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QUATERNARY AMMONIUM COMPOUNDS

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18 Claims. (Cl. 260—127)

This invention relates to the manufacture of quaternary ammonium compounds which display bactericidal and fungicidal properties.

U. S. Letters Patent No. 2,108,765, issued February 15, 1938 (application Serial No. 719,592, filed April 7, 1934), refers to quaternary ammonium compounds containing at least one higher molecular aliphatic hydrocarbon radical attached to the nitrogen atom, which compounds are characterized by their bactericidal and fungicidal properties.

In further development of the said invention we have now found that among the ammonium compounds particularly also the formerly not described polyammonium compounds which contain at least one higher molecular aliphatic hydrocarbon radical attached to a quaternary nitrogen atom display considerable bactericidal and fungicidal properties, particularly with regard to antiseptic action. Therefore they can be used as disinfecting and preserving media for various purposes, for instance, as a mouth-wash, for disinfecting hands, dental prostheses and the like, animal material, such as meat, skins, blood, glands or other organs, for disinfecting table utensils, store-vessels, medical instruments, bandages, laundry, floors, walls, etc.

The higher aliphatic hydrocarbon radical which is present in the new compounds at least once preferably contains from 8 to 18 carbon atoms. Sometimes it is advantageous that the said radical is present in the form of that mixture which results when manufacturing the new polyammonium compounds by means of those higher alkylamines or alkylhalides which are obtained in the known manner from the mixture of fatty acids obtained by saponification of natural fats and resins, such as coconut oil, palm oil and colophony. The other radicals may be saturated or unsaturated alkyl groups or aralkyl groups, such as methyl, ethyl, propyl, isopropyl, butyl, allyl, crotyl, benzyl, phenylethyl and the like.

The new polyammonium compounds specified are preferably used in the form of their salts with acids, such as the hydrohalic acids, sulfuric and sulfonic acids, for instance, alkyl- and aryl-sulfonic acids, such as methane, ethane, benzene or toluene sulfonic acids, furthermore nitric and phosphoric acids or carboxylic acids, such as formic, acetic, lactic, citric, tartaric, benzoic acid and the like. These salts as well as the free ammonium bases in general readily dissolve in water and alcohols.

The substances specified kill coli-bacteria and staphylococci within a short time in concentra-

tions between about 1:1000 and 1:100000, and hinder the growth of the said bacteria in still lower concentrations.

The polyammonium compounds of the above specified kind may be used in substance as well as in solution or emulsion, eventually also in admixture with one another or with other active or inert substances, such as powders, ointment-bases, creams and the like.

The new polyammonium compounds containing at least one higher molecular aliphatic hydrocarbon radical are prepared for instance by causing aliphatic compounds containing at least two reactive substituents to react with tertiary amines. In this case at least one of the reagents must contain a higher aliphatic hydrocarbon radical. The aliphatic compounds above specified containing at least two reactive substituents are preferably the esters of polyvalent alcohols, for instance, with halogen hydracids or aromatic sulfonic acids.

On the other hand, also tertiary polyamines in which one or more nitrogen atoms may be nuclearly bound as is the case with tertiary piperazines, may be caused to react with reactive esters of alcohols, for instance alkyl halides or alkyl esters of sulfonic acids. In this case it is again required that at least one of the reagents contains a higher aliphatic hydrocarbon radical. The transformation of the tertiary polyamines into quaternary ammonium compounds may be carried out in several stages.

The new polyammonium compounds containing higher molecular aliphatic hydrocarbon radicals may likewise be obtained by reacting upon a tertiary amine with a quaternary ammonium compound containing a hydrocarbon radical with a reactive substituent. Also in this case one of the reagents must contain a higher aliphatic hydrocarbon radical. It is, for instance, possible to cause a trialkylammoniumalkyl halide to react upon a tertiary amine containing a higher aliphatic hydrocarbon radical. A higher aliphatic hydrocarbon radical may also be contained in the quaternary trialkylammoniumalkyl halide or also in both reagents.

The polyammonium compounds thus obtainable may contain substituents, such as hydroxyl groups, sulfhydryl groups and further, for instance, halogen atoms. The aliphatic radicals, in particular the higher aliphatic radicals, may likewise contain ether-like bound oxygen atoms or sulfur atoms.

It is understood that when using in the specification and in the appended claims the term

"higher molecular aliphatic radical" this term is intended to include also the said substitution products and the radicals which contain ether-like bound oxygen or sulfur atoms.

5 The invention is further illustrated by the following examples without being restricted thereto:

Example 1.—116 parts by weight of tetramethyl-ethylenediamine are heated with 498 parts by weight of dodecylbromide to 100° C. for several hours. After cooling the viscous sirup formed, which after prolonged standing solidifies to crystals, is dissolved in 9 times its weight of distilled water. In this manner a 10% aqueous solution of tetra-methyl-didodecyl-ethylenediammonium bromide is obtained.

10 The same compound is also obtained by causing methyl bromide to react upon symmetrical dimethyldidodecyl-ethylene-diamine in molecular quantities (2 mols of methyl bromide +1 mol. of dimethyldidodecyl-ethylenediamine) in a closed vessel at about 100° C.

15 The above described tetramethyl-didodecyl-ethylene-diammonium bromide may be transformed into the corresponding thiocyanate, nitrate or cyanide by reacting thereupon with 2 mols of potassium thiocyanate, silver nitrate or sodium cyanide. The free base may be obtained by treating the aqueous solution of the bromide with the calculated quantity of freshly precipitated silver hydroxide. After separating the silver bromide formed the base may be obtained by evaporating the solution.

