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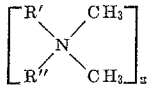
MICROBIOLOGICALLY ACTIVE QUATERNARY AMMONIUM COMPOUNDS

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The present invention has for its object the preparation of relatively water-insoluble, microbiologically active compounds by reaction of certain quaternary ammonium hydroxides or their water-soluble salts with nitro derivatives of aromatic carboxylic acids or their water-soluble salts.

The quaternary ammonium compounds used in the process of this invention are all bacteriologically active, having a phenol coefficient of at least 100 with respect to both *Staphylococcus aureus* and *Salmonella typhosa* at 20° C., when determined by the standard method given in the United States Department of Agriculture Circular No. 198. They contain at least one carbon chain having from 8 to 22 carbon atoms and also possess at least one benzyl radical attached to the quaternary nitrogen atom. The benzyl radical may, if desired, be substituted by alkyl groups or halogen atoms. The quaternary ammonium compounds, moreover, possess only non-heterocyclic nitrogen atoms. In general, the quaternary ammonium compounds used in the present invention comply with the formula:



where R′ is an alkyl radical containing from 8 to 22 carbon atoms, an alkyl benzyl radical in which the benzyl group may contain a substituent methyl radical and in which the alkyl group contains 8 to 22 carbon atoms, or an alkyl phenoxy ethoxy ethyl radical in which the phenyl group may contain a substituent methyl radical and R″ is a benzyl or substituted benzyl radical, or a methyl group if R′ is an alkyl benzyl radical containing eight or more carbon atoms in its alkyl substituent. X in the above formula is chlorine, bromine, iodine, sulfate, methosulfate, ethosulfate and the like.

Typical examples of these quaternary ammonium compounds are alkyl dimethyl benzyl ammonium chloride in which the alkyl group may have from 8 to 22 carbon atoms, alkyl dimethyl substituted benzyl ammonium chlorides, in which the alkyl radical contains from 8 to 22 carbon atoms and in which the benzyl radical is substituted with one or more side chains containing from 1 to 5 carbon atoms such, for example, as methyl, dimethyl, trimethyl, tetramethyl, ethyl, diethyl, isopropyl, tertiary butyl and isoamyl or with one, two or more halogen atoms such as chlorine and bromine, alkyl dimethyl menaphthyl ammonium chloride and alkyl dimethyl tetrahydromenaphthyl ammonium chloride in which the alkyl radical contains from 8 to 22 carbon atoms, alkyl benzyl trimethyl ammonium chloride in which the alkyl radical contains from 8 to 22 carbon atoms and in which the aromatic nucleus of the benzyl radical may, if desired, be substituted by one or more methyl or other lower alkyl groups, alkyl phenoxy ethoxy ethyl dimethyl benzyl ammonium chloride in which the alkyl radical may be isooctyl or nonyl, and mixtures of the aforesaid quaternary ammonium compounds.

The aromatic nitro monocarboxylic acids which are used in the present invention correspond to the general formula $RZCO_2H$, where R is a mono- or poly-nitro substituted benzene or naphthalene nucleus or the nitro substituted nucleus of diphenyl or diphenyl oxide and Z is $(CH_2)_n$ or $(CH_2)_n$—2H, where n is any number from zero to four.

Typical examples of the nitro aromatic carboxylic acids which may be used in the practice of this invention include o-, m- and p-nitro benzoic acids, 3, 4, 5 and 6 nitro salicyclic acids, the various isomers of nitro phenyl acetic and nitro phenyl butyric acids, nitro cinnamic and nitro hydrocinnamic acids, the isomeric forms of mono and poly nitro diphenyl carboxylic acid and of the various nitro alpha and beta naphthoic acids, the dinitro and trinitro benzoic acids, the mono-, di- and tri-nitro toluic acids and the like.

The compounds of this invention may be prepared by mixing an aqueous solution of the quaternary ammonium salt or hydroxide of the kind defined above with an aqueous solution of the acid in question or with any of its water-soluble salts.

After thorough mixing, the organic product layer is separated from the aqueous layer (as with a separatory funnel) since two distinct phases are formed. Separation may be facilitated by the addition of an organic solvent immiscible with water. The product layer may be washed with water to remove any residual by-product salt or unreacted materials. The solvent, if any, may be evaporated and the product air or vacuum dried to a paste, wax, oil or solid.

It is not necessary to use an aqueous medium. Any solvent or solvent mixture in which the starting materials are soluble will be satisfactory. Non-aqueous solvents facilitate the separation of by-product inorganic salt and reduce the need for vacuum drying to get an anhydrous product. When a non-aqueous medium is employed, it is usually necessary to add a small amount of water to facilitate ionic reaction.

The product may be used, if desired, without drying since any entrapped water is irrelevant to the microbiological activity of the compounds. In other applications, removal of water may be essential for reasons not related to biological activity.

