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FUNGICIDE

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This invention relates to materials adapted to inhibit fungi, in particular the growth of fungi on plants in foliage. The invention is especially concerned with preparing and placing in the hands of the ultimate user, at a low cost, a fungicide base material or concentrate from which the user may easily and quickly prepare an efficient water-base fungicide of low phytotoxicity containing glyoxalidines as the active ingredient. The invention is also concerned with the spray material thus prepared.

It has been proposed to inhibit fungi by applying to plants, water-base sprays containing glyoxalidines. Difficulties arise, however, in preparing and using such sprays. Those glyoxalidines and glyoxalidine derivatives, for instance the glyoxalidine salts, which are water soluble, that is materials which have a water solubility of more than 0.05 part by weight in 100 parts of water at 25° C., may be unsatisfactory, at least for field use as fungicides, because they wash off of the plant too readily during a rain occurring shortly after their application. Glyoxalidines having a heptadecyl group connected to the carbon at the 2-position in the glyoxalidine ring, with or without a short chain saturated carbonaceous group connected to the nitrogen at the 1-position, for instance 2-heptadecyl glyoxalidine, 1-aminoethyl-2-heptadecyl glyoxalidine, and 1-hydroxyethyl-2-heptadecyl glyoxalidine are good fungicides of which 2-heptadecyl glyoxalidine is the most satisfactory for general field use, being highly fungicidal and combining low phytotoxicity with hydrophobic characteristics. It is a soft, waxy, somewhat greasy, soap material with a melting point of about 94° C. The 1-hydroxyethyl-2-heptadecyl glyoxalidine (melting point about 50° C.) is somewhat like 2-heptadecyl glyoxalidine only softer, more waxy, greasy and soapy, while 1-aminoethyl-2-heptadecyl glyoxalidine is a liquid at ordinary temperatures (25° C.). Both of these glyoxalidines have hydrophilic characteristics and are not so desirable for general field use as the hydrophobic 2-heptadecyl glyoxalidine.

The saturated carbon chain at the 1-position on the glyoxalidine ring may contain up to 3 carbon atoms and there may be saturated substituents containing up to about 4 carbon atoms for one or all of the hydrogens at the 4 and 5 positions but the character of the substituents at the 1 and 2 positions appears to have the greatest effect on those properties of the glyoxalidine which enable them to operate satisfactorily on plants in foliage. Shorter chains

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than a 17 carbon atom chain at the 2-position render the glyoxalidine more phytotoxic. Chains longer than 17 carbon atoms at the 2-position make the material less fungicidal. Chains longer than 3 carbon atoms at the 1-position render the glyoxalidine more phytotoxic. Unsaturation of the substituents at either the 1- or the 2-position promotes phytotoxicity. Cyclic groups at either the 1- or 2-position are to be avoided as they either decrease fungistatic action or increase phytotoxicity.

Thus 2-pentadecyl glyoxalidine, a material which is soft, waxy, somewhat greasy and soapy, (melting point about 92° C.) quite like 2-heptadecyl glyoxalidine, is more phytotoxic than the heptadecyl glyoxalidine as is 2-heptadecenyl glyoxalidine, a material which is quite soft, waxy, greasy and lard-like (melting point 52° C.). Both of these materials are hydrophobic and desirable for field use from this point of view.

From a practical point of view the manufacturer must supply the orchardist with a low cost concentrate or spray base in such form that merely by mixing with water and other low cost materials readily available to the orchardist at the time of use, he will have an easily prepared spray, in the present case of glyoxalidines. To be practical, the base composition or concentrate should be entirely or substantially homogeneous as packaged, easily removed from the container, easily measured with primitive equipment, capable of being dispersed in water easily and quickly, free of foaming difficulties when agitated with water, stable physically at least over the extreme range of atmospheric temperatures, chemically stable to retain potency over an extended storage period and yield a spray composition, when mixed with water, having the toxicant in a form most toxic to fungi, yet non-phytotoxic to plants in foliage. It is contemplated that the orchardist may also mix with the base or the spray such special additives, for instance arsenates, the various rotenone and nicotine products, the various carbamates, DDT, and the like, as his particular spray schedule may require. Certain glyoxalidines and mixtures of glyoxalidines work well with these fungicides and insecticides, being compatible and non-reactive with them, even though the glyoxalidine ring is unsaturated, to yield sprays which are effective yet not too phytotoxic.

In accordance with the present invention I provide a low cost base meeting these requirements for both base and spray. In the preferred embodiment of the invention, commercial "stearic

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acid," which may contain palmitic acid or oleic acid or both in addition to stearic acid, is reacted with ethyl alcohol and the esters so formed are reacted with ethylene diamine or equivalent to yield a mixture of hydrophobic glyoxalidines. This glyoxalidine mixture is reacted with acetic acid in isopropanol to yield a liquid solution of the acetates in the alcohol. It has been found that the salts can be concentrated quite highly in such a solution, enabling the base thus prepared to be stored and shipped easily, and at a low cost per pound of active material and, further, that the glyoxalidine salts are quite stable in such a solution even though the base contains water. The orchardist is thus supplied with a concentrate from which he can prepare a fungicidal spray merely by mixing with water, preferably with the addition of lime to precipitate the glyoxalidines from the salts and as much more lime as the orchardist requires to safen the mixture when used with arsenates, for instance lead arsenate and the like. Even without lime or with only sufficient lime to precipitate the glyoxalidines, sprays may be prepared from such a solution and be highly fungicidal yet not too phytotoxic even after the solution has been stored several months.

