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DODECYL-DIMETHYL-1,2,4,5-TETRAMETHYL-BENZYL AMMONIUM CHLORIDE

Samuel B. McFarlane, Summit, N.J., assignor to Millmaster Onyx Corporation, New York, N.Y., a corporation of New York

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This application is a continuation-in-part of application Serial No. 174,672, filed February 21, 1962, and now abandoned.

This invention relates to a quaternary ammonium compound of high microbicidal potency which is crystalline and nondeliquescent in nature, the advantages of which will appear hereinafter.

Quaternary ammonium compounds of certain classes are well known to the art for their antimicrobial powers, which may vary from a few times to many hundred times the efficacy of the same amount by weight of phenol. The greater number of these compounds are of the nature of gels or of soft sticky solids which tend to absorb atmospheric moisture and to deliquesce. Certain other compounds are light fluffy powders which are unpleasant or hazardous to handle because they are easily air-floated to a dust which is irritating to the mucous membrane. Still others have a limited life since they tend to decompose slowly and thus lose their potency. Some of the known powder quaternaries are salts of bromime, and therefore excessively costly. The microbicidal powers of these quaternary ammonium compounds are widely variable, and the great majority of them are to be found near the middle of the range of potency. They are also sensitive to the inhibiting effect of the constituents of hard water, which inactivates them at normally microbicidal concentrations.

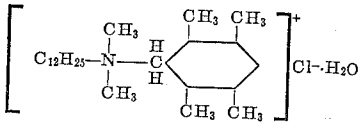
It is the object of the present invention to provide an antimicrobial quaternary ammonium compound which avoids the shortcomings of the known compounds.

A primary object of the invention is the provision of a chemically stable quaternary ammonium compound which is a crystalline solid and which is non-dusting when pulverized, and which is physically stable at ordinary ambient temperatures without caking or deliquescing.

Another object of the invention is the provision of such a compound which is a potent microbicide in extremely dilute solutions and which retains its microbicidal power in the presence of the constituents of hard water.

Another object is to provide the aforesaid crystalline product at a reasonably low cost.

The compound of this invention which achieves these objects is dodecyl dimethyl durenyl ammonium chloride which conforms to the following structure:



although it may also be prepared anhydrous.

Unlike other quaternary ammonium compounds of similar constitution and similar antimicrobial properties, alkyl dimethyl durenyl chloride, and specifically the dodecyl dimethyl durenyl chloride of this invention, is a stable solid of crystalline structure, which may be crushed or powdered if desired and necessary to a free-

flowing powder without the formation of an objectionable amount of fines, and which may therefore be handled freely without dusting. Whether as crystals or as powder, it does not absorb moisture from the atmosphere and hence does not cake or become adherent or sticky from deliquescence.

The aforesaid highly desirable crystallinity is very surprising in view of the prior art. British Patent No 977,099, December 2, 1964, recites (page 1, lines 32–40): "Mere drying of a typical long chain quaternary ammonium compound results in a more or less sticky or pasty semi-solid mass, or an amorphous powder tending to agglomerate. The typical long chain quaternary ammonium compound is not by nature crystalline, at least in that state of purity generally provided in commercial production.

"Other approaches to the preparation of dry particulate forms of quaternary ammonium compounds have hitherto suffered from disadvantages of either cost or of physical form. Illustrative of some disadvantages are excess handling, mechanical attrition (dusting), inhomogeneity, incomplete penetration (caking), and degradation."

U.S. Patent No. 2,700,683, issued January 25, 1955, to Tesoro et al., and relating to alkyl dimethyl alkyl-benzyl ammonium chloride, recites among others "Ar-tetramethyl benzyl n-dodecyl dimethyl ammonium chloride" (column 2, line 25). It recites further (column 3, lines 45–69): "It is extremely difficult to isolate the prepared compounds in pure form inasmuch as they are usually deliquescent and rapidly absorb water from the atmosphere and even from mixtures with absolute (over 96%) ethanol . . . . The boiling down of concentrated aqueous solutions of these materials is not feasible . . . . High concentrations (90% or over) of the new quaternary compounds can be prepared by carrying out the quaternization in relatively volatile solvents . . . . Such 90% preparations are clear, pale yellow, extremely viscous syrups . . . . The syrups are extremely soluble in water . . . ."

The product of this invention therefore very surprisingly differs from Tesoro's products in that it is a crystalline white material with a water solubility of less than 1% instead of a yellow syrup, extremely soluble in water, and also that it is easily recoverable from aqueous solution by evaporation or by crystallization from aqueous solution. It is non-deliquescent and stable under normal atmospheric conditions. It can be provided in the form of free-flowing non-dusting powder which can be readily handled without causing skin, eye, or mucous-membrane irritation. It is free of deliquescent isomers.

As will appear hereinafter, the compound of this invention is bacteriostatic and bactericidal at extremely high dilution and possesses a high hard water tolerance.

