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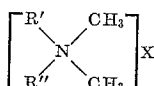
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MICROBIOLOGICALLY ACTIVE QUATERNARY AMMONIUM COMPOUNDS

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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 amino-substituted 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. 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 iso-

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octyl or nonyl, and mixtures of the aforesaid quaternary ammonium compounds.

The aromatic amino-substituted monocarboxylic acids which are used in the present invention correspond to the general formula RZCOOH, where R is an amino-substituted benzene or naphthalene nucleus or the amino-substituted nucleus of diphenyl or diphenyl oxide and Z is (CH₂)_n or (CH₂)_n—2H, where n may be any number from zero to four.

Typical examples of the aromatic amino acids which may be used in the practice of this invention include o-, m- and p-amino benzoic acid, 3-, 4- and 5-amino salicylic acid, the various amino alpha and beta naphthoic acids, the amino phenyl acetic acids, -phenyl propionic acids, -phenyl butyric acids, o-, m- and p-amino cinnamic acid 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 ex-

ample, 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 characteristics 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 them 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 retardant 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 microorganisms, 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 cellulose, cardboard, fibre-board, 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 non-ionic 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 sterilized in an autoclave. One cc. solution of the microbiologically active compound 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 weight percent of the sodium salt of m-amino benzoic acid. To a vigorously agitated aliquot of this solution containing 0.126 equivalent weights of the compound was added the chemically equivalent amount of a 10% 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% C₁₂, 30% C₁₄, 17% C₁₆, 3% C₁₈). 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 a brown paste of alkyl dimethyl ethyl-benzyl ammonium m-amino benzoate in 94% theoretical yield. Similar products were prepared by replacing the m-amino benzoic acid with p-amino benzoic acid and o-amino benzoic acid.

Example II

A stock solution was prepared containing 10 weight percent of the sodium salt of p-amino salicylic acid. To a vigorously agitated aliquot of this solution containing 0.114 equivalent weights of the compound was added the chemically equivalent weight of a 10% solution of a commercial grade of alkyl dimethyl benzyl ammonium chloride (Onyx Chemical Corporation's "BTC-824" in which the alkyl distribution is 60% C₁₄, 30% C₁₆, 5% C₁₂, 5% C₁₈). The agitated mixture was transferred to a separatory funnel and separated into two phases. The organic layer was removed and dried in a vacuum oven to yield an orange-colored paste of alkyl dimethyl benzyl ammonium p-amino salicylate in 99% yield.

Example III

Two hundred ml. of the stock solution of sodium p-amino salicylate of Example II containing 0.114 equivalent weights of the compound was reacted by adding, with vigorous agitation, a chemically equivalent weight of the solution of alkyl dimethyl ethyl-benzyl ammonium chloride used in Example I. The reaction mixture was transferred to a separatory funnel and separated into two phases. The organic product layer was removed and dried in a vacuum oven to yield a yellow paste of alkyl dimethyl ethyl-benzyl ammonium p-amino salicylate in 97% of the theoretical yield.

Example IV

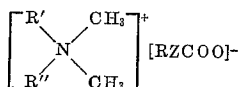
The results of static dilution tests performed on products of Examples I to III are shown in the following table in which *S.a.* signifies *Staphylococcus aureus*, *S.t.*, *Salmonella typhosa* and *A.n.*, *Aspergillus niger*.

BACTERIOSTATIC ACTIVITY OF VARIOUS QUATERNARY AMMONIUM
SALTS OF AMINO-SUBSTITUTED AROMATIC MONOCARBOXYLIC
ACIDS

Quaternary	Acid	Reciprocal of Static Dilution Level of Product vs.—		
		S.a.	S.t.	A.n.
Alkyl Dimethyl Ethyl-Benzyl Ammonium Chloride.	o-Amino Benzoic....	>10 ⁸	10 ⁵	10 ³
	p-Amino Benzoic....	1	10 ⁵	10 ⁴
	m-Amino Benzoic....	10 ⁶	10 ⁵	10 ³
	p-Amino Salicylic....	10 ⁶	10 ⁵	10 ³
Alkyl Dimethyl Benzyl Ammonium Chloride.	p-Amino Salicylic....	10 ⁷	10 ⁵	10 ⁴

We claim:

1. A compound having the structure:



wherein R is a member of the group consisting of amino-substituted benzene, amino-substituted naphthalene, amino-substituted diphenyl and amino-substituted diphenyl oxide, Z is a member of the group consisting of (CH₂)_n and (CH₂)_n-2H wherein n is a number from 0 to 4, R' is a member of the group consisting of alkyl, alkyl benzyl, alkyl methyl-benzyl, wherein the alkyl in each case 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 having a methyl substituent on the phenyl group, and R'' is a member of the group consisting of benzyl and lower alkyl-substituted benzyl, and methyl if R' is alkyl benzyl.

2. The compound of claim 1 wherein the anionic moiety is the residue of an aromatic amino acid selected from the group consisting of o-, m- and p-amino benzoic acids, 3-, 4- and 5-amino salicylic acids, amino alpha and beta naphthoic acids, amino phenyl acetic acids, amino phenyl propionic acids, amino phenyl butyric acids, and o-, m-, and p-amino cinnamic acids.

3. Alkyl dimethyl ethyl-benzyl ammonium m-amino

benzoate, wherein the alkyl contains 12 to 18 carbon atoms.

4. Alkyl dimethyl ethyl-benzyl ammonium p-amino benzoate, wherein the alkyl contains 12 to 18 carbon atoms.

5. Alkyl dimethyl ethyl-benzyl ammonium o-amino benzoate, wherein the alkyl contains 12 to 18 carbon atoms.

6. Alkyl dimethyl benzyl ammonium p-amino salicylate, wherein the alkyl contains 12 to 18 carbon atoms.

7. Alkyl dimethyl ethyl-benzyl ammonium p-amino salicylate, wherein the alkyl contains 12 to 18 carbon atoms.

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