was therefore quite unexpected to discover that quaternaries containing N-alkylbenzyl groups of proper size could be improved as to fungitoxicity and lack of phytotoxicity with specific dichloro- or trichloro-benzyl groups. The unpredictable nature of the balance of these desired qualities is particularly evident when one notes that both fungi and apple trees are vegetative.

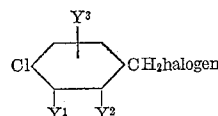
Quaternary ammonium salts which meet the above strict requirements have been defined by the structural Formula I given above. They are prepared conveniently by reacting a tertiary amine

(II)



with a polychlorobenzyl halide

(III)

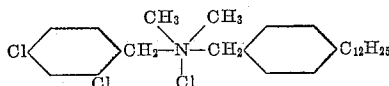


This may be desirably done in an inert organic solvent, such as acetone, methyl hexyl ketone, acetonitrile, nitromethane, ethyl acetate, benzene, toluene, or a naphtha. About equivalent amounts of the two reactants are mixed and reacted together. Temperatures for reaction lie between 25° and 150° C. In some cases the quaternary ammonium salt precipitates as it is formed and can be separated and freed of solvent. In other cases, solvent may be distilled from the reaction mixture to leave a residue which can be used as obtained or may be purified as by precipitation, extraction, charcoaling, or recrystallization.

Preparations of typical compounds are shown in the following examples which are presented for purposes of illustration and not limitation. Parts are by weight unless otherwise noted.

Example 1

There are mixed 25 parts of dodecylbenzyl-dimethylamine, 16.1 parts of 2,4-dichlorobenzyl chloride, and 100 parts of acetone. This mixture is heated under reflux for 3.5 hours. The reaction mixture is cooled to about 25° C. with separation of a solid, which is collected, washed with anhydrous diethyl ether, and dried. There is thus obtained 14.2 parts of product, which melts at 132-135° C. and which corresponds by analysis to dodecylbenzyl-dimethyl-2,4-dichlorobenzylammonium chloride



Nitrogen content is 2.7% and total chlorine is 21.0%

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(2.8% and 21.3% respectively by theory). Ionic chlorine is 7.0% (theory 7.1%).

The above preparation is repeated with substitution of 28.3 parts of dodecylbenzyl-diethylamine for the dodecylbenzyl-dimethylamine. The product, dodecylbenzyl-diethyl-2,4-dichlorobenzylammonium chloride, is similar in properties to the above compound. It is quite as safe on tender foliage and about as fungitoxic.

In fungitoxicity tests by the slide germination method, the above compound, dodecylbenzyl-dimethyl-2,4-dichlorobenzylammonium chloride, has ED_{50} values of 1-10 p.p.m. against *Alternaria solani* and *Monolinia fruticola*, and of less than 1 p.p.m. against *Stemphylium sarcinaeforme*.

When a 0.1% solution is applied to young tomato plants, there is no evidence of phytotoxicity. On young apple trees, there is no evidence of phytotoxicity at 0.12%.

Against apple scab (*Venturia inaequalis*) on apple tree seedlings, there is 99% protection and 99% eradication when this compound is applied from a spray containing 1.00 pound per 100 gallons of water. Protection remains at 98% even after simulated rain.

This compound is also highly active against such typical pathogens as *Agrobacterium tumefaciens* (plant galls), *Erwinia amylovora* (fire blight), *Erwinia carotovora* (vegetable soft rot), *Xanthomonas phaseoli* (bean blight), *Xanthomonas pruni* (bacterial soft spot of plum and peach), *Corynebacterium flaccumfaciens* (bacterial wilt of beans), and *Xanthomonas vesicatoria* (bacterial spot of peppers and tomatoes).

Furthermore, the above prepared compounds give very favorable values in standard antibacterial tests. In the broth titre test, for example, they are effectively bacteriostatic at 1/100,000 against *S. typhosa* and bactericidal at the same dilution. Against *S. aureus*, they are bacteriostatic at 1/400,000 and bactericidal at 1/200,000.

