This invention relates to antibacterial quaternary ammonium salts of polymerized epichlorohydrin and to a method of preparing the same. More particularly, this invention relates to salts having the following structural formula:

\[
\text{R}^\text{N} - \text{R} \quad \text{R}^\text{N} - \text{R}'
\]

wherein \( R \) is an aliphatic group containing from 1 to about 24 carbon atoms. \( R' \) and \( R'' \) each are aliphatic groups containing from 1 to about 4 carbon atoms. \( R' \) and \( R'' \) can be different in the same compound. \( R, R' \) and \( R'' \) have this definition throughout the description of this invention; they are preferably \( n \)-alkyls. \( n + m \) ranges from 2 to 50; \( n \) ranges from 1 to 50; \( m \) ranges from 0 to 49. \( n + m +1 \) the number of carbon atoms in \( R \) must be greater than 12. Preferably \( n + m \) has a value of 4 to 15, \( n \) a value of 1 to 15, and \( m \) a value of 0 to 14. \( n, m, \) and \( n + m \) are average values by the nature of the reaction forming the polymers; therefore, \( n, m, \) and \( n + m \) can have fractional values.

Antibacterial quaternary ammonium chlorides are known to the art. Antibacterial compounds of the above structural formula, however, are not.

It is, therefore, an object of this invention to provide polyquaternary ammonium compounds having the above structural formula which are outstandingly active as antibacterial agents.

It is a further object of this invention to prepare such compounds by reacting acyclic tertiary amines with polyepichlorohydrin.

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

Antibacterial acyclic polyquaternary ammonium compounds, none of which are known to be described in the prior art and exemplary of those within the present invention, are set forth in Table I below wherein the tertiary amine, \( m \) and \( n \) are applied in the structural formula set forth above.

### Table I

<table>
<thead>
<tr>
<th>Acyclic tertiary amine</th>
<th>Moles epichlorohydrin in polymer=( n+m )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Octyldimethyl</td>
<td>5</td>
</tr>
<tr>
<td>Decyldimethyl</td>
<td>5</td>
</tr>
<tr>
<td>Dodecyldimethyl</td>
<td>5</td>
</tr>
<tr>
<td>Dodecylmethylethyl</td>
<td>5</td>
</tr>
<tr>
<td>Octodecylmethylethyl</td>
<td>5</td>
</tr>
<tr>
<td>Trimethyl</td>
<td>12.5</td>
</tr>
<tr>
<td>Tripropyl</td>
<td>12.5</td>
</tr>
<tr>
<td>Triethyl</td>
<td>37.5</td>
</tr>
<tr>
<td>Triethyldimethyl</td>
<td>37.5</td>
</tr>
<tr>
<td>Octadeoxyldimethyl</td>
<td>37.5</td>
</tr>
</tbody>
</table>

In the above table the value of \( m \) can be 0, 1 or range up to \( n+m-1 \).

The preferred compound within the scope of the invention is:

\[
\text{R}^\text{N} - \text{R} \quad \text{R}^\text{N} - \text{R}'
\]

Composed similar to those of the present invention but with \( R' \) and/or \( R'' \) containing more than about 4 carbon atoms apparently cannot be formed in a reasonable amount of time.

The degree of polymerization \((n+m)\) is arbitrarily limited to 50 because of difficulty in producing compounds with \( n+m \) greater than 50. If a tertiary amine is reacted with epichlorohydrin, the tertiary amine catalyzes polymerization, and the monomer apparently cannot be formed. If \( n + m +1 \) the number of carbon atoms in \( R \) is not greater than 12, compounds similar to those of the present invention can be formed. However, such compounds do not have antibacterial properties. Thus, for antibacterial properties in polymers having a low degree of polymerization, a long chain length \( R \) is necessary.

The degree of quaternization on \( n \) must at least be 1. No increase in antibacterial efficacy is apparent over \( n=1 \) as the value of \( n \) is raised. The precise value of \( m \) within the above stated ranges is not critical.

These antibacterial acyclic polyquaternary ammonium compounds can be produced by a variety of methods. It is preferable to start with polymerized epichlorohydrin. The polymerized epichlorohydrin is reacted with an acyclic tertiary amine, either in the presence of a solvent or with no solvent present, together with a suitable quaternization catalyst. If a solvent is present, the reaction can be carried out at the reflux temperature of the solvent. If no solvent is present, the boiling point of the acyclic tertiary amine is the limiting reaction temperature. Mixtures of acyclic tertiary amines can be employed or different amines meeting the limitations herein can be added sequentially. Generally, reaction temperatures range from 60° F. to 300° F.

