OLIGOMERIC QUATERNARY AMMONIUM ANTIMICROBIAL AGENTS

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Field of Search ..............260/567.6 R, 567.6 P

ABSTRACT
Quaternary ammonium compounds of the general formula

\[
\begin{align*}
\text{R} & \quad \text{CH} \quad \text{N} \quad \text{CH} \quad \text{R'} \\
& \quad \text{CH} \quad \text{OCH} \quad \text{CH} \quad \text{OCH(OH)} \\
& \quad \text{CH} \quad \text{OH} \\
\end{align*}
\]

wherein R and R' are the same and are selected from the group consisting of \( \text{R''OCH}_2\text{CH(OH)} \) and \( \text{R''CH(OH)} \) wherein R'' is an n-alkyl group of from about four to about 20 carbon atoms, X is a halide ion, and y has a value of from about 2 to about 4 possess significantly greater antibacterial activity than the corresponding monomers, i.e., when y has a value of 1 and there is no R' group.

3 Claims, No Drawings
OLIGOMERIC QUATERNARY AMMONIUM ANTIBACTERIAL AGENTS

BACKGROUND OF THE INVENTION

This invention relates to improved antibacterial compositions. More particularly, it relates to the discovery that certain polymeric quaternary ammonium compounds possess antibacterial activity significantly greater than that possessed by the corresponding monomers.

THE PRIOR ART

Antibacterial quaternary ammonium halides are known to the art. See, for example, Rohm & Haas British Patents Nos. 812,140, granted on Apr. 22, 1959; 815,745, granted on July 1, 1959; and 834,410, granted on May 11, 1960. The latter patent has a U.S. counterpart, U.S. Pat. No. 2,810,713, granted to Melamed on Oct. 22, 1957. Additional patents include British Pat. No. 1,120,523, granted on July 17, 1968, and U.S. Pat. No. 3,428,680, granted on Feb. 18, 1969 to Walker et al. Although the above references disclose certain polymeric quaternary ammonium compounds as antibacterials, the specific antibacterial compounds of the present invention are not disclosed nor suggested.

It is, therefore, an object of this invention to provide polymeric quaternary ammonium compounds which possess a high degree of antibacterial activity.

This and other objects will become apparent as the invention is hereafter described in more detail.

SUMMARY OF THE INVENTION

These objects are achieved by the present invention with is directed towards polymeric 2-hydroxyalkyl quaternary ammonium halides with greatly improved antibacterial properties. More specifically, it has been found that polymeric compounds having the formula

\[
\text{CH}_3 + \text{R} - \text{CH} - \text{N} - \text{CH}_2 - \text{H} \text{R}
\]

wherein R and R' are the same and are selected from the group consisting of \(\text{CH}_2\text{OCH}_2\text{CH(OH)-}\) and \(\text{CH(OH)-}\) wherein R' is an n-alkyl group of from about four to about 20 carbon atoms, X is a halide ion selected from the group consisting of bromine, chlorine, iodine and fluoride, and Y has a value of from about 2 to about 4, possess greater antibacterial activity than the corresponding monomers, i.e., when Y has a value of 1, and R' is not present.

The process by which the novel compositions of the present invention are made is no part of the present invention, as they can be made by methods known in the art. For purposes of the present invention, it is preferable to begin with an N-methylated polyamine of the general formula \(\text{H}[(\text{CH}_3)_2\text{CH} \text{CH}_2\text{NH}]\). The amine is reacted with an epoxide selected from the group consisting of 1,2-epoxy-3-alkoxy-propanes and 1,2-epoxyalkanes in the presence of a solvent. A benzyl halide is subsequently added, and the reaction is continued until completion.

The reaction is carried out using specific mole ratios. The number of moles of epoxide used is twice the number of moles of amine. The number of moles of benzyl halide used is the number of moles of amine multiplied by the number of nitrogen atoms in the amine.

Examples of preferred amines that can be used to produce the compositions within the scope of the present invention include: N,N',N'-dimethylethlenediamine; N,N',N'-trimethylethlenetetramine; N,N',N',N'-tetramethylethlenetetramine.