An alternative method for the preparation of compounds especially applicable to the treatment of fabric, ropes, net, woven and non-woven fabric and reticulated or convoluted materials involves a two-step process. In the first step, the material is passed through a bath containing the anionic moiety. Excess solution is removed by methods well known to those skilled in the art. The treated material is then passed through a second bath wherein the concentration of quaternary ammonium compound is such that the material pickup will result in an equivalent amount of quaternary ammonium compound reacting with the anionic moiety, depositing the product in the most intimate way on the surface and in the interstices, convolutions and reticulations of the material.

The method of adjustment of solution concentration to achieve the required pickup is well known to those skilled in the art. The order of treatment may be reversed without affecting the biological activity or durability of the product on the material. The products of this invention may be formulated as water dispersions by dissolving them in a water-miscible organic solvent such as acetone or methanol and diluting with water or by dissolving them in emulsifiable oils such, for example, as sulfonated castor oil or pine oil and diluting with water. In preparing aqueous dispersions, emulsifying agents such, for example, as ethylene oxide condensates of alkyl phenols may be used with or without organic solvents.

It is surprising that the compounds of this invention exhibit high microbiological activity despite their relative insolubility in water. Because of their unusual combination of physical and microbiological properties, they can be used to impart laundry-resistant anti-microbial char-

acteristics to textiles. They can also be used as the active agent in antimildew finishes for textiles which are resistant to leaching with water.

Although the compounds have low water solubility, they are compatible with various organic solvents, plasticizers and high molecular weight compounds. Consequently, they may be incorporated as anti-microbial agents in synthetic resins and plastics. The compounds are compatible with natural and synthetic rubber latices. Therefore, they may be used to prepare bacteriostatic films and molded objects deposited from such latices.

The compounds can be incorporated into cutting and grinding fluids without precipitation. Also, they blend well with non-ionic and anionic surface active agents. In such compositions they retain their microbiological activity.

It will be understood that the properties of the products described herein will vary depending upon the nature of the quaternary ammonium compound used in their preparation as well as the aromatic carboxylic acid or salt reacted therewith.

The chemical, physical and biological properties of the products of our invention make then especially appropriate for the following applications when suitably incorporated in active amounts in an appropriate vehicle, binder, medium or substrate:

(1) Mildewproofing fabric, canvas, ropes, textiles, awnings, sails, tenting and other woven and non-woven reticulated materials.

(2) Paint mildewstats.

(3) Jet plane fuel additive to control growth of microorganisms.

(4) Odor preservative agents for clothes and shoes.

(5) Mildew reardant and odor suppressant for shoes and other leather products.

(6) Topical antiseptics.

(7) Antidandruff agents.

(8) Disinfection agents for hair and gut of man and beast.

(9) Bacteriostatic furniture dressing.

(10) Surface finishes for stone, plaster, tile, cement, brick and other inorganic building materials, to retard growth of mircroorganisms, fungi, mold and algae.

(11) Wool preservative.

(12) Plant and tree spray to combat fungi.

(13) Antimycotic agents for soap wrappers.

(14) Self-sanitizing brushes.

(15) Mildewproofing agent in and on plastic and film.

(16) Mildewproofing of cellulosics, cardboard, fibreboard, paper and cordage.

(17) Contact biostat for application to film, waxes and cloth to preserve cheese, meats and vegetables and other food products.

(18) Algal inhibition, especially on surfaces and in solution where low foaming is desirable.

(19) Paper pulp slime control.

(20) Sanitizing agent for rug, carpet, curtains.

(21) Egg preservation.

(22) Adhesive preservation.

(23) Preservation of latex paints.

(24) Preservation of metal-working compounds.

(25) Additives for soap and for both anionic and nonionic detergents in liquid, bar, powder, bead, solution and other forms to impart bacteriostatic and fungistatic properties thereto.

The microbiological activity of our compounds has been evaluated for microbiological stasis by the Standard Tube Dilution Test, the technique for which is common knowledge to those skilled in the art. A Difco Bacto CSMA Broth #0826 was used in the study. This test is used to determine the lowest concentration of microbiologically active compounds which will inhibit the growth of the organism in question. For a wide range of applications, the inhibition of growth rather than outright kill is satisfactory.

Briefly put, the Tube Dilution Test consists in placing 9 cc. of the CSMA Broth in a test tube which is then sterilzed in an autoclave. One cc. solution of the microbiologically active compund at an appropriate concentration is added to the test tube which is then inoculated with 0.1 cc. of a twenty-four hour old culture of the organism under study. The test tube is then incubated at 37° C. for forty-eight hours and observed for bacterial growth.

The same procedure is followed for fungi. In such tests, however, the tubes are incubated for fourteen days at a temperature suitable for optimum fungal growth, usually 25° C.