Examples of acyclic tertiary amines that can be used to produce compositions within the scope of the present invention are trimethylamine, triethylamine, tripropylamine, methylpropylamine, tributylamine, hexylidimethylamine, octylidimethylamine, decylidimethylamine, dodecyldimethylamine, dodecylmethylethylamine, dodecylidimethylamine, dodecylethylbutylamine, octadecklydi-
methylamine, octadecylmethylbutylamine, eicosylmethyl amine and docosylmethylamine.

The polymerized epichlorohydrin referred to above has the following structure:

\[
\text{HO}_2\text{CH-CH-O}^\text{CH}^\text{CHCl}^\text{CH}_{n+m}
\]

wherein \(n+m\) is the degree of polymerization. The \(-\text{CH}_2\text{Cl}\) group in the polyci- plorohydrin structure will hereafter be referred to as a pendant chloromethyl group and the \(-\text{Cl}\) atom in the polyci- plorohydrin structure as a pendant chlorine atom.

Examples of catalysts that can be used in a process to produce the compounds of the present invention are alkali- line substances such as sodium bicarbonate, sodium hy- droxide, potassium bicarbonate, potassium hydroxide and mixtures of these. The amount of catalyst to be used ranges from 0.1 to 6% by weight of polyci- plorohydrin.

Suitable solvents for such a process include water, acetone, benzene and lower primary alcohols such as methyl, ethyl, propyl, isopropyl, butyl and iso-butyl alcohols.

In the preferred method, polyci- plorohydrin, e.g. where \(n+m=12.5\), is refluxed in aqueous isopropanol in the presence of NaHCO\(_3\) catalyst with sufficient molar quantities of an acyclic tertiary amine, e.g. trimethyl- amine, to quantize from 1 to \(m+n\) of the pendant chlorine atoms in the pendant chloromethyl groups. This is shown in the following representative equation:

\[
\text{HO}_2\text{CH-CH-O}^\text{CH}^\text{CHCl}^\text{CH}_{n+m} + RRR'RN \rightarrow \text{NaHCO}_3 \rightarrow \text{HO}_2\text{CH-CH-O}^\text{CH}^\text{CHCl}^\text{CH}_{n+m} + RRR'RN
\]

Also epichlorohydrin can be refluxed in a solvent such as benzene with an acyclic tertiary amine, e.g. trimethyl- amine, as a polymerization catalyst followed by the quan- terization of the polyci- plorohydrin thus formed by the same amine. This is shown in the following representa- tive equation, e.g., wherein \(n+m=12.5\):

\[
\text{HO}_2\text{CH-CH-O}^\text{CH}^\text{CHCl}^\text{CH}_{n+m} + RRR'RN
\]

The following specific examples are illustrative of the present invention, but are not limiting thereof:

**EXAMPLE I**

A mixture of 100 parts (0.087 mole) of polyci- plorohydrin with an average molecular weight of 1150, equiv- alent to 12.5 moles epichlorohydrin monomer in the poly- mer or \(n+m=12.5\) (Polyglycol 166–1150), 78.4 parts of 25% aqueous solution of 

\[
\text{NaHCO}_3
\]

and 6 parts sodium bicarbonate of 6% by weight, based on polyci- plorohydrin was refluxed for a total of seven hours. The reac- tion mixture was cooled to room temperature and 

\[
\text{NaHCO}_3
\]

removed by filtration. Removal of isopropyl al- cohol under aspirator vacuum yielded a tan waxy mate- rial that was completely water soluble and ether insoluble. Ionizable chloride content: actual 9.4%; theory, 10.2%; this indicates a high degree of quantization of 92.0%. The formed compound had the general structural formula set forth above with \(n+m=12.5\), \(n=4\), and the tertiary amine = trimethylamine; it is effective as an antibacterial agent.

**EXAMPLE II**

A mixture of 100 parts (0.087 mole) of polyci- plorohydrin similar to that used in Example I was refluxed with 33.90 parts (0.335 mole) of triethylamine together with 133.9 parts of isopropyl alcohol and 6 parts of sodium bicarbonate for a total of seven hours. The product ob- tained after removal of the sodium bicarbonate by filtration at room temperature, and the isopropyl alcohol by evaporation, was a light tan waxy solid that was water soluble and ether insoluble. The ionizable chloride content was 8.25% while the theoretical content was 9.10%, indicating a quantization of 90.5%. The formed compound had the general structural formula set forth above with \(n+m=12.5\), \(n=4\), and the tertiary amine = triethyl- amine; it is effective as an antibacterial agent.