Examples of preferred epoxides that can be used to produce the novel compositions of the present invention include: 1,2-epoxyhexane; 1,2-epoxyheptane; 1,2-epoxyoctane; 1,2-epoxydecane; 1,2-epoxytetradecane; 1,2-epoxyhexadecane; 1,2-epoxyoctadecane; 1,2-epoxyeicosane; 1,2-epoxy-3-hexyloxypropane; 1,2-epoxy-3-heptyloxypropane; 1,2-epoxy-3-octyloxypropane; 1,2-epoxy-3-nonyloxypropane; 1,2-epoxy-3-decyloxypropane; 1,2-epoxy-3-dodecyloxypropane; 1,2-epoxy-3-tetradecyloxypropane; 1,2-epoxy-3-hexadecyloxypropane; 1,2-epoxyoctadecyloxypropane.

Most preferred are 1,2-epoxy-3-octyloxypropane and 1,2-epoxydecane.

Examples of suitable solvents for the purposes of the present invention include methanol, ethanol, isopropanol, butanol, or any other suitable polar solvent.

Examples of suitable benzyl halides are benzyl bromide, benzyl chloride, benzyl fluoride and benzyl iodide. Benzyl bromide is most preferred.

PREFERRED EMBODIMENTS

The following examples sets forth and illustrate in more detail the nature and objects of the present invention but are not limiting thereof.

EXAMPLE I

Preparation of the diquaternary analog of 2-hydroxy-3-octyloxypropyl dimethylbenzlammonium bromide.

2.37 grams (0.0269 moles) of N,N'-dimethylethlenediamine (Aldrich Chemical Co., Inc.) and 10 grams (0.0538 moles) of 1,2-epoxy-3-octyloxypropane (Chemical Procurement Labs Inc.) were dissolved in 50 ml of ethanol and heated at reflux temperature for 16 hours. 9 grams (0.0538 moles) of benzyl bromide were subsequently added and the refluxing was continued for an additional 24 hours. The mixture was then cooled to about room temperature and the ethanol subsequently evaporated off to yield a light-colored, hygroscopic crystalline solid. The residue was subsequently washed with ether and dried. The result was the diquaternary analog of 2-hydroxy-3-octyloxypropyl dimethylbenzlammonium bromide which is effective as an antibacterial agent, and which possesses significantly greater effectiveness than the corresponding monomer.

EXAMPLE II

Preparation of the triquaternary analog of 2-hydroxy-3-octyloxypropyl dimethylbenzlammonium bromide.

Utilizing substantially the same procedures as in Example I, 1.0 g (0.00689 moles) of N,N',N'-trimethyl-diylenetetramine, 2.56 g (0.01378 moles) of 1,2-
3,719,711

3,719,711 epoxy-3-octyloxypropane, were reacted in 25 ml of ethanol. 3.53 g (0.02067 moles) of benzyl bromide were subsequently added as in Example I. The resulting composition was the triquaternary analog of 2-hydroxy-3-octyloxypropyl dimethylbenzylammonium bromide, said compound being an effective antibacterial agent and having significantly greater effectiveness than the corresponding monomer.

EXAMPLE III

Preparation of the tetraquaternary analog of 2-hydroxy-3-octyloxypropyl dimethylbenzylammonium bromide

Utilizing substantially the same procedures as in Example I, 1.0 g (0.00494 moles) of N,N',N''-tetramethyliethyltrimethylenetetramine, 1.84 g (0.00988 moles) of 1,2-epoxy-3-octyloxypropane, and 3.38 g (0.01976 moles) of benzyl bromide were reacted in the presence of 25 ml of ethanol. The result was the tetraquaternary analog of 2-hydroxy-3-octyloxypropyl dimethylbenzylammonium bromide, which is effective as an antibacterial agent possessing significantly greater activity than the corresponding monomer.

Effective agents are also obtained by substituting the following compounds for the 1,2-epoxy-3-octyloxypropane utilized in Examples I-III: 1,2-epoxyhexane; 1,2-epoxyheptane; 1,2-epoxyoctane; 1,2-epoxydodecane; 1,2-epoxytetradecane; 1,2-epoxyhexadecane; 1,2-epoxyoctadecane; 1,2-epoxyeicosane; 1,2-epoxy-3-hexyloxypropane; 1,2-epoxy-3-heptyloxypropane; 1,2-epoxy-3-nonlyoxypropane; 1,2-epoxy-3-decylxypropane; 1,2-epoxy-3-dodecylxypropane; 1,2-epoxy-3-tetradecylxypropane; 1,2-epoxy-3-hexadecylxypropane; 1,2-epoxyoctadecylxypropane. Similar results are also achieved by substituting the following compounds for the benzyl bromide utilized in Examples I-III: benzyl chloride, benzyl fluoride, and benzyl iodide to form the corresponding di-, tri-, and tetraquaternary halides. Similar results are also achieved by substituting the following compounds for the ethanol utilized in Examples I-III: methanol, isopropanol, butanol, and other suitable polar solvents.