Apple whips were sprayed with solutions containing 0.75 pound per 100 gallons of the above compounds at one-week intervals for a period of four weeks. No evidence of phytotoxicity was observed even though the whips were held under humid conditions.

Apples were treated with a solution containing one pound of the above compounds per 100 gallons of water. The apples were stored for 24 hours under high humidity, then dried, and stored for seven days. No stains developed on the apples. At the same time, apples thus treated with dodecyl-dimethylbenzylammonium chloride developed "ghost rings" or brown stains.

Another method of evaluation distinguishes the action of dodecylbenzyl-dimethyl-2,4-dichlorobenzylammonium chloride and the like from that of dodecylbenzyl-dimethylbenzylammonium chloride and of dodecyl-dimethylbenzylammonium chloride as comparison compounds. In this method of evaluation, spores are obtained from lesions of leaves from the eradication test by washing leaves having lesions with water and collecting spores. These spores are applied to standard coated slides such as used in the slide spore germination test. The inoculated slides are stored under conditions favorable for germination for 24 hours and then examined. With the comparison compounds, there occurs about 50% germination of the spores, while in the case of spores from lesions of leaves treated with dodecylbenzyl-dimethyl-2,4-dichlorobenzylammonium chloride there is no germination.

Example 2

There are mixed 30.3 parts of dodecylbenzyl-dimethylamine, 20 parts of 3,4-dichlorobenzyl chloride, and 120 parts of acetone. The mixture is stirred and heated under reflux for 2.5 hours. Solvent is evaporated to give 38.1 parts of a viscous oil, which contains 21.2% of chlorine and 3% of nitrogen (theory 21.3% and 2.8% respectively for dodecylbenzyl-dimethyl-3,4-dichlorobenzylammonium chloride).

Similar compounds are prepared with ethyl or hydroxyethyl groups in the place of the above methyl groups.

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The above compound, evaluated by the slide-germination method, has an ED_{50} value of less than 5 p.p.m. against *Alternaria solani*, *Monolinia fruticola*, and *Stemphylium sarcinaeforme*. It shows no phytotoxicity when applied to young tomato plants in aqueous sprays containing 0.1% or even 1% of the compound.

The tests for control of apple scab on McIntosh seedlings show 99% protection with sprays containing one pound in 100 gallons of water and 93% protection at 0.25 pound per 100 gallons. Eradication at 0.75 pound per 100 gallons is above 87%.

This compound shows superior performance in controlling tomato late blight (*Phytophthora infestans*), requiring only 29 p.p.m. to give an ED_{50} value. It has unusual persistence in tests in which plants are sprayed with water to simulate rain.

In the fruit injury above described, there is no evidence of phytotoxicity.

In the test for viability of spores treated with solutions of the above compound, there was no germination on the test slides.

In the broth titre test, the above compound is bacteriostatic against *S. typhosa* at 1/100,000 and against *S. aureus*, *Micrococcus pyogenes*, var. *aureus*, at 1/400,000. It is bactericidal against *S. typhosa* at 1/10,000 and against *S. aureus* at 1/400,000.

Example 3

There are mixed 26.1 parts of nonylbenzyl-dimethylamine, 19.6 parts of 3,4-dichlorobenzyl chloride, and 80 parts of acetone. The mixture is heated at reflux temperatures for 3.5 hours and cooled in an ice bath. Solid forms and is collected, washed with cold acetone and dried to give 25.3 parts of a product which by analysis corresponds to nonylbenzyl-dimethyl-3,4-dichlorobenzylammonium chloride. The chlorine content found is 23.9% (23.3% theory) and the nitrogen content is 3.0% (3.1% theory).