Commercial stearic acid of the usual type contains from about 2% to 5% by weight of oleic acid for the triple pressed grade, about 5% to 10% oleic acid for the double pressed grade, and about 10% to 15% for the single pressed grade. The remaining fatty acids in the commercial stearic acid run from about 5% to 55% by weight of palmitic acid and from about 5% to 45% of stearic acid. The commercial stearic acid contains very minor and negligible amounts of fatty acids having less than 16 carbon atoms and more than 18 carbon atoms, usually totalling not more than 0.5% by weight of the combined weight of stearic, palmitic and oleic acids. Commercial stearic acids prepared by processes involving hydrogenation may contain no, or only a trace of, oleic acid. The commercial stearic acids thus run from about 4% to 55% palmitic acid, about 38% to 95% stearic acid and about zero to 15% oleic acid. I have found that upon properly reacting any commercial stearic acids of the types mentioned, even though they contain the maximum of palmitic and oleic acids, with an alcohol and then with ethylene diamine, a mixture of 2-substituted glyoxalidines is obtained in approximately the same ratio as the acids appeared in the original commercial stearic acid but that even though substantially all of the glyoxalidines remain as such and do not deteriorate into the corresponding acyclic compounds, the mixture of glyoxalidines obtained from commercial stearic acid is not too phytotoxic for use even under such conditions that a spray of water and the glyoxalidines, containing more of the mixed glyoxalidine than will dissolve in the water, is applied to the plant.

The glyoxalidine product thus obtained is not packaged or used as a fungicide; it is a soft, waxy, greasy, hydrophobic material having a melting point of about 85° C. It cannot practically be ground to a dry, free-flowing powder. Also, if reduced to small particles, the particles have a decided tendency to pack and agglomerate so that the orchardist would not obtain a free-flowing powder even though the manufacturer packaged the material as a powder. Further, even when the material is added to water as a powder, the particles have a tendency to agglomerate in

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the water due to the properties of the material whereby the particles repel water and adhere to one another. These properties, however, make the glyoxalidine product a desirable fungicide as it remains a solid at any temperature encountered in the field; being somewhat adhesive it adheres well to the plant and being hydrophobic it does not dissolve in rain to any appreciable extent although it does dissolve in rain, dew or water of guttation to the extent necessary to inhibit fungi. But the orchardist must be given a glyoxalidine product in such form that he can easily prepare a water-base spray having the glyoxalidines in extremely finely-divided state and in the condition most toxic to the fungi. Because of costs, the commercial stearic acid must be used as a source of glyoxalidines and a feature of the invention is that this is possible and yet produce a satisfactory base as well as a sufficiently non-phytotoxic spray.

In attempts to prepare a satisfactory base, I have ground the glyoxalidine product in water to prepare a paste which could be dispersed in more water to prepare a water-base spray but, under storage conditions, the glyoxalidines hydrolyze and the hydrolyzed products do not control apple scab. I have dissolved the glyoxalidines in various solvents, for example alcohols, ketones, oils and the like and poured the solution into water to prepare a spray but this is not feasible commercially; the low cost alcohols and ketones, for instance methanol, ethanol, propanol, isopropanol, butanol, acetone, methyl ethyl ketone, and the like, hold so little glyoxalidines that the cost of the solvent is too great; the oils are somewhat phytotoxic and are not universally usable in a spray schedule. I have ground the glyoxalidines in solvents, for instance alcohols and ketones, for example methanol, ethanol, propanol, isopropanol, butanol, and other alcohols, acetone, methyl ethyl ketone and other ketones using sufficient of the glyoxalidines to make a paste and thus lower the solvent cost but the disadvantages of this are that upon mixing with water to form a spray, the water-soluble solvent with which the paste is made is leached out by the spray water and the glyoxalidine agglomerates into lumps which will not disperse.

To prepare a satisfactory base, the glyoxalidine mixture is reacted with a low cost organic acid, for instance acetic acid, to yield a mixture of the organic acid salts of the respective glyoxalidines; and the mixture of such salts is dissolved in a low cost alcohol, for instance isopropanol, having the property of holding a large amount of the salt and not appreciably reacting with it, to give a highly concentrated solution which is the fungicide base.

I have found that there are practical limitations on both the acids and alcohols which can be used. The glyoxalidines must be in the form of organic acid salts because the glyoxalidines per se are found to be so insoluble even in low cost non-phytotoxic solvents that the cost of the solvent is too large to be practical should it be attempted to prepare, package, store and ship a solution of the glyoxalidines. The salts should be those of organic acids as the mineral acid salts are not practical; they are quite insoluble in the low cost non-phytotoxic alcohols and too much solvent is required to allow a solution of glyoxalidine salts of mineral acids to be used. The acids should be substantially non-phytotoxic, they should not react to any appreciable extent with metal, and their salts, at least those of cal-

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cium, should be substantially non-phytotoxic. It is contemplated that the base will be a highly concentrated liquid solution of the glyoxalidine acetates in isopropanol and that it will be packaged in metal containers. Mineral acids and highly active organic acids, for instance formic acid, which react readily with metals would corrode a metallic container, particularly any free acid which might be present, and upon storage of the base, the metal would even sequester the acid from the salts thereby not only causing corrosion and leaks in the container but yielding a precipitate of free glyoxalidines which would give a non-homogeneous base product. Acetic, propionic, butyric, valeric, 2-ethyl butyric, n-hexanoic, heptanoic, octanoic, and 2-ethyl hexanoic acids, that is monocarboxylic acids having from 2 to 8 carbon atoms, are the only practical acids; higher molecular weight acids yield salts which are too insoluble.