EXAMPLE IV

Preparation of the diquaternary analog of 2-hydroxy dodecylmethylbenzylammonium bromide

1.0 g (0.01136 moles) of N,N'-dimethylethylendiamine and 4.19 g (0.02272 moles) of 1,2-epoxydodecane were refluxed in 25 ml of ethanol for about 20 hours. 3.88 g (0.02272 moles) of benzyl bromide were then added and refluxing continued for about an additional 2 hours. The ethanol was stripped off by rotary evaporation, leaving a heavy syrup. The syrup was washed several times with ether and dried in a desicator. The resulting composition was the diquaternary analog of 2-hydroxy-dodecylmethylbenzylammonium bromide which is an effective antibacterial agent possessing significantly greater effectiveness than the corresponding monomer.

EXAMPLE V

Preparation of the triquaternary analog of 2-hydroxy dodecylmethylbenzylammonium bromide

Utilizing substantially the same procedures as in Example IV, 1.0 g (0.00689 moles) of N,N',N''-trimethyl-diethylenetriamine, 2.54 g (0.01378 moles) of 1,2-epoxydodecane, and 3.53 g (0.02067 moles) of benzyl bromide were reacted in 25 ml of ethanol. The resulting compound was the triquaternary analog of 2-hydroxy-dodecylmethylbenzylammonium bromide which is an effective antibacterial agent possessing significantly greater antibacterial effectiveness than the corresponding monomer.

Agar Incorporation Minimal Inhibitory Concentration Test

The antibacterial efficacies of the antibacterial compositions of the present invention were established and can be demonstrated by determining the bacteriostatic breakpoint also known as the minimal inhibitory concentration (MIC). The test is designed to determine the minimum concentration of an antibacterial composition which just prevents the growth of a test organism through incubation. This is expressed as the "MIC" or "Bacteriostatic Breakpoint" and is expressed in parts per million (ppm).

In this test, plates containing a medium of trypticase soy agar (TSA) and varied concentrations of the antibacterial agents to be tested were prepared. The plates were subsequently inoculated with prepared trypticase soy broth (TSB) cultures of an inoculum. In the present test, the inoculum against which the compounds of the present invention were tested were Staphylococcus aureus (Gm +) and Escherichia coli (Gm -). The inoculated plates were incubated for about 48 hours at 37°C and subsequently examined for
growth. The lowest concentration of the antibacterial agent being tested which shows no growth of the inoculum is the MIC expressed in parts per million. In this test, 2-hydroxy-3-octyl oxypropyl dimethylbenzylamonium bromide and the corresponding di-, tri-, and tetraquaternary analogs were evaluated. Also evaluated was 2-hydroxy dodecyl dimethyl benzyl ammonium bromide and the corresponding di-, tri-, and tetraquaternary analogs thereof. The results of tests are disclosed below in Table I wherein y1 denotes the monomer, y2 the diquaternary analog, y3 the triquaternary analog, and y4 the tetraquaternary analog.

Table I

<table>
<thead>
<tr>
<th>Compound</th>
<th>Staphylococcus aureus ppm</th>
<th>(MIC)</th>
<th>Escherichia coli ppm</th>
<th>Broth</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1</td>
<td>pH 5.8</td>
<td></td>
<td>pH 6.8</td>
<td></td>
</tr>
<tr>
<td>Y1</td>
<td>&gt;10</td>
<td>&gt;20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Y2</td>
<td>2.5</td>
<td>20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Y3</td>
<td>2.5</td>
<td>20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Y4</td>
<td>10</td>
<td>20</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

B2

| Y1       | 10                        | >20   |                      |       |
| Y2       | 2.5                       | 20    |                      |       |
| Y3       | 2.5                       | 20    |                      |       |
| Y4       | 10                        | 20    |                      |       |

1. A — 2-hydrox y-3-octyl oxypropyl dimethylbenzylammonium bromide
2. B — 2-hydroxy dodecyl dimethyl benzyl ammonium bromide

From the above table, it can be seen that the higher analogs, i.e., the di- (y2), tri- (y3), and tetraquaternary (y4) analogs, generally exhibit lower MIC values than the corresponding monomers (y1) indicating greater antibacterial effectiveness.