In the slide germination tests ED_{50} values are found of 1 to 10 p.p.m. against *Alternaria solani* and *Monolinia fruticola*, and of less than 1 p.p.m. against *Stemphylium sarcinaeforme*. There is no evidence of any phytotoxicity when young tomato plants are sprayed with 0.12% solution of this quaternary ammonium salt. Similarly, apple seedlings show no evidence of phytotoxicity with 0.1% solutions. Apple scab is eradicated to an extent of over 75% and protection of about 90% is obtained from sprays with 0.75 pound in 100 gallons.

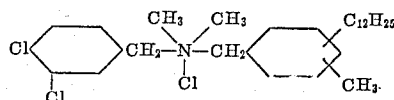
Compounds of the above type with smaller alkylbenzyl groups exhibit some phytotoxicity and fall off in fungitoxicity rapidly as the alkyl group is decreased in size.

The nonylmethylbenzyl-dimethyl-3,4-dichlorobenzylammonium salts, where the anion is chloride, bromide, acetate, sulfate, methylsulfate, or the like, are somewhat more active than the above nonylbenzyl compound and quite safe on foliage.

Effectiveness increases somewhat with increase in the size of the R^1 group when the R^2 substituent is a nonyl group. Thus, nonylethylbenzyl-dimethyldichlorobenzylammonium chloride or bromide and nonylbutylbenzyl-dimethyldichlorobenzylammonium chloride or bromide are both effective in controlling fungi and bacteria which attack growing plants and are also safely used thereon, even with repeated applications.

Example 4

In the same way as in Example 2, there are reacted 33 parts of dodecylmethylbenzyl-dimethylamine and 19.6 parts of 3,4-dichlorobenzyl chloride in 120 parts of acetone. After removal of solvent, there is obtained 51 parts of a yellow oil which corresponds in composition to



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The chlorine content is 21.3% and the nitrogen content is 2.7%.

This compound gives an ED₅₀ value of 1 to 10 p.p.m. against *Alternaria solani*, *Monolinia fruticola*, and *Stemphylium sarcinaeforme*.

It gives an excellent performance against *Phytophthora infestans* on tomatoes with an ED₅₀ value below 30 p.p.m. It shows no evidence of phytotoxicity at 0.2% or even at 1.0% on young tomatoes or at 0.12% on apple seedlings.

It gives 99% protection against *Venturia inaequalis* on McIntosh apple seedlings and an eradication of about 80%. In the tests for persistence, it gives 97% protection.

In the tests for fruit injury there was no staining and no development of "ghost rings."

In the broth titre tests, this compound was both bacteriostatic and bactericidal to *S. typhosa* at 1/100,000 and was both bacteriostatic and bactericidal to *S. aureus* at 1/800,000.

Example 5

A trichlorobenzyl chloride is prepared by chloromethylating a commercial trichlorobenzene which contains about 70% 1,2,4-trichlorobenzene and 30% 1,2,3-trichlorobenzene. This benzyl chloride is mainly 2,4,5-trichlorobenzyl chloride.

There are reacted 23 parts of the above chloride and 30 parts of dodecylbenzyltrimethylamine by heating under reflux in acetone. The acetone is then removed by distillation to give an oil, which by analysis is chiefly dodecylbenzyltrimethyltrichlorobenzylammonium chloride.

It gives ED₅₀ values under 10 p.p.m. against *Alternaria solani*, *Monolinia fruticola*, and *Stemphylium sarcinaeforme*. It is effective in controlling *Phytophthora infestans* on tomatoes, giving ED₅₀ values of 30-60 p.p.m. and showing very good persistence under simulated rain. It protects apple seedlings against *Venturia inaequalis* to the extent of 85% with an eradication of about 77%. It shows no evidence of phytotoxicity at 0.12% on young tomato plants or apple seedlings.

For preparation of aqueous sprays of the above compound, it may be desirable to take it up with a small proportion of a non-ionic wetting agent such as octylphenoxypolyethoxyethanol to ensure good dispersion on foliage. The application of other of the polychlorobenzyl-containing quaternaries of this invention may also be improved in this way.