The preferred solvent, represented by isopropanol, is of low cost, completely water-soluble, non-phytotoxic in the amounts in which it will appear in the spray, holds in solution a large amount of the organic acid salts of the glyoxalidines, is saturated, monohydric and noncyclic, has low viscosity and freezing point, boiling point within 20° C. of that of water at 760 mm., vapor pressure within 20 mm. of mercury of that of water at 20° C., non-foaming when beaten with water and has 3 or 4 carbon atoms. The solvent should also be quite inert toward the glyoxalidine salts so that the glyoxalidine ring remains intact so far as possible.

Alcohols with more than 4 carbon atoms are generally not completely water-soluble. Boiling points and vapor pressures near those of water facilitate the preparation of the salt solutions and enable the preparation of aqueous sprays from which the alcohol is readily expelled when the spray is applied to the plant, thus eliminating the possibility of phytotoxicity due to the solvent, as the spray dries on the leaves. Unsaturated and cyclic alcohols are more phytotoxic than saturated acyclic alcohols and are more apt to be toxic to warm-blooded animals and are generally not completely water-soluble. Low viscosities (below 2.92 centipoises at 20° C.) and low freezing points (below 0° C.) enable the preparation of a spray base which remains quite fluid at relatively low temperatures. Polyhydric alcohols are not practical; they cost more than the monohydric alcohols, they have too little solvent power for the salts and they are too viscous. The base should be a non-viscous, mobile liquid at temperatures as low as about 5° C., this being the lowest temperature at which early season spraying is done, and preferably such a liquid at temperatures below 0° C. A solution composed of 26 parts by weight of isopropanol (99.2%, by volume, isopropanol, 0.8% water; 99% and 1%, respectively, by weight) and 74 parts of the acetates of the glyoxalidines prepared from a typical commercial stearic acid (41.4% stearic acid, 50.6% palmitic acid, 8% oleic acid, by weight) solidified at +8° C. but where the isopropanol was replaced by 26 parts of ethylene glycol the solution solidified at 24° C. A solution of 50 parts by weight of the glyoxalidine acetates in 50 parts of isopropanol melted at -5° C. The maximum solubility of the glyoxalidine mixture from which the acetates were prepared was only 12 parts by weight in 100 parts of isopropanol at 20° C. Methanol, ethanol, the propanols and the butanols are the lowest cost alcohols and of these,

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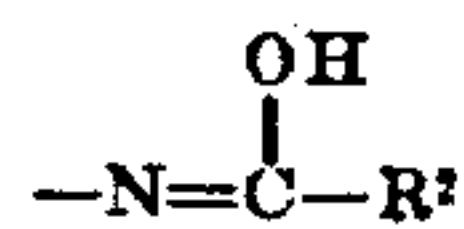
isopropanol is preferred. Methanol, ethanol and the propanols are also completely soluble in water. The butanols may be used to replace a part or all of the propanol but the most common, the normal, butanol is not completely soluble in water and when the spray is applied to the leaves, the butanol does not volatilize as quickly as either of the propanols. However, butanol gives salt solutions with about the same solidifying temperatures as isopropanol. Methanol is usable but undesirable because of its toxicity to warm-blooded animals. Ethanol is undesirable because its use requires the incorporation of denaturants which may affect the operability of the fungicide.

Ketones, for instance acetone, methyl ethyl ketone and the like are unusable; they form addition compounds with the glyoxalidine salts upon storage and the ketones per se may suffer condensation if the solution of the solids is alkaline.

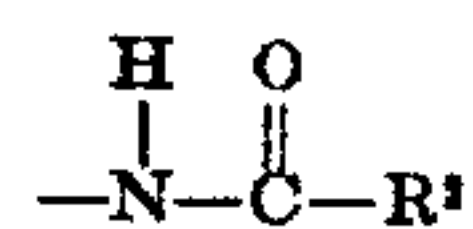
An important feature of the invention is the chemical stability of the glyoxalidine ring when the organic acid salts are dissolved in those alcohols which are herein contemplated as practical solvents, that is isopropanol, ethanol and butanol, in the order named. In the presence of water alone, the glyoxalidines and their salts hydrolyze with a breaking of the ring and the formation of the corresponding straight chain amine-amide or salt. Thus, upon hydrolysis, the bond breaks between the nitrogen at the 1 position and the carbon at the 2 position, giving a group



at the 1-position, and a group



at the 2-3 position which is in equilibrium with its amide form



The glyoxalidines formed from ethylene diamine and the typical commercial stearic acid having the analysis given, when in an aqueous colloidal dispersion containing 84% by weight of water and 16% of glyoxalidines, hydrolyzed to the extent of 50% when held at 100° C. for 30 minutes. Such a dispersion was entirely hydrolyzed upon standing 10 days at normal temperatures of from 20° C. to 25° C. The hydrolyzed glyoxalidines are not effective against apple scab, *Venturia inaequalis*, and are less effective than the unhydrolyzed glyoxalidines against substantially all fungi.

For an isopropanol solution of the acetates (65.9 parts, by weight, of acetates, 33.7 parts of anhydrous isopropanol, and 0.4 part of water) the deterioration was 50% only after 160 hours at 100° C. and while there was a little hydrolysis and/or alcoholysis it was not over 1% of the weight of the glyoxalidine salts, upon standing 10 weeks at the normal temperatures. In alcoholysis, the group at the 1-position is



the R_x being the residue from the alcohol.

For a n-butanol solution of the acetates (65.9 parts, by weight, of acetates, 33.7 parts of anhydrous n-butanol, and 0.4 part of water) there was

a little hydrolysis and/or alcoholysis but less than 1% of the weight of the glyoxalidine salts, upon standing 10 weeks at the normal temperatures.