EXAMPLE VIII

Bactericidal Test

This test is designed to determine bactericidal effectiveness of antibacterial agents. A stock solution of the antibacterial agent being tested and dimethyl formamide (DMFA) was prepared, the concentrations of antibacterial agent being 10 ppm and 100 ppm. After the tubes were heated in a water bath for about 20 minutes at about 37°C, they were inoculated by a trypticase soy broth culture containing the test organisms, Staphylococcus aureus and Escherichia coli. Aliquots were removed from the samples and were put into Petri plates containing molten trypticase soy agar containing 5 percent Tween 80 and 1 percent horse serum. The plates were allowed to harden and were subsequently incubated for 48 hours at 37°C. The plates were then examined and the number of bacterial colonies formed were counted using a Quebec Colony Counter. The results of the tests expressed as percent cidal kill are found in Table II below, wherein y1 indicates the monomer, y2 the diquaternary analog, y3 the triquaternary analog, and y4 the tetraquaternary analog.

Table II

<table>
<thead>
<tr>
<th>Compound</th>
<th>Staphylococcus aureus</th>
<th>Escherichia coli</th>
</tr>
</thead>
</table>

From the above table, it can be seen that the higher analogs, i.e., the di- (y2), tri- (y3), and tetraquaternary (y4) analogs show greater cidal kill percentages at lower concentrations indicating greater antibacterial effectiveness than the corresponding monomers (y1).

It has also been found that the above-disclosed polymeric quaternary ammonium antibacterial agents possess antibacterial properties whereby a lasting antibacterial effect is obtained particularly in soap and non-soap synthetic detergent compositions, and other products where an antibacterial action is desired. Such compositions containing combinations of the present invention in amounts of from about 0.1 to about 5 percent, preferably about 2 percent, are particularly effective.

The term "soap" as used herein is meant to designate alkali metal soaps such as the sodium and potassium salts of the higher fatty acids of naturally occurring plant or animal esters, e.g., palm oil, coconut oil, babasu oil, soybean oil, castor oil, tallow, whale and fish oils, grease and lard and mixtures thereof. Sodium and potassium soaps can be made by direct saponification of the fats and oils or by the neutralization of the fatty acids which are prepared in a separate manufacturing process. Examples of suitable soaps are the sodium, potassium, ammonium and alkylammonium salts of higher fatty acids (C10–C18). Particularly useful are the sodium and potassium salts of the mixtures of fatty acids derived from coconut oil and tallow, i.e., sodium or potassium tallow and coconut soap.

Anionic synthetic detergents which can be used with the antibacterial combinations of the present invention can be broadly defined as the water-soluble salts, including the alkali metal, ammonium and substituted ammonium salts, of organic sulfuric reaction products having in their molecular structure an alkyl radical containing from about eight to about 22 carbon atoms and a radical selected from the group consisting of sulfonic acid and sulfuric acid ester radicals.

Important examples of the synthetic detergents which can be used with the compositions of the present invention are the following: an alkali metal (e.g., sodium and potassium) ammonium and substituted ammonium (e.g., lower alkyl ammonium) salts; alkyl sulfates, especially those obtained by sulfating the higher alcohols produced by reducing the glycerides of tallow or coconut oil; random paraffin sulfonates, in which the alkyl group contains from about eight to about 22 carbon atoms, prepared by treating random paraffin hydrocarbons in sulfur dioxide and chlorine in the presence of light followed by treating with a base; branched or linear alkyl benzene sulfonates, in which
the alkyl group contains from about eight to about 18 carbon atoms, preferably from about 10 to about 14 carbon atoms, especially those of the types described in U.S. Pat. Nos. 2,220,099, and 2,477,383; sodium alkyl glyceryl ether sulfonates, especially those ethers of the higher alcohols derived from tallow and coconut oil; coconut oil fatty acid monoglyceride sulfates and sulfonates; sulfuric acid esters of the reaction product of one mole of a higher fatty alcohol (e.g., tallow or coconut alcohols) and from about 1 to about 6, preferably about 3 moles of ethylene oxide; alkyl phenol ethylene oxide ether sulfates with about 4 units of ethylene oxide per molecule and in which the alkyl radicals contain about nine carbon atoms; the reaction product of fatty acids esterified with isethionic acid and neutralized with sodium hydroxide where, for example, the fatty acids are derived from coconut oil; fatty acid amides of the methyl taurine in which the fatty acids, for example, are derived from coconut oil; sulfonated olefins of U.S. Pat. No. 3,332,880; and others known in the art, a number being specifically set forth in U.S. Pat. Nos. 2,486,921, 2,486,922 and 2,396,278.