**EXAMPLE III**

One hundred parts (0.22 mole) of polyci- plorohydrin (Polyglycol 166–450, average molecular weight = 450, equivalent to 5 moles of epichlorohydrin in the polymer or \(n+m=5\)), 141 parts of dodecylmethylamine (0.66 mole) and 6 parts of sodium bicarbonate were heated together under a nitrogen atmosphere for a total time of five hours between the temperatures of 150 and 160°C. The reaction mixture was freed from sodium bi- carbonate by filtration and was soluble in isopropanol and in water but was ether insoluble. Ionizable chloride content of 8.25% compared to the theoretical value of 9.75% indicated that a quantization completeness of 84.5% was obtained. The formed compound had the general structural formula set forth above with \(n+m=5\), \(n=3\) and the tertiary amine = dodecylmethylamine; it is effective as an antibacterial agent.

**EXAMPLE IV**

One hundred parts of polyci- plorohydrin (0.22 mole) as in Example III, 46.86 parts (0.22 mole) dodecyl- dimethylamine, 147 parts isopropyl alcohol, and 6 parts of sodium bicarbonate were refluxed together for seven hours. The product of this reaction was freed from sodium bicarbonate by filtration when cool and the alcohol was removed under vacuum. The resulting material was water soluble and ether insoluble. The ionizable chloride content of 3.58% compared with the theoretical value of 5.35% indicated that quantization to the extent of 67% had occurred. The formed compound had the general structural formula set forth above with \(n+m=5\), \(n=1\) and the tertiary amine = dodecylmethylamine; it is effective as an antibacterial agent.

**EXAMPLE V**

One hundred parts (0.22 mole) of polyci- plorohydrin as in Example III, 140.58 parts (0.66 mole) of dodecy- dimethylamine (mole ratio amine to polyci- plorohydrin = 3/1), 240 parts of isopropyl alcohol and 6 parts of sodium bicarbonate were refluxed together for a total time of five hours. The polyci- plorohydrin was added in two portions; one-half at the start of reflux and one- half after two hours had elapsed. After working up the reaction product as described in the previous example, a tan waxy gum was obtained that dissolved in water or isopropanol but was ether insoluble. The ionizable chlo- ride content of 8.40% indicated a quantization com- pleteness of 86%. The formed compound had the general structural formula set forth above with \(n+m=5\),
3,428,680

5

n=3 and the tertiary amine=dodecyldimethylamine; it is effective as an antibacterial agent.

EXAMPLE VI

Epichlorohydrin, 115.6 parts (1.25 moles), was dissolved in 275.6 parts of benzene and the mixture was brought to the reflux temperature. 106.5 parts (0.5 mole) of dodecyldimethylamine was added slowly to the refluxing mixture. After a total reflux time of 7 hours, the product was freed from benzene in a rotary evaporator under vacuum and the orange waxy residue thus obtained was water soluble and ether insoluble and contained 19% oxirane oxygen compared to the initial value of 8.3% indicating 77% utilization of the epichlorohydrin. The molecular weight (ebullioscopic) was 890 indicating that approximately two dodecyldimethylamine molecules were attached to a polychlorohydrin molecule containing five monomer units. The formed copolymer had the general structural formula set forth above with \( n + m = 5 \); \( n = 2 \) and the tertiary amine=dodecyldimethylamine; it is an effective antibacterial agent.

Effective agents are also obtained by substituting in the foregoing examples various other previously described acyclic tertiary amines for the amines there employed. Similar results are also achieved by replacing the solvent and the catalyst of the preceding examples with other solvents and catalysts of the character hereinbefore indicated.

EXAMPLE VII

As indicated previously, the polyquaternary ammonium compounds described herein have been discovered to be valuable antibacterial agents. The antibacterial activity of these compounds was determined by conducting "Standard Tube Dilution Tests." Such tests are conducted in vitro and consist essentially of preparing test tubes of a standardized broth medium containing serial dilutions (diminishing concentrations) of a compound being tested, inoculating each tube with a preselected microorganism and after an incubation period, determining the growth of bacteria in each tube.