The compound of this invention may be synthesized by alkylating dodecyl dimethyl amine, an article of commerce, with 1,2,4,5-tetramethyl-benzyl chloride. The latter may be prepared from the hydrocarbon durene obtained from the refining of petroleum, by chloromethylating it by methods well known to the art. The reactants are both of reasonable cost. Such reaction makes it possible to produce a substantially pure crystalline non-deliquescent lauryl dimethyl durenyl ammonium chloride free of other isomers which may cause deliquescence.

Antimicrobial quaternary ammonium compounds have found wide acceptance in the field of sanitization, disinfection and sterilization. Large quantities are used in the

food handling industries to sanitize vessels and utensils; fabrics such as diapers and hospital linens and other textile materials are treated with them to prevent the propagation or transmission of pathogenic or putrefactive microorganisms; walls, floors and other surfaces are washed with them for disinfection and deodorization; where chemically compatible they are used as preservatives in cosmetic, latex and other applications; they may be employed topically, for example, to combat the microorganisms which cause dandruff and athlete's foot.

A wide field of application is in the treatment of water supplies, such as water for paper making, in swimming pools and other bodies of water, in brine or water for flooding in secondary oil recovery, in recirculated water in cooling towers, air-conditioners, humidifiers and the like, and for the sterilization of drinking water for animals, such as poultry. These compounds are not usually used to sterilize drinking water for human consumption because of the taste which they impart to the water in microbicidal concentration.

In order to be effective for the treatment of water for the aforesaid purposes, these quaternary ammonium compounds should be compatible with the normal constituents of natural water supplies such as the mineral salts which account for water hardness. It is well known to the art of sanitization that quaternary ammonium germicides which are quite effective in soft water will fail to inhibit the growth of bacteria, fungi or algae in hard water except in greatly increased concentration. Under such conditions, the cost of treating water may be greatly increased; hence an agent which is not so inhibited by hard water presents economic and generally practical advantages.

The product of this invention is of moderate water solubility, but of a magnitude many times that required for microbicidal effect; it is also slow to dissolve, so that it may be applied in calculated dosages and permitted to leach out gradually. Because of its physical nature, this compound lends itself to compression into tablets or briquettes which may be readily and safely transported and used at low cost; or it may be measured out into bags or envelopes and similar inexpensive containers which occupy a minimum of space and the weight of which does not materially increase the cost of transportation of the compound in relatively small units of weight. The packaged compound may be stored without special precautions over long periods of time without deterioration of the compound or the packing material. It may be safely handled by the user without dangers inherent in fluid materials. It does not irritate the skin, eyes, and mucous-membranes of the person who handles it during its use.

It lends itself exceedingly well to admixture with other pulverulent materials, such materials either having synergistic, auxiliary or other properties, or on the other hand having no more desirable property than that of diluent, in order to facilitate handling where extremely small amounts of the active ingredient are required, or where a certain low level of concentration is required.

The family of compounds of which the product of this invention is the outstanding example may be prepared by reacting stoichiometric amounts of alkyl dimethyl amine and 1,2,4,5-tetramethyl-benzyl chloride. The reaction is exothermic and will proceed in the absence of any solvent. However, since the product is solid, this is not a practical method of preparation. A solvent such as water, methanol, ethanol, isopropanol, propylene glycol, dioxane, benzene and other solvents which will readily suggest themselves to those skilled in the art, will facilitate the control of the reaction and the recovery of the pure product.

While stoichiometric proportions are required, it is desirable to have a small excess of amine present to maintain the reaction mixture on the faintly alkaline side.

Water is the cheapest solvent possible and is quite suitable. The amount of water is not critical; it must be in sufficient quantity for fluidity in order to permit of agitation and control of temperature by heating or cooling, but not so much in excess as to interfere with the recovery of the product by crystallization. It is feasible to complete the reaction in a sufficiency of water, and then to evaporate the solution to dryness. This however yields a product which contains such impurities as those present in the reactants, the small residues of unreacted material, and the possible by-products from hydrolysis or pyrolysis. Re-solution and crystallization would be necessary in this case.

By using an optimum amount of water, the greater part of the product may be recovered by cooling the solution upon completion of the reaction to such temperature where, spontaneously or upon seeding with a crystal of the product, crystallization will occur. The solution may, if desired, be chilled further to increase the yield. The crystals can then be recovered by filtration, followed by washing with cold water and drying. A pure product of better than 99% quality may be obtained thus.

The following examples are illustrative, but are not intended to limit the invention:

EXAMPLE I

54.7 grams or 0.25 mole of a technical grade of lauryl dimethyl amine having an equivalent weight of 219; 44.8 grams or 0.245 mole of durenyl chloride; and 50 milliliters of water were heated under agitation in a reaction vessel to a temperature of about 92° C. The reactants which were at first not soluble in the water entered into solution during the course of the reaction and the viscosity of the mixture increased to a point where stirring became difficult or impossible. In order to increase the fluidity at about 92° C., more water to the extent of 167 milliliters was added gradually as required. Reaction was continued for a total of one hour and forty minutes, when the reaction was 95.9% completed, as determined by argentometric titration of the chloride ion. Since after only 43 minutes the titration indicated 95.7% of the theoretical, the reaction was considered to be completed.

On standing overnight, the reaction mass solidified. The mixture was melted and transferred to an evaporating dish and dried to constant weight in a vacuum oven.