The nonionic synthetic detergents which can be used with the antibacterial combinations of the present invention may be broadly defined as compounds produced by the condensation of alkylamine oxide groups (hydrophilic in nature) with an organic hydrophobic compound which may be aliphatic or alkyl-aromatic in nature. The length of the hydrophilic or polyoxyalkylene radical which is condensed with any particular hydrophobic group can be readily adjusted to yield a water-soluble compound having the desired degree of balance between hydrophilic and hydrophobic elements.

For example, a well-known class of nonionic synthetic detergents is made available on the market under the trade name of "Pluronic." These compounds are formed by condensing ethylene oxide with a hydrophobic base formed by the condensation of propylene oxide with propylene glycol. The hydrophobic portion of the molecule which, of course, exhibits water insolubility has a molecular weight of about 1,500 to about 1,800. The addition of polyoxyethylene radicals to this hydrophobic portion tends to increase the water solubility of the molecule as a whole and the liquid character of the products is retained up to the point where polyoxyethylene content is about 50 percent of the total weight of the condensation product.

Other suitable nonionic synthetic detergents include:

1. The polyethylene oxide condensates of alkyl phenols, e.g., the condensation products of alkyl phenols having an alkyl group containing from about six to 12 carbon atoms in either a straight chain or branched chain configuration, with ethylene oxide, the said ethylene oxide being present in amounts equal to 10 to 60 moles of ethylene oxide per mole of alkyl phenol. The alkyl substituent in such compounds may be derived from polymerized propylene, diisobutylene, octane, or nonane, for example.

2. Those derived from the condensation of ethylene oxide with the product resulting from the reaction of propylene oxide and ethylene diamine — products which may be varied in composition depending upon the balance between the hydrophobic and hydrophilic elements which is desired. For example, compounds containing from about 40 to about 80 percent polyoxyethylene by weight and having a molecular weight of from about 5,000 to about 11,000 resulting from the reaction of ethylene oxide groups with a hydrophobic base constituted of the reaction product of ethylene diamine and excess propylene oxide, said base having a molecular weight of the order of 2,500 to 3,000, are satisfactory.

3. The condensation product of aliphatic alcohols having from 8 to 18 carbon atoms, in either straight chain or branched chain configuration, with ethylene oxide, e.g., a coconut alcohol ethylene oxide condensate having from 10 to 30 moles of ethylene oxide per mole of coconut alcohol, the coconut alcohol fraction having from 10 to 14 carbon atoms.

4. Long chain tertiary amine oxides corresponding to the following general formula, \( R_1RN_1R_3 \rightarrow O \), wherein \( R_1 \) contains an alkyl, alkenyl or monohydroxy alkyl radical of from about eight to about 18 carbon atoms from 0 to about 10 ethylene oxide moieties, and from 0 to 1 glycerol moiety, and \( R_2 \) and \( R_3 \) contain from one to about three carbon atoms and from 0 to about 1 hydroxy group, e.g., methyl, ethyl, propyl, hydroxyethyl, or hydroxypropyl radicals. The arrow in the formula is a conventional representation of a semi-polar bond. Examples of amine oxides suitable for use in this invention include dimethyldecyldimethylamine oxide, oleyldi(2-hydroxyethyl)amine oxide, dimethylglycolamine oxide, dimethyldodecylamine oxide, di-(2-hydroxyethyl)-tetradecylamine oxide, 3-dodecoxy-2-hydroxypropyl(3-hydroxypropyl)amine oxide, dimethyhexadecylamine oxide.