The broth medium employed in these assay tests was an FDA phenol coefficient test nutrient broth. Stock solutions of the test product were then prepared in sterile distilled water. Serial dilutions of the test stock solution and then placed into the tubes containing the nutrient broth.

The broth tubes were inoculated with a bacterial suspension prepared in the following manner. A 24 hour broth culture of gram-positive Staphylococcus aureus FDA 209 was prepared. One-tenth milliliter quantities of the broth culture were added per each previously prepared broth tube containing the test materials. Gram-negative Escherichia coli ATCC 10536 cultures were prepared as inoculum in a similar manner.

Treatment tubes were incubated for 48 hours at 37°C and then observed for the presence or absence of growth. The smallest concentration of test material completely inhibiting growth is the end point. This concentration (parts per million of bacteriocidal agent) is called the bacteriostatic breakpoint. Appropriate sterility and inoculum controls were incorporated.

In order to allow for a comparison of the relative bacteriostatic effectiveness of the novel acyclic polyquaternary ammonium compounds, similar in vitro tests were run on heterocyclic polyquaternary ammonium compounds prepared as shown in Wittcoff, U.S. Letters Patent 2,483,749, granted Feb. 24, 1948.

Such heterocyclic compounds were prepared using pyridine and quinoline tertiary amines.

The results of the in vitro tests described above are tabulated in Table II.

<table>
<thead>
<tr>
<th>Moles Epichlorohydrin in</th>
<th>Tertiary Amine</th>
<th>Bacteriostatic Breakpoints (parts per million)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram Positive Micro-</td>
<td>Gram Negative Micro-</td>
<td></td>
</tr>
<tr>
<td>organism (^1)</td>
<td>organism (^2)</td>
<td></td>
</tr>
<tr>
<td>-------------------------</td>
<td>-------------------</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>0.5</td>
<td>0.1</td>
</tr>
<tr>
<td>5</td>
<td>1.0</td>
<td>0.2</td>
</tr>
<tr>
<td>5</td>
<td>2.0</td>
<td>0.3</td>
</tr>
<tr>
<td>5</td>
<td>4.0</td>
<td>0.4</td>
</tr>
<tr>
<td>5</td>
<td>6.0</td>
<td>0.5</td>
</tr>
</tbody>
</table>

\(^1\) Staphylococcus aureus FDA 209.
\(^2\) Escherichia coli ATCC 10536.

Similar antibacterial results to those displayed by the compounds which are effective antibacterial agents. These in Table II are displayed by compounds with the previously described structural formula and wherein \( n + m = 37.5 \); \( n = 1 \) and the tertiary amines are dodecyldimethylbenzylamine, octadecyldimethylbutylamine, eicosyldimethylamine and docosyldimethylamine.

As can be seen from Table II, the acyclic polyquaternary ammonium compounds described above have superior bacteriostatic properties to the heterocyclic polyquaternary ammonium compounds of U.S. 2,483,749. This is especially true in the case of the polymers produced by reacting the polyepichlorohydrin of molecular weight 450 (\( n + m = 5 \)) with octyldimethylamine, decyldimethylamine and dodecyldimethylamine where the bacteriostatic breakpoints are less than 1 p.p.m. as compared with greater than 1,000 p.p.m. in the case of the quinoline and pyridine compounds made according to U.S. 2,483,749. In fact, the above-mentioned polymers of the present invention compare favorably with Roccal, a \((C_8-C_{18}) \) alkyl-dimethyl-benzyl ammonium chloride and which is an effective germicidal agent.
There is thus provided by this invention a class of new compounds which are effective antibacterial agents. These compounds can be dissolved in water in the range of about 500 to about 1,000 p.p.m. and the solution used as antibacterial compositions. The water can contain a nonionic or surfactant if desired.

These new compounds further unexpectedly retain their antibacterial properties when combined with certain detergent compositions. Thus, an effective antibacterial detergent composition can be formulated which consists essentially of about 0.1% to about 10% of an acyclic polyquaternary ammonium compound of the present invention and from about 5% to about 95% of an alkaline builder salt. Alkaline builder salts include the sodium and potassium phosphates, silicates, carbonates, bicarbonates, borates and polyphosphates. The balance of the detergent composition can be water, nonionic detergents and diluents as sodium sulfate.