The yield was 90.5 grams of dry powder of lauryl dimethyl-1,2,4,5-tetramethyl-benzyl ammonium chloride, corresponding to a yield of 92%. It was found to have a melting point of 172° C.

EXAMPLE II

In a similar manner, the corresponding homologous compounds were prepared, substituting for lauryl dimethyl amine, the hexyl, octyl, decyl, myristyl, cetyl and stearyl dimethyl amines, respectively. All were obtained as powders.

EXAMPLE III

The products of Examples I and II were tested bacteriologically by the Standard Phenol Coefficient Method as described in the "Official Methods of Analysis of the Association of Official Agricultural Chemists," 9th edition, pages 63–65. The phenol coefficients of benzalkonium chloride, U.S.P., are included for the purpose of comparison:

Table I

PHENOL COEFFICIENTS AT 20° C., DDAC=DIMETHYL DURENYL AMMONIUM CHLORIDE

	Staphylococcus aureus	*Salmonella typhosa*
Hexyl DDAC	16.6	11.1
Octyl DDAC	41.4	33.3
Decyl DDAC	121	194
Lauryl DDAC	1,083	556
Myristyl DDAC	116	223
Cetyl DDAC	41.4	27.2
Stearyl DDAC	25.0	19.4
Benzalkonium Chloride, U.S.P	500	300

The above table demonstrates that lauryl dimethyl durenyl ammonium chloride is a surprisingly and phenomenally more potent germicide than its homologs.

Benzalkonium chloride, U.S.P., which is alkyl dimethyl (unsubstituted) benzyl ammonium chloride, and which is a widely accepted and largely sold germicide of this class, is only half as effective.

EXAMPLE IV

In order to prepare a dodecyl dimethyl durenyl ammonium chloride of higher purity, a high quality commercially available dodecyl dimethyl amine of 96% grade was employed. 108.6 grams of the amine, or 0.51 mole, was reacted with 91.3 grams of durenyl chloride, or 0.50 mole, in the presence of 600 grams of water in an agitated reaction vessel. The temperature was maintained at 85–90° C. for one hour when the reaction was found to be 95% complete, by argentometric titration, and about 98% complete at the end of another half hour. The mixture was allowed to cool spontaneously until its viscosity became noticeably greater. At this point a few small crystals of dodecyl dimethyl durenyl ammonium chloride were introduced and the agitation was stopped. When the nuclei showed signs of growth, the mixture was agitated for a minute or two, and crystal growth was allowed to proceed without further disturbance.

On the following morning, the flask contained an almost solid slurry of crystals. This was broken up and filtered on a Buchner funnel, after which the compressed cake was washed three times with small portions of cold distilled water. The thoroughly drained precipitate was dried in a current of air at 60° C. in a tray drier.

The product was obtained in a yield of 170 grams or 81% of the theoretical. It assayed better than 99% as dodecyl dimethyl - 1,2,4,5 - tetramethyl - benzyl ammonium chloride monohydrate.

The product had a solubility of a few tenths of one percent at room temperature. It was tested bacteriologically by the Standard Phenol Coefficient Test Method of the Association of Official Agricultural Chemists (1955), pages 87–91, and by the Hard Water Tolerance Test of the United States Department of Agriculture, Interpretation No. 21, Federal Register (September 1956). For the purpose of comparison, the performance of benzalkonium chloride, U.S.P., is appended.

Table II

S.a.=Staplylococcus aureus
S.t.=Salmonella typhosa

Product	Phenol Coefficient vs.		Hard Water Tolerance, p.p.m.
	S.a.	*S.t.*	
Dodecyl-dimethyl-1,2,4,5-tetramethylbenzyl ammonium chloride	1,285	845	1,200
Benzalkonium Chloride, U.S.P	500	300	350

The product is therefore outstandingly superior in microbicidal properties as evidenced by the above tests.

The amount of the compound to be employed may vary depending on the use to which it is to be applied, but will range from 2 to 200 parts per million in the treatment of water, and up to about 1,000 parts per million for other microbicidal applications. It may be sprinkled upon the water surface of a swimming pool or other body of water, or it may be introduced into circulating water as tablets or briquettes to disperse gradually, or it may be introduced into the water in bags or envelopes which will disintegrate. It may be combined with other substances as a component of a powder composition. It may be packed in bags or other light weight containers and stored for indefinite periods and shipped at a minimum expense for use at a desired time or place, in bulk or in measured amount for dosage. It will not deteriorate under the influence of the atmosphere nor will it unfavorably influence the packing material in which it is stored. And it may be handled in all these forms without hazard to personnel.

I claim:

1. Free-flowing crystals of dodecyl dimethyl-1,2,4,5-tetramethyl-benzyl ammonium chloride free of any deliquescent isomers thereof.

2. Free-flowing crystals of dodecyl dimethyl-1,2,4,5-tetramethyl-benzyl ammonium chloride monohydrate free of any deliquescent isomers thereof.

References Cited by the Examiner

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CHARLES B. PARKER, *Primary Examiner.*
ROBERT V. HINES, *Assistant Examiner.*