5. Long chain tertiary phosphine oxides corresponding to the following general formula \( RR''\rightarrow O \), wherein \( R \) contains an alkyl, alkenyl or monohydroxyalkyl radical ranging from eight to 18 carbon atoms in chain length, from 0 to about 10 ethylene oxide moieties and from 0 to 1 glycerol moiety and \( R'' \) are each alkyl or monohydroxyalkyl groups containing from one to three carbon atoms. The arrow in the formula is a conventional representation of a semi-polar bond. Examples of suitable phosphine oxides are: dodecyltrimethylphosphine oxide, tetradecylmethylphosphine oxide, tetradecylmethylphosphine oxide, 3,6,9-triaoxaundecylmethylphosphine oxide, cetyltrimethylphosphine oxide, 3-dodecoxy-2-hydroxypropyl(2-hydroxyethyl)phosphine oxide, stearyldimethylphosphine oxide, cetyldimethylphosphine oxide, oleyldimethylphosphine oxide, dodecyldimethylphosphine oxide, tetradecylmethylphosphine oxide, dodecylcyclohexylphosphine oxide, dodecylcyclohexylphosphine oxide, tetradecylcyclohexylphosphine oxide, cetyldimethylphosphine oxide, 2-hydroxydodecylmethylphosphine oxide.

6. Long chain dialkyl sulfides containing one short chain alkyl or hydroxy alkyl radical of one to about three carbon atoms (usually methyl) and one long
hydrophobic chain which contains alkyl, alkenyl, hydroxy alkyl, or keto alkyl radicals containing from about eight to about 20 carbon atoms, from 0 to about 10 ethylene oxide moieties and from 0 to 1 glyceryl moiety. Examples include:

- octadecyl methyl sulfoxide, 2-ketotridecyl methyl sulfoxide,
- 3,6,9-trioxaocadecyl 2-hydroxyethyl sulfoxide,
- dodecyl methyl sulfoxide,
- oleoyl 3-hydroxy propyl sulfoxide,
- tetradeyl methyl sulfoxide,
- 3-methoxytridecyl methyl sulfoxide,
- 3-hydroxytridecyl methyl sulfoxide,
- 3-hydroxy-4-dodecoxybutyl methyl sulfoxide.

The zwitterionic synthetic detergents useful with the antibacterial agents of the present invention can be broadly described as derivatives of aliphatic quaternary ammonium, phosphonium, and sulfonium compounds, in which the aliphatic radicals can be straight chain or branched, and wherein one of the aliphatic substituents contains from about eight to about 18 carbon atoms and one contains an anionic water solubilizing group, e.g., carboxy, sulfonate, sulfate, phosphate, or phosphonate. A general formula for these compounds is:

\[
\text{R}^*\text{Y}^*\text{CH}_{2}\text{R}\text{Z}^*\]

wherein \( \text{R}^* \) contains an alkyl, alkenyl, or hydroxy alkyl radical of from about eight to about 18 carbon atoms, from 0 to about 10 ethylene oxide moieties and from 0 to 1 glyceryl moiety; \( \text{Y} \) is selected from the group consisting of nitrogen, phosphorous, and sulfur atoms; \( \text{R}^2 \) is an alkyl or monohydroxyalkyl group containing one to about three carbon atoms; \( x \) is 1 when \( \text{Y} \) is a sulfur atom and 2 when \( \text{Y} \) is a nitrogen or phosphorous atom, \( \text{R}^4 \) is an alkylene or hydroxyalkylene of from one to about four carbon atoms and \( \text{Z} \) is a radical selected from the group consisting of carboxy, sulfonate, sulfate, phosphate, and phosphonate groups.

Examples include:

- 4-[N,N-di(2-hydroxyethyl)-N-octadecylammonio]butane-1-carboxylate,
- 5-[S-3-hydroxypropyl-S-hexadecylsulfonio]-3-hydroxypentane-1-sulfate,
- 3-[P,P-diethyl-P-3,6,9-trioxaetraoxycphosphonio]-2-hydroxypropane-1-phosphate,
- 3-[N,N-dipropyl-N-3-dodecoxy-2-hydroxypropylammonio]-propane-1-phosphonate,
- 3-(N,N-dimethyl-N-hexadecylammonio)propane-1-sulfonate,
- 3-(N,N-dimethyl-N-hexadecylammonio)-2-hydroxypropane-1-sulfonate,
- 4-[N,N-di(2-hydroxyethyl)-N-(2-hydroxydodecyl)ammonio]-butane-1-carboxylate,
- 3-[S-ethyl-S-(3-dodecoxy-2-hydroxypropyl)sulfonio]-propane-1-phosphate,
- 3-[P,P-dimethyl-P-dodecphosphonio]-propane-1-phosphonate; and
- 5-[N,N-di(3-hydroxypropyl)-N-hexadecylammonio]2-hydroxypentane-1-sulfate.