Of the completely water-soluble alcohols which hold large amounts of the salts, for instance ethanol, isopropanol, and n-butanol, the alcohol may contain up to 1% by weight of water and still not hydrolyze an otherwise anhydrous glyoxalidine salt more than 1% by weight, even after 10 weeks at 25° C. Such an alcohol is considered to be substantially anhydrous for the purposes of this invention and solutions of the glyoxalidine salts referred to herein in completely water-soluble solvents referred to herein are considered to be substantially anhydrous when they contain no more than 0.4 mol of water per mol of the salt, this being the critical amount of water which is permissible in the salt solution and not have more than 40% of the salt hydrolyzed, this being the critical permissible amount of hydrolysis for yielding a glyoxalidine fungicide practically effective against apple scab.

The base is preferably neutral or slightly acidic but may have pH's ranging up to 7.5. Slightly acidic solutions having about 1% excess acid are preferred as maintaining the glyoxalidine in the form of the salt and, although more acidic solutions may be used, the excess acid is merely waste. The solutions are preferably not too basic as the glyoxalidines might precipitate. Any free acid should not appreciably attack the lead-tin alloy coatings, known as "terne-plate" (cf. Terne-plate, The Condensed Chemical Dictionary, Third Edition, 1942, Reinhold Publishing Corp.) at temperatures as high as 110° F. Solutions with pH values between 6.5 and 7.5 are preferred. The glyoxalidine salts of the practical organic acids do not hydrolyze in weakly aqueous alcohol solution as readily as the free glyoxalidines, and free acid keeps the glyoxalidine in the salt form. In the preferred base, represented by an isopropanol solution of the acetates of the glyoxalidines from commercial stearic acid, both the acid and the solvent are completely water-soluble.

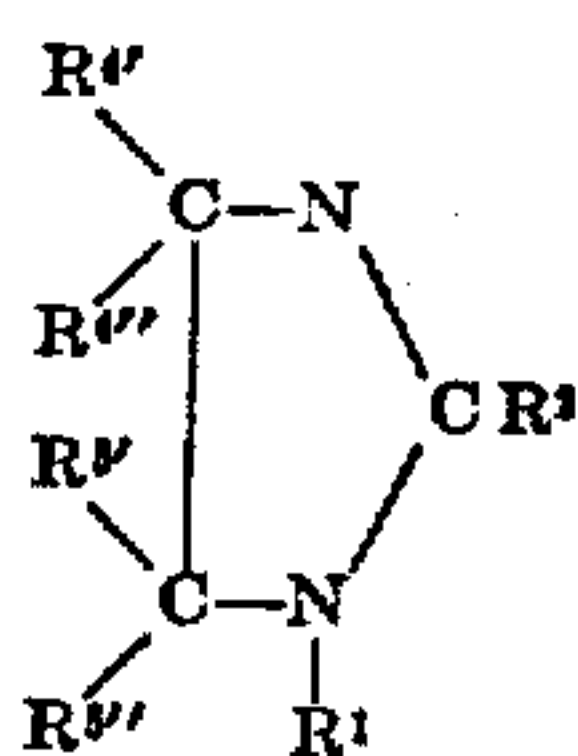
In a water-base spray, by means of which the glyoxalidines are most conveniently applied to plants in foliage, the glyoxalidines should be in the condition most toxic to fungi and as finely-divided as possible. It is contemplated that the ultimate user of the glyoxalidine salt solution will produce a water-base spray merely by mixing the salt solution with water and with sufficient alkaline material to neutralize such free acid as may be present and to free the glyoxalidine from its salt and thus precipitate the free glyoxalidine in a finely-divided, preferably colloidal or substantially colloidal, state. It has been found that a glyoxalidine spray composition, prepared directly before use, is highly effective, as insufficient time elapses between the time the glyoxalidine salts are mixed with the spray-water and base and the use of the spray, for the glyoxalidines to hydrolyze to any appreciable extent. Also, the glyoxalidines are precipitated in the spray-water in a finely-divided condition, the particle size being substantially colloidal; and when the glyoxalidine particles are prepared in this manner, that is by precipitation from their organic acid salts directly in the spray water which also contains the alkaline salt of the organic acid, they do not agglomerate in the water of the spray as do previously-prepared glyoxalidine particles which are added to water.

For best results in the use of the spray, it is

important that certain alkaline materials be used to neutralize the acid of the concentrate. The preferred and representative basic material is lime although barium oxide, magnesium oxide, and the carbonates of either may be used. Lime is of low cost and it is non-phytotoxic, in reasonable amounts, so that if the orchardist wishes to use more lime than is sufficient to neutralize the acid of the concentrate, no harm is done. In fact, lime is a safening agent frequently used in connection with lead arsenate and a large excess of lime over that required to neutralize the acid, may be used. Only 1.45 ounces of CaO are necessary to react with the glyoxalidine acetates in a quart (weight 1.8 pounds) of isopropanol concentrate containing 1.2 pounds by weight of the acetates. A quart of such a concentrate in 100 gallons of water yields a satisfactory fungicidal spray against apple scab. But up to 4 pounds of lime may be used in the 100 gallons of water. The spray should not be too strongly basic, as it might be if excess sodium or potassium hydroxides were used else the spray would be too phytotoxic. Furthermore, sodium and potassium acetates are phytotoxic. The pH of the spray will be about 11.5 where the amount of lime used is that necessary to neutralize any free acetic acid plus that theoretically necessary to neutralize the glyoxalidine acetates, and 11.87 and 12.1, respectively, where 50% and 100% more lime is used than that necessary to neutralize the salts. The glyoxalidine spray having a pH within this range and containing lime or barium or magnesium oxides or their carbonates, is not phytotoxic to apple and the free glyoxalidines do not coagulate. The alkali which is used is preferably quite insoluble in water, having a solubility within the range from magnesium oxide to barium oxide. The preferred alkali is also more water-soluble than the free glyoxalidine; and the alkali salt which is formed when it neutralizes the acid of the concentrate is more water-soluble than either the alkali or the free glyoxalidine. Thus, when the orchardist applies to a plant, a water-base spray prepared by neutralizing the glyoxalidine acetates in the concentrate with lime (or barium or magnesium oxides, or their carbonates) and the spray contains excess alkali, the spray contains finely-divided free glyoxalidines and free lime (which term includes hydrated lime) in suspension and free lime and calcium acetate in solution. The excess lime assures that all of the glyoxalidine acetates have been decomposed into free glyoxalidines and calcium acetate, and prevents the reformation of the water-soluble glyoxalidine acetates on the plant since the first rains or heavy dews wash away the acetic acid in the form of its calcium salt while the more insoluble lime and that part of the hydrated lime converted to carbonate by carbon dioxide in the air remain in situ on the plant. Other alkalis which are safening agents are the aforementioned magnesium oxide and barium oxide and their carbonates; and the salts formed by the metals of these alkalis with the organic acids referred to herein as suitable for forming glyoxalidine salts, are non-phytotoxic.