The compatibility of the acyclic polyquaternary ammonium compounds of the present invention with detergent compositions containing the above-stated amounts of alkaline builders is shown in the following example:

**EXAMPLE VIII**

"Standard Tube Dilution Tests" similar to those in Example VII were conducted; however, 50 p.p.m. of a detergent composition containing 5% diethanolamide of coconut oil fatty acid, 7% potassium toluene sulfonate, 12% potassium pyrophosphate and 76% water was added to the nutrient broth. The acyclic polyquaternary ammonium compound tested for compatibility was one with \(n+m=5\), \(n=2\) and the tertiary amine = decyldimethylamine. The bacteriostatic breakpoint for *Staphylococcus aureus* FDA 209 was about 0.6 p.p.m. and for *Escherichia coli* ATCC 10536 was less than 0.5 p.p.m. These breakpoints are substantially the same as those in Table II where no detergent composition was added and such similar results show the compatibility of the acyclic polyquaternary ammonium compounds of the present invention with detergent compositions containing alkaline builders.

The compounds of the present invention are further useful as antistatic agents, emulsifying agents and dispersing assistants.

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 spirit and scope of the invention.

What is claimed is:

1. A polyquaternary ammonium salt of a polymerized epichlorohydrin, the polyquaternary ammonium salt having the following unit structure:

\[
\text{HO} - \text{CH_2-CH-O--CH_2-CH-O--H} \\
\text{CH}_3 \\
\text{R'--N--R''} \\
\text{Cl} \\
\text{Cl}^+ \\
\text{R}
\]

wherein \(R\) is an alkyl group containing 8, 10, or 12 carbon atoms and \(R'\) and \(R''\) are each alkyl groups containing from 1 to about 4 carbon atoms; wherein \(n\) plus \(m\) ranges from 5 to about 12.5, \(n\) ranges from 1 to about 12.5, and \(m\) ranges from 0 to about 11.5 when \(R\) contains either 8 or 10 carbon atoms; and wherein \(n\) plus \(m\) is about 5, \(n\) ranges from 1 to about 5, and \(m\) ranges from 0 to about 4 when \(R\) contains 12 carbon atoms.

2. The polyquaternary ammonium salt according to claim 1 wherein \(R\) is an octyl group, \(R'\) and \(R''\) are each methyl groups, \(n\) plus \(m\) is equal to 5, \(n\) is equal to 2, and \(m\) is equal to 3.

3. The polyquaternary ammonium salt according to claim 1 wherein \(R\) is a decyl group, \(R'\) and \(R''\) are each methyl groups, \(n\) plus \(m\) is equal to 5, \(n\) is equal to 2, and \(m\) is equal to 3.

4. The polyquaternary ammonium salt according to claim 1 wherein \(R\) is a dodecyl group, \(R'\) and \(R''\) are each methyl groups, \(n\) plus \(m\) is equal to 5, \(n\) is equal to 1, and \(m\) is equal to 4.

5. The polyquaternary ammonium salt according to claim 1 wherein \(R\) is a decyl group, \(R'\) and \(R''\) are each methyl groups, \(n\) plus \(m\) is equal to 5, \(n\) is equal to 5, and \(m\) is equal to 2.

6. The polyquaternary ammonium salt according to claim 1 wherein \(R\) is a dodecyl group, \(R'\) and \(R''\) are each methyl groups, \(n\) plus \(m\) is equal to 5, \(n\) is equal to 5, and \(m\) is equal to zero.

References Cited

**UNITED STATES PATENTS**

<table>
<thead>
<tr>
<th>Patent Number</th>
<th>Date</th>
<th>Inventor(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2,483,743</td>
<td>10/1949</td>
<td>Wittcoff</td>
</tr>
<tr>
<td>2,876,217</td>
<td>3/1959</td>
<td>Paschall</td>
</tr>
</tbody>
</table>

**FOREIGN PATENTS**

<table>
<thead>
<tr>
<th>Patent Number</th>
<th>Date</th>
<th>Country</th>
</tr>
</thead>
<tbody>
<tr>
<td>213,383</td>
<td>2/1961</td>
<td>Austria</td>
</tr>
<tr>
<td>626,245</td>
<td>6/1963</td>
<td>Belgium</td>
</tr>
</tbody>
</table>

CHARLES B. PARKER, Primary Examiner.
R. V. HINES, Assistant Examiner.

U.S. Cl. X.R.

260—348, 583, 633; 167—65, 22; 424—82