Example 6

The method of Example 1 is followed to react dodecylmethylbenzyltrimethylamine and 2,4-dichlorobenzylchloride to form dodecylmethylbenzyltrimethyl-2,4-dichlorobenzylammonium chloride, a yellow oil, which contains 21.0% of chlorine and 2.7% of nitrogen. The yield is practically quantitative.

This compound has an ED₅₀ value of about 1-10 p.p.m. against *Monolinia fruticola* and between 10 and 50 against *Alternaria solani* and *Stemphylium sarcinaeforme*.

The compound eradicates completely 70% of the lesions of *Venturia inaequalis* on apple seedlings. It has a protective value of 87% and a 93% value in persistence tests.

The above chlorides may be converted into other salts by exchanging the chloride ion for other anions, such as sulfate, methyl sulfate, acetate, phosphate, benzenesulfonate, toluenesulfonate, naphthalenesulfonates, or like anions.

To assist in the solution and dilution of the compounds

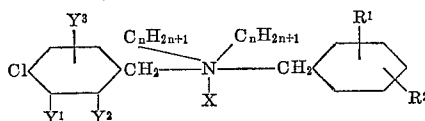
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of this invention, particularly in the field, it is desirable to prepare so-called emulsion concentrates. For example, the above quaternary ammonium compounds can be taken up with about an equal volume of isopropanol. This solution (80 parts) is mixed with 16 parts of xylene or an aromatic naphtha and 4 parts of a solvent- and water-soluble alkylphenoxypolyethoxyethanol wetting agent to provide a self-emulsifying composition.

In general such emulsion concentrate may contain from about 20% to about 60% of a defined quaternary ammonium salt, about 40% to 75% of organic solvent for said salt, and 0% to 10% of a non-ionic emulsifier soluble in the solvent-salt mixture. In addition to the above-mentioned alkylphenoxypolyethoxyethanols, there may be used ethylene oxide condensates of long-chained alcohols, mercaptans, fatty acids, hydroxy esters or amines or mixed ethylene oxide-propylene oxide condensates of these and similar materials.

I claim:

1. A compound of the formula



wherein R¹ is selected from the class consisting of hydrogen and alkyl groups of not over four carbon atoms, R² is an alkyl group of 9 to 15 carbon atoms, the total number of carbon atoms in R¹ and R² being not over 16 carbon atoms, Y¹ and Y² are selected from the class consisting of hydrogen and chlorine, at least one of these being chlorine, Y³ is selected from the class consisting of hydrogen and chlorine, the total number of chlorine atoms on the phenyl group carrying the Y substituents being two to three, n is an integer with a value of one to two, and X is an anion from the class consisting of chloride and bromide.

2. Dodecylbenzyltrimethyl - 2,4 - dichlorobenzylammonium chloride.

3. Dodecylbenzyltrimethyl - 3,4 - dichlorobenzylammonium chloride.

4. Dodecylmethylbenzyltrimethyl - 3,4 - dichlorobenzylammonium chloride.

5. Nonylmethylbenzyltrimethyl - 3,4 - dichlorobenzylammonium chloride.

6. Dodecylbenzyltrimethyltrichlorobenzylammonium chloride.

References Cited in the file of this patent

UNITED STATES PATENTS

2,097,640	Piggott	Nov. 2, 1937
2,569,803	De Benneville	Oct. 2, 1951
2,664,444	Kwartler	Dec. 29, 1953
2,691,676	Hallock	Oct. 12, 1954
2,694,715	Stayner	Nov. 16, 1954
2,763,589	O'Brien et al.	Sept. 18, 1956
2,787,573	Newcomer	Apr. 2, 1957

FOREIGN PATENTS

647,258	Great Britain	Dec. 6, 1950
285,479	Switzerland	Jan. 16, 1953

OTHER REFERENCES

65	Braun et al.: Ann. der Chemie, col. 507, pages 1-13 (1933).
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