Glyoxalidines may be prepared by a reaction wherein a commercial stearic acid is reacted with ethanol to give a mixture of ethyl stearate, ethyl palmitate and ethyl oleate in proportions corresponding to the amounts of the respective acids in the acid reactant. The mixed esters are then reacted with ethylene diamine to give the corresponding N-(2-aminoethyl) stearamide and

the corresponding monoamides in the cases of the other acids. The mixture of amides is then heated to close the ring and drive off the water which is formed and finally to distill the glyoxalidines. During this heating a portion of the glyoxalidines are decomposed to the corresponding diamides or a portion of the monoamides form the corresponding diamides while another portion of the monoamides form the corresponding glyoxalidines. The diamides are undesirable in the fungicide base and are preferably eliminated. The distillate from the heating step contains, as a major portion, a mixture of glyoxalidines and a minor amount of the diamides corresponding to the stearic, palmitic and oleic acids in the original commercial stearic acid. The general structural formula of the glyoxalidines is:



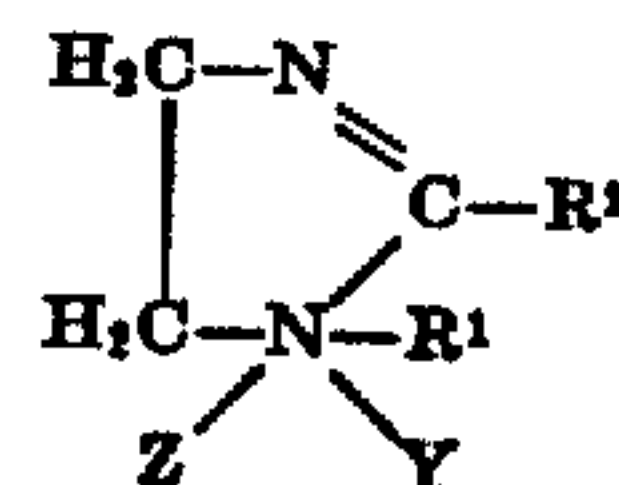
Substituted glyoxalidine

The superscripts indicate the numbers of the positions on the glyoxalidine ring. In the above formula, R^2 must be an organic radical but R^1 may be hydrogen or an organic radical as may also be $R^{4'}$, $R^{4''}$, $R^{5'}$, and $R^{5''}$. Where the acid is stearic acid, $R^{4'}$, $R^{4''}$, $R^{5'}$, and $R^{5''}$ are H, and R^1 is H or aminoethyl or hydroxyethyl, the product is 2-heptadecyl glyoxalidine or 1-aminoethyl-2-heptadecyl glyoxalidine or 1-hydroxyethyl-2-heptadecyl glyoxalidine, respectively. Where the acid is oleic acid, the corresponding heptadecenyl glyoxalidines are formed and where the acid is palmitic acid, the corresponding pentadecyl glyoxalidines are formed. In making the hydrophobic glyoxalidine product with which the present invention is principally concerned, the diamine is unsubstituted ethylene diamine, the acid is commercial stearic acid and the average glyoxalidine product is a mixture of about 55 parts, by weight, of 2-heptadecyl-, 45 parts of 2-pentadecyl- and 5 to 8 parts of 2-heptadecenyl-glyoxalidines, the variations being those previously indicated for the composition of commercial stearic acid.

To form the fungicide concentrate and eliminate any undesirable amounts of diamides, I treat the distillate previously referred to with isopropanol and acetic acid or with those materials previously indicated as satisfactory. The acetic acid should be at least glacial containing not more than 0.5% water and the alcohol should contain not more than 1% water, by weight, so that the concentrate contains no more than 0.4 mol of water per mol of glyoxalidine. Acetic anhydride and anhydrous isopropanol may be used but are generally too expensive. The distillate may be treated with the acid and alcohol in any order but preferably the acid and alcohol are mixed in a vessel equipped with devices for adequate cooling and stirring. The molten glyoxalidine mixture is added at such a rate that the temperature of the solution does not rise above 40° C., else too much hydrolysis or alcoholysis occurs. At least sufficient acid is used to react with all of the glyoxalidines and a slight excess may be added. The diamides do not react with the acid but remain in suspension in the liquid

phase. If desired the diamides may be removed by filtering and the filtrate is a clear solution of the glyoxalidine acetates in the isopropanol.

The formation of the mixed acetates is exothermic. The reaction proceeds smoothly to give a glyoxalidonium (a quaternary ammonium salt) compound of the type



where Z is —H, and Y is —O.CO.CH₃ in the case of acetic acid.