The amphoteric synthetic detergents useful in the present invention can be broadly described as derivatives of aliphatic secondary and tertiary amines in which the aliphatic radical can be straight chain or branched and wherein one of the aliphatic substituents contains from about eight to about 18 carbon atoms and one contains an anionic water solubilizing group, e.g., carboxy, sulfonate, sulfate, phosphate, or phosphonate. Examples of compounds falling within this definition are sodium 3-dodecylamino propionate, sodium 3-dodecylamino propionate sulfonate, dodecy1-β-alanine, N-alkyltaurines such as the one prepared by reacting dodecylamine with sodium isethionate according to the teaching of U.S. Pat. No. 2,658,072, N-hexyl alky arsatic acids such as those produced according to the teaching of U.S. Pat. No. 2,438,091, and the products sold under the trade name "Miranol" and described in U.S. Pat. No. 2,528,378.

Detergent formulations containing the antibacterial compositions of the present invention can also contain from about 0 to about 90 percent, preferably from about 10 to about 90 percent of water-soluble alkaline detergency builder salts, either of the organic or inorganic types. Examples of such builder salts can be found in U.S. Pat. No. 3,336,233, issued Aug. 15, 1967, column 9, lines 29–66, which is incorporated herein by reference.

The detergent formulations can also contain any of the usual adjuvants, diluents, and additives, for example, perfumes, anti-tarnishing agents, anti-redeposition agents, dyes, fluorescers, suds builders, suds depressors and the like without detracting from the advantageous properties of the antibacterial compositions of the present invention.

Examples of diluents which may be incorporated into a synthetic detergent bar in amounts of up to about 80 percent of the bar include soap, especially heavy metal insoluble soaps, (metallic salts of higher fatty acids); starches such as cornstarch; and clays such as china clay or fuller's earth. Other diluents include inorganic salts such as sodium and potassium chlorides and sulfates. Such diluents add bulk to the bar and improve its cosmetic properties without impairing its detergent or cohesive properties.

**EXAMPLE IX**
A milled toilet detergent bar is prepared in accordance with methods known and used in the art and having the following composition:

<table>
<thead>
<tr>
<th>Component</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium alkyl glyceryl ether sulfate (alkyl group derived from the middle cut of alcohol obtained by catalytic reduction of coconut oil)</td>
<td>8.0</td>
</tr>
<tr>
<td>Potassium alkyl sulfate (alkyl group derived from the middle cut of alcohol obtained by catalytic reduction of coconut oil)</td>
<td>20.0</td>
</tr>
<tr>
<td>Magnesium soap of 80:20 tallow:coconut fatty acids</td>
<td>17.0</td>
</tr>
<tr>
<td>Inorganic salts (sodium and potassium chlorides and sulfates)</td>
<td>32.0</td>
</tr>
<tr>
<td>Diquaternary analog of 2-hydroxy-3-octylxoxypyrophydimethylbenzylammonium bromide</td>
<td>2.0</td>
</tr>
<tr>
<td>Water and minor balance to 100</td>
<td></td>
</tr>
</tbody>
</table>

*Middle-cut coconut alcohols having a chain length distribution substantially as follows: 2% C₁₂, 66% C₁₄, 23% C₁₆, and 9% C₁₈.
This bar cleans well and exhibits good odor reducing properties evidencing antibacterial effectiveness. It reduces the number of bacteria on the skin and does not discolor significantly.

Substantially equivalent results are achieved when the diquaternary analog of 2-hydroxy-3-octylxypropyl dimethylbenzylammonium bromide is substituted by the tri-, and tetraquaternary analogs thereof. Similar desirable antibacterial effectiveness is also achieved when the diquaternary analog of 2-hydroxy-3-octylxypropyl dimethylbenzylammonium bromide is replaced by the di-, tri-, and tetraquaternary analogs of 2-hydroxy dodecyl(dimethylbenzyl)ammonium bromide.

EXAMPLE X

A granular built synthetic detergent composition having the following formulation can be prepared and the antibacterial compositions of the present invention can be incorporated therein.

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium dodecylbenzene sulfonate</td>
<td>17.5</td>
</tr>
<tr>
<td>Sodium tripolyphosphate</td>
<td>50.0</td>
</tr>
<tr>
<td>Sodium sulfate</td>
<td>14.0</td>
</tr>
<tr>
<td>Sodium silicate (SiO₂·Na₂O=2:1)</td>
<td>7.0</td>
</tr>
<tr>
<td>Diquaternary analog of 2-hydroxy dodecyl-</td>
<td>3.0</td>
</tr>
<tr>
<td>dimethylbenzylammonium bromide</td>
<td></td>
</tr>
<tr>
<td>Water and minors</td>
<td>balance to 100</td>
</tr>
</tbody>
</table>

This composition, in addition to performing well in its cleaning capacity, imparts considerable antibacterial activity to fabrics cleansed in its solution.