The invention is illustrated by, but not restricted to, the following examples:

EXAMPLE I

A stock solution was prepared containing 10% of the sodium salt of p-nitro phenyl acetic acid. To a vigorously agitated aliquot of this containing 0.0294 equivalent weights of the compound was added the chemically equivalent amount of an 11% solution of a commercial grade of alkyl dimethyl ethyl-benzyl ammonium chloride (Onyx Chemical Corporation's "BTC–471" in which the alkyl distribution is 50% C_{12}, 30% C_{14}, 17% C_{16}, 3% C_{18}). The agitated mixture was transferred to a separatory funnel and separated into two phases. The organic product layer was removed and vacuum dried to yield a brown paste in 89% of the theoretical yield of alkyl dimethyl ethyl-benzyl ammonium p-nitro phenyl acetate.

EXAMPLE II

A stock solution was prepared containing 10% of the sodium salt of 3-nitro-4-chlorobenzoic acid. To an aliquot of this solution containing 0.027 equivalent weights of the compound was added a chemically equivalent amount of an 11% solution of the alkyl dimethyl ethyl-benzyl ammonium chloride of Example I, with vigorous agitation. The agitated mixture was poured into a separatory funnel and separated into two phases. The organic product layer was removed and vacuum dried to yield an orange-colored paste in theoretical yield of alkyl dimethyl ethyl-benzyl ammonium 3-nitro-4-chlorobenzoate.

EXAMPLE III

Sixty ml. of the solution of the sodium salt of 3-nitro-4-chlorobenzoic acid of Example II was treated in the same manner with a chemically equivalent amount of an 11% solution of a commercial grade of alkyl dimethyl benzyl ammonium chloride (Onyx Chemical Corporation's "BTC–824" in which the alkyl distribution is 60% C_{14}, 30% C_{16}, 5% C_{12}, 5% C_{18}). The organic product layer was vacuum dried to yield 15 g. of an orange-colored paste of alkyl dimethyl benzyl ammonium 3-nitro-4-chlorobenzoate, in theoretical yield.

EXAMPLE IV

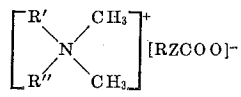
The products of Examples I through III were tested by the Standard Tube Dilution Test described above against *Staphylococcus aureus* (*S.a.*), *Salmonella typhosa* (*S.t.*) and *Aspergillus niger* (*A.n.*). Results are shown in Table I.

TABLE I

Product	Reciprocal of Static Dilution of Product vs.—		
	S.a.	*S.t.*	*A.n.*
Alkyl Dimethyl Ethyl-Benzyl Ammonium 3-Nitro-4-Chlorobenzoate	10^5	10^5	10^4
Alkyl Dimethyl Benzyl Ammonium 3-Nitro-4-Chlorobenzoate	10^5	10^5	10^5
Alkyl Dimethyl Ethyl-Benzyl Ammonium p-Nitro Phenyl Acetate	10^5	10^6	10^4

We claim:

1. A compound having the structure:



wherein R′ is a member of the group consisting of alkyl containing 8 to 22 carbon atoms, alkyl benzyl wherein the alkyl contains 8 to 22 carbon atoms, alkyl methyl-substituted benzyl wherein the alkyl contains 8 to 22 carbon atoms, alkyl phenoxy ethoxy ethyl wherein the alkyl is isooctyl or nonyl, and alkyl phenoxy ethoxy ethyl wherein the alkyl is isooctyl or nonyl and in which the phenyl has a substituent methyl, wherein R″ is a member of the group consisting of benzyl, lower alkyl-substituted benzyl and methyl, R″ being methyl when R′ is alkyl benzyl, wherein R is a member of the group consisting of nitro-substituted benzene, nitro-substituted naphthalene, nitro-substituted diphenyl and nitro-substituted diphenyl oxide, and wherein Z is a member of the group consisting of $(CH_2)_n$ and $(CH_2)_n$—2H where n is 0 to 4.

2. The compound of claim 1, wherein the nitro-substituted aromatic carboxylic anion is derived from the group consisting of o-, m- and p-nitro benzoic acids, 3, 4, 5 and 6 nitro-salicylic acids, nitro phenyl acetic acids, nitro phenyl butyric acids, nitro cinnamic acids, nitro

hydrocinnamic acids, mono- and poly-nitro diphenyl carboxylic acids, nitro alpha and nitro beta naphthoic acids, dinitro and trinitro benzoic acids, and mono-, di- and trinitro toluic acids.

3. Alkyl dimethyl ethyl-benzyl ammonium p - nitro phenyl acetate wherein the alkyl contains 12 to 18 carbon atoms.

4. Alkyl dimethyl ethyl-benzyl ammonium 3 - nitro-4-chloro-benzoate wherein the alkyl contains 12 to 18 carbon atoms.

5. Alkyl dimethyl benzyl ammonium 3-nitro-4-chloro-benzoate wherein the alkyl contains 12 to 18 carbon atoms.

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