The invention may be illustrated by the following example based upon an isopropanol solution of the acetates of the mixed glyoxalidines from commercial stearic acid containing about 55 parts, by weight, of stearic acid, 45 parts of palmitic acid and 5 to 8 parts of oleic acid, this solution later being mixed with water and lime to form a water-base spray, it being understood that other glyoxalidine salts, solvents and alkalis may be used, as previously explained.

A charge of five mols of commercial stearic acid (1420 grams, the reactant being considered as wholly stearic acid), 30 mols of ethanol (maximum water content 0.2% by weight), 1000 cc. of benzene and 1 cc. of concentrated sulfuric acid as a catalyst (1.73+ grams anhydrous H₂SO₄) was heated in a kettle equipped with a column connecting to a decanting head. The mixture was refluxed at atmospheric pressure, a kettle temperature of 75° C. and a head temperature of 65° C., this being the temperature at which a ternary mixture of water, ethanol and benzene passes the head. The water was removed as the lower layer of the condensate. When water ceased to appear in the condensate, the head temperature rose to 66° C. which is the constant boiling point of a binary of ethanol and benzene. At this point 5 grams of sodium acetate were added to the kettle to neutralize the sulfuric acid. The distillation was continued at atmospheric pressure to remove acetic acid, ethanol and benzene, the kettle temperature finally rising to 98° C. and the head temperature to 78° C., the boiling point of ethanol, sufficient alcohol having been used to allow for the removal of other volatiles and finish with the distillation of only the alcohol. While other alcohols may be used, ethanol is preferred as it forms a relatively low boiling, constant boiling point mixture with water. Also, substantially anhydrous reactants are preferred so that there is a minimum amount of water to be removed.

The ethyl esters of stearic, palmitic and oleic acids thus formed were distilled over a head temperature range of 148° C. to 165° C. at an absolute pressure of 1.5 mm. of mercury. The yield of esters was 95% based on the original acid content.

A charge of 1 mol (312 grams) of the mixed esters obtained as previously described and 5 mols (300 grams) of ethylene diamine was heated in a kettle equipped with a reflux condenser. The mixture was heated with total reflux for 8 hours at a kettle temperature of 125° C. at atmospheric pressure. The excess ethylene diamine was then stripped off, at atmospheric pressure, by distilling to a final kettle temperature of 215° C. The kettle residue was predominantly a mixture of N-(2-aminoethyl) stearamide and the corresponding amides of palmitic and oleic acids.

Minor amounts of the corresponding glyoxalidines and diamides are formed in this step as well as tars, decomposition products and the like. The reactants are preferably substantially anhydrous although they need not be entirely so. The presence of water slows the formation of the monoamides and favors the formation of the undesirable diamides.

The impure mixture of monoamides was then heated under reduced pressure to form and distill the glyoxalidines. From a kettle the vapors passed through a column of the Claissen type, which could be heated, and then to a receiver which was connected to a cold trap, the entire system being maintained under a vacuum. The first vapors which came off were water generated as the rings closed and the glyoxalidines formed from the monoamides. The vacuum remained at about 10 mm. until the majority of the water was removed. As the rate of generation of water decreased, the temperature of the kettle mix rose until it reached 200° C., the temperature at the head of the column was 180° C. and the pressure had lowered to 2 mm. The glyoxalidines then began to distill, the temperature of the kettle finally rising to 275° C. and the head temperature to 210° C. at which point the distillation was stopped. The rise in kettle temperature was due to the formation of diamides and the formation of tars and decomposition products and their concentration. The kettle residue contained the tars and the majority of the diamides. The yield of glyoxalidines was 76% based on the amount of esters originally charged. The yield of diamides was about 12% of which about 2% was found with the glyoxalidine distillate and 10% in the kettle residues.

An isopropanol solution of the glyoxalidine acetates was made in the manner previously stated, incorporating acetic acid in the stoichiometric proportion of 12 parts, by weight, of glacial acetic acid (99.5% acetic acid, 0.5% water) to 54 parts by weight of the glyoxalidines together with 34 parts by weight of isopropanol (99% isopropanol, 1% water, by weight) thereby forming the acetates (melting point 40° C.) in a weakly aqueous isopropanol solution. If desired, anhydrous alcohol or acid or the anhydride may be used and either acid or anhydride may be used in greater than stoichiometric proportion, as previously explained. Any amount of alcohol may be incorporated depending upon the solidification temperature and other characteristics required of the concentrate. A sufficient portion of the acid may be in the form of the anhydride to react with any water present to form the acid and then form the glyoxalidine salt. To maintain low costs, it is contemplated that completely anhydrous alcohols will not be used.

The cooled alcohol solution, prepared as previously described, contained a precipitate, but even if the precipitate represents up to about 5% of the weight of the glyoxalidines it need not be removed for practical purposes. The alcohol solution may, however, be filtered to yield a clear solution of the acetates. Thus the alcohol and acid treatment yields a liquid concentrate which is stable both physically and chemically, easily measured with primitive equipment and from which the orchardist, by the addition of water and lime, may easily and quickly prepare a fungicidal spray having the glyoxalidines freshly precipitated in colloidal, non-agglomerating and potent condition.

The concentrate previously described prepared

by incorporating 34 parts, by weight, of isopropanol with 12 parts of glacial acetic acid and 54 parts of the mixed glyoxalidines, is preferred over other compositions both with respect to materials and their quantities. Such a solution solidifies at 6° C., contains, per 100 parts by weight, 66 parts of the acetates, 0.4 part of water, 33.6 parts of anhydrous isopropanol, no free acetic acid, and has a pH of 7.3. A quart of the solution (1.8 pounds) added to 100 gallons (834 pounds) of water with sufficient lime to precipitate the glyoxalidines yields a satisfactory spray containing a pound of colloiddally suspended glyoxalidines. No hydrolysis or alcoholysis or other deterioration of the glyoxalidines or the acetates greater than 1% by weight of the glyoxalidines or salts could be detected in such a concentrate after a storage period of 70 days at 25° C.