Substantially equivalent results are obtained when the diquaternary analog of 2-hydroxy dodecyl(dimethylbenzyl)ammonium bromide is replaced with the tri-, and tetraquaternary analogs thereof. Substantially equivalent results are also obtained when the diquaternary analog of 2-hydroxy dodecyl(dimethylbenzyl)ammonium bromide of Example X is replaced by the di-, tri-, and tetraquaternary analogs of 2-hydroxy-3-octylxypropyl dimethylbenzylammonium bromide.

Substantially equivalent results are obtained, i.e., good cleaning and good odor reducing properties, when the sodium dodecylbenzene sulfonate of Example X is replaced, on an equal weight basis, by the following:

sodium tallowalkyl sulfate;
potassium cocostalkyl glyceryl ether sulfonate;
sodium salt of randomly sulfonated paraffin containing an average of 15.2 carbon atoms;
ammonium tridecyl sulfate;
condensation product of octyl phenol with 15 moles of ethylene oxide per mole of octyl phenol;
dimethyldodecylamine oxide;
dodecyl(dimethyl)phosphine oxide;
tetradecyl methyl sulfoxide;
3-(N,N-dimethyl-N-hexadecylammonio)propane-1-sulfonate;
3-dodecylaminopropionate; and
dodecyl-β-alanine.

EXAMPLE XI

A granular built synthetic detergent composition having the following formulation can be prepared and the antibacterial compositions of the present invention incorporated therein.

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>The reaction product of coconut alcohol and about 30 moles of ethylene oxide</td>
<td>9.0</td>
</tr>
<tr>
<td>Sodium tripolyphosphate</td>
<td>58.5</td>
</tr>
<tr>
<td>Sodium sulfate</td>
<td>14.0</td>
</tr>
<tr>
<td>Sodium silicate (SiO₂·Na₂O=2:1)</td>
<td>7.0</td>
</tr>
<tr>
<td>Diquaternary analog of 2-hydroxy-3-octylxypropyl dimethylbenzylammonium bromide</td>
<td>1.0</td>
</tr>
<tr>
<td>Water</td>
<td>10.5</td>
</tr>
</tbody>
</table>

The composition possesses good cleaning capacity and desirable antibacterial effectiveness on fabrics cleansed in the solution.

Substantially equivalent results are achieved when the diquaternary analog of 2-hydroxy-3-octylxypropyl dimethylbenzylammonium bromide is substituted by the tri-, and tetraquaternary analogs thereof. Similar desirable antibacterial effectiveness is also achieved when the diquaternary analog of 2-hydroxy-3-octylxypropyl dimethylbenzylammonium bromide is replaced by the di-, tri-, and tetraquaternary analogs of 2-hydroxy dodecyl(dimethylbenzyl)ammonium bromide.

The foregoing description of the invention has been presented describing certain operable and preferred embodiments. It is not intended that the invention should be so limited, since variations and modifications thereof will be obvious to those skilled in the art, all of which are within the scope and spirit of the invention.

What is claimed is:

1. Polymeric antibacterial 2-hydroxyalkyl quaternary ammonium halide compounds having the structural formula:

   \[
   \begin{array}{c}
   \text{R} \\
   \text{CH₃} \\
   \text{N}^- \\
   \text{CH₃} \\
   \text{CH₃} \\
   \text{X}^- \\
   \text{Y}
   \end{array}
   \]

   wherein R and R' are the same and are selected from the group consisting of R'"OCH₂CH(OH)— and R'"CH(OH)— wherein R'" is an n-alkyl group containing from four to 20 carbon atoms, X is a halide ion, and y has a value of from 2 to 4.

2. The polymeric antibacterial compound of claim 1 wherein R and R' are C₆H₁₃ — O — CH₂CH(OH)—, X is Br⁻ and y has a value of from 2 to 4.

3. The polymeric antibacterial compound of claim 1 wherein R and R' are C₁₆H₃₃CH(OH)—, X is Br⁻, and y has a value of from 2 to 4.

   * * * * *