To prepare a water-base spray, a quart of the acetate solution is mixed in 100 gallons of water and from 1.45 ounces to 4 pounds of lime (calculated as CaO) are beaten into the water containing the acetates. The lower amount of lime is necessary to neutralize the combined acetic acid in the concentrate and all lime above this amount is excess but from 1 to 4 or more pounds of lime are preferred per pound of free glyoxalidines for the phytotoxic safening action, particularly where arsenates or other phytotoxic addends are incorporated. Upon mixing the lime into the water and the concentrate, the free glyoxalidines are obtained as a substantially colloidal suspension. The reaction of the lime with the acetates goes substantially to completion. The pH of the spray was 11.55 where only enough lime was used to neutralize the acid and was 12.1 where the spray contained free lime in suspension. For the control of apple scab, slurries containing from ½ pint to 1½ quarts of the preferred concentrate wherein the glyoxalidine salts are somewhat but not more than 10% hydrolyzed or alcoholized (¼ pound to 1½ pounds of mixed free glyoxalidines or slightly less depending upon the amount of hydrolysis or alcoholysis) and for the control of cherry leaf spot, slurries containing from ¼ pint to 1½ pints of the concentrate, per 100 gallons of water, have proven satisfactory. Such slurries containing no more lime than is necessary to neutralize the acid, are not too phytotoxic for use on apples and cherries even though about 10% of the glyoxalidine weight is 2-heptadecenyl glyoxalidine and up to 55% of the remaining glyoxalidine is 2-pentadecyl glyoxalidine. The amount of 2-heptadecyl glyoxalidine appears to be sufficient and the minimum amount necessary to overcome such phytotoxicity due to the pentadecyl and heptadecenyl glyoxalidines as may be serious on these plants in the absence of safening agents when using the maximum concentration of active ingredient given above.

In tests against late blight on tomatoes, water-base spray compositions containing 0.2% by weight of the mixed glyoxalidines, prepared from the previously-mentioned typical commercial stearic acid, were used. In composition A the spray was prepared by mixing sufficient powdered mixed glyoxalidines into water to give the 0.2% by weight. In composition B the spray was prepared by mixing lime, water, and the amount of mixed glyoxalidine-acetates, in isopropanol, necessary to give 0.2% of mixed glyoxalidines in the composition. Composition B contained 20%, by weight, of lime over that which was necessary to neutralize free and combined acid.

In both sprays the proportions of one glyox-

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alidine to another were the same. Each type of spray was applied to several different tomato plants so that no plant had more than one type of spray applied to it. The sprayed plants and untreated plants were then inoculated with the blight. The results were:

	Percent Disease Following 0.2% Spray, Late Blight Test	
	#1	#2
Composition A.....	4	11
Composition B.....	0	0

Untreated check plants showed from 300 to 400 lesions per check or control plant. The figures represent the percent of disease lesions on the sprayed plants considering the number of disease lesions on untreated or control plants as 100%. The method of testing is more completely explained in a paper by McCallan and Wellman, Contributions from Boyce Thompson Institute, vol. 13, pages 93-134, 1943. The tests show good control of late blight by sprays made from the powdered glyoxalidines from the typical commercial stearic acid but perfect control by sprays in which the glyoxalidines from the same commercial acid are freshly precipitated from a concentrate of their salts prepared in accordance with the present invention.

A fungicidal spray prepared from the glyoxalidines of commercial stearic acid is highly advantageous for practical field use not only because of its potency and low cost but because all of the glyoxalidines are hydrophobic and therefore do not readily dissolve in rain or dew and wash off of the plant in solution. It must be recognized that there is some loss of glyoxalidines due to physical wash-off, wind and the like and that there is also a loss of glyoxalidines by hydrolysis due to rain, dew and the like. But in the case where the glyoxalidine salt concentrate is properly prepared, for instance in the manner described, from commercial stearic acid and from substantially anhydrous low cost materials, and although the glyoxalidines are usually slightly hydrolyzed or alcoholized, they can be kept for several months with not more than 10% deterioration and the concentrate yields a spray composition having hydrophobic glyoxalidines in a colloidal, non-agglomerating and most potent form which is maintained for effective field use at least as long as the glyoxalidines physically remain in situ on the plant. Also, the orchardist is given a highly concentrated base which is easily and freely measurable under any condition of temperature that he might encounter during the spraying season and from which he may easily prepare a water-base spray.

What is claimed is:

1. A concentrate adapted to be made into a spray for combatting plant pests by the addition of water and an alkaline material, comprising a mixture of glyoxalidine salts of aliphatic, monocarboxylic acids having from 2 to 8 carbon atoms, in solution in an alcohol, the salts being principally those of 2-heptadecyl glyoxalidine and 2-pentadecyl glyoxalidine substantially in the proportion of from 5% to 55% of 2-pentadecyl glyoxalidine salt and from 95% to 45% of 2-heptadecyl glyoxalidine salt, the alcohol being a monohydric, acyclic saturated alcohol having from 1 to 4 carbon atoms inclusive.

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2. A concentrate adapted to be made into a spray for combatting plant pests by the addition of water and an alkaline material, comprising a mixture of glyoxalidine salts of aliphatic, monocarboxylic acids having from 2 to 8 carbon atoms, in solution in an alcohol, the salts being principally those of and substantially in the proportion of from 4% to 55% of 2-pentadecyl glyoxalidine salt, from 95% to 38% of 2-heptadecyl glyoxalidine salt and from a trace to 15% of 2-heptadecenyl glyoxalidine salt, the alcohol being a monohydric, acyclic saturated alcohol having from 1 to 4 carbon atoms inclusive.

3. A concentrate adapted to be made into a spray for combatting plant pests by the addition of water and an alkaline material, comprising a mixture of a glyoxalidine salt of an aliphatic, monocarboxylic acid and a member of the group consisting of alcoholysis and hydrolysis products thereof, in solution in an alcohol, there being a larger proportion of the salt than of a member of said group, the organic acid having from 2 to 8 carbon atoms, the alcohol being a monohydric, acyclic saturated alcohol having from 1 to 4 carbon atoms inclusive.

4. A concentrate adapted to be made into a spray for combatting plant pests by the addition of water and an alkaline material, comprising a mixture of a glyoxalidine salt of an aliphatic, monocarboxylic acid and an hydrolysis product thereof, in solution in an alcohol, there being a larger proportion of the salt than of the hydrolysis product, the organic acid having from 2 to 8 carbon atoms, the alcohol being a monohydric, acyclic saturated alcohol having from 1 to 4 carbon atoms inclusive.

5. A concentrate adapted to be made into a spray for combatting plant pests by the addition of water and an alkaline material, comprising a mixture of glyoxalidine salts of aliphatic, monocarboxylic acids having from 2 to 8 carbon atoms and a member of the group consisting of alcoholysis and hydrolysis products of said salts, in solution in an alcohol, the salts and said products being principally those of 2-heptadecyl glyoxalidine and 2-pentadecyl glyoxalidine, there being a larger proportion of the salts than of said products, the alcohol being a monohydric, acyclic saturated alcohol having from 1 to 4 carbon atoms, inclusive.

6. A composition for combatting plant pests comprising water, a mixture of a glyoxalidine, a salt of the group consisting of the barium, calcium and magnesium salts of aliphatic, monocarboxylic acids containing from 2 to 8 carbon atoms, and a monohydric, acyclic saturated alcohol having from 1 to 4 carbon atoms, inclusive; the glyoxalidine being a member of the group consisting of 2-heptadecyl glyoxalidine and 2-pentadecyl glyoxalidine.

7. A composition for combatting plant pests comprising water, a mixture of glyoxalidines, a salt of the group consisting of the barium, calcium and magnesium salts of aliphatic, monocarboxylic acids containing from 2 to 8 carbon atoms, and a monohydric, acyclic saturated alcohol having from 1 to 4 carbon atoms, inclusive; the glyoxalidines being principally 2-heptadecyl glyoxalidine and 2-pentadecyl glyoxalidine, not more than about 55% of the weight of the glyoxalidines being 2-pentadecyl glyoxalidine.

8. A composition for combatting plant pests comprising water, a mixture of glyoxalidines, a salt of the group consisting of the barium, calcium and magnesium salts of aliphatic, mono-

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carboxylic acids containing from 2 to 8 carbon atoms, and a monohydric, acyclic saturated alcohol having from 1 to 4 carbon atoms, inclusive; the glyoxalidines being principally and in the proportion of from 4% to 55% of 2-pentadecyl glyoxalidine, from 95% to 38% of 2-heptadecyl glyoxalidine and from a trace to 15% of 2-heptadecenyl glyoxalidine.

9. Method of preparing a composition for combatting plant pests which comprises reacting ethanol with commercial stearic acid containing from about 4% to 55% by weight of palmitic acid, from about 38% to 95% of stearic acid and from about zero to 15% of oleic acid, and obtaining a mixture of the corresponding esters; reacting the mixture of esters with ethylene diamine to obtain a mixture of the corresponding N-(2-aminoethyl) amides; subjecting the mixture of amides to distillation at a temperature between about 180° C. and 210° C. at an absolute pressure of about 2 mm. of mercury to form and deliver to a receiver 2-pentadecyl glyoxalidine, 2-heptadecyl glyoxalidine and 2-heptadecenyl glyoxalidine in the proportions of about 4% to 55% of 2-pentadecyl glyoxalidine, 95% to 38% of 2-heptadecyl glyoxalidine, and zero to 15% of 2-heptadecenyl glyoxalidine; reacting the mixture of glyoxalidines thus obtained with an aliphatic, monocarboxylic acid containing from 2 to 8 carbon atoms to form the corresponding mixture of glyoxalidine salts, and dissolving the salts in a monohydric, acyclic, saturated alcohol having from 1 to 4, inclusive, carbon atoms for purposes of stabilization during storage; and immediately prior to use mixing the alcohol solution thus obtained with water containing at least sufficient of a member of the group consisting of barium, calcium and magnesium oxides and carbonates to react with the combined and any

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free acid of the alcohol solution to precipitate in the water glyoxalidines corresponding to the salts in the alcohol solution.

10. Method of producing a spray for combatting plant pests which comprises mixing with water a member of the group consisting of barium, calcium and magnesium oxides and their carbonates, and a concentrate comprising a mixture of glyoxalidine salts of aliphatic, monocarboxylic acids having from 2 to 8 carbon atoms in solution in an alcohol; the salts being principally those of 2-heptadecyl glyoxalidine and 2-pentadecyl glyoxalidine substantially in the proportion of from 5% to 55% of those from 2-pentadecyl glyoxalidine and from 95% to 45% of those from 2-heptadecyl glyoxalidine, the alcohol being a monohydric, acyclic saturated alcohol having from 1 to 4 carbon atoms, there being at least a sufficient quantity of a member of said group to react with the combined and any free acid of the concentrate.

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