20 Example 2.—116 parts by weight of tetramethyl-ethylenediamine are triturated with 469 parts by weight of dodecyloxymethyl chloride. After the reaction temperature has fallen the tetramethyl-didodecyloxymethyl-ethylene-diammonium chloride formed is recrystallized from benzene. It forms a crystalline powder of indefinite melting point, which is soluble in water and forms strongly foaming solutions.

25 Example 3.—501 parts by weight of dodecylthiomethyl chloride are added to 116 parts by weight of tetramethyl-ethylenediamine. The mixture is heated for several hours on the water bath. After cooling the reaction product is triturated and washed with cold benzene. The tetramethyl-di-dodecylthiomethyl-ethylenediammonium chloride thus obtained forms a yellowish white powder and yields strongly foaming solutions when dissolved in water.

30 Example 4.—284 parts by weight of tetrabutyl-ethylenediamine are triturated with 469 parts by weight of do-decyloxymethyl chloride. The mixture is then treated in accordance with the directions given in Example 2. The tetrabutyl-di-dodecyloxymethyl-ethylenediammonium chloride thus obtained forms a viscous sirup which is soluble in water.

35 Example 5.—146 parts by weight of N-tetramethyl-β-hydroxy-propylenediamine are treated with 498 parts by weight of dodecyl bromide and heated for 12 hours on the water bath. The tetramethyl-didodecyl-β-hydroxy-propylene-diammonium bromide is thus obtained in the form of a colorless viscous sirup which is soluble in water to a clear solution and the concentrated solution of which forms a highly viscous liquid.

40 The same compound is obtained by heating 426 parts by weight of dimethyldodecylamine with 218 parts by weight of glycerine-dibromhydrin at a temperature of 80–90° C.

45 Example 6.—590 parts by weight of dimethyloleylamine are heated with 281 parts by weight of tribromhydrin in a closed vessel for 12 hours

to 90–100° C. The viscous sirup formed is dissolved in water after cooling. In this manner a viscous solution of tetramethyl-dioleoyl-β-bromopropylenediammonium bromide is obtained.

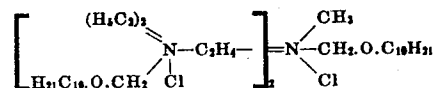
5 Example 7.—146 parts by weight of tetramethyl-β-hydroxy-propylenediamine are heated with 557 parts by weight of β-hydroxy-γ-dodecyloxy-propyl chloride for 12 hours to 100° C. The viscous sirup thus formed is dissolved in 19 times its weight of distilled water. In this manner a 10 5% solution of tetramethyl-di-(dodecyloxy-β-hydroxy-propyl)-β-hydroxy-propylene-diammonium chloride is formed.

15 Example 8.—454 parts by weight of symmetrical dimethyl-di-dodecyl-β-hydroxypropylenediamine are heated with 253 parts by weight of benzyl chloride for 10 hours to 100° C. The dimethyl-dibenzyl-di-dodecyl-β-hydroxypropylenediammonium chloride obtained forms a yellowish brown viscous sirup the aqueous solution of which 20 foams strongly.

Example 9.—229 parts by weight of methyl-bis-diethyl-aminoethyl-amine of the formula



25 are stirred with 619 parts by weight of decyloxymethyl chloride. After cooling the bis-(diethyl-decyloxymethyl-chloroammonium-ethyl)-methyl-decyloxymethyl-ammonium chloride of the formula



30 forms a yellowish viscous mass which is readily soluble in water.

35 Example 10.—424 parts by weight of symmetrical dimethyl-di-dodecylethylenediamine are heated with 341 parts by weight of benzylthiomethyl chloride for 3 hours to 80° C. After cooling the resin-like reaction product is dissolved in 9 times its quantity of distilled water. A clear solution of dimethyl-di-dodecyl-dibenzylthiomethyl-ethylenediammonium chloride is thus obtained.

40 Example 11.—135 parts by weight of diethyl-amino-ethyl chloride are heated with 171 parts by weight of benzyl bromide for 4 hours to 70–80° C. 213 parts by weight of dimethyl dodecylamine are added and the mixture is again heated for 6 hours to 90–100° C. After cooling the reaction product is dissolved in four times the quantity by weight of distilled water. In this manner a 20% solution of α-(dimethyl-dodecyl-chloroammonium) - β - (diethyl - benzyl - bromoammonium) - 45 ethane is obtained.

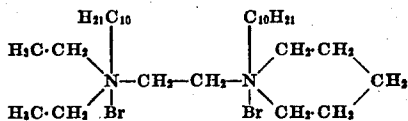
50 Example 12.—594 parts by weight of dimethyloctadecylamine are dissolved in 1000 parts by weight of dry benzene. The mixture is treated with an ice cold solution of 127 parts by weight of symmetrical dichloroacetone in 1000 parts by weight of dry benzene. After the reaction is complete the benzene is distilled off in vacuo and the tetramethyl-dioctadecyl-β-oxopropylene-diammonium chloride formed is dissolved in nine times the quantity by weight of distilled water.

55 Example 13.—114 parts by weight of N,N-dimethylpiperazine are triturated with 558 parts by weight of dodecyloxymethyl bromide. After the reaction temperature has fallen the mixture is dissolved in distilled water. A clear solution of dimethyl-di-dodecyloxy-methyl-piperazinium di-bromide is thus obtained.

60 Example 14.—342 parts by weight of symmetrical dimethyl-dioctyl - β - hydroxypropylenedia-

mine (prepared by reacting upon 2 mols of methyloctylamine with 1 mol. of glycerine-dibromohydrin) are heated with 242 parts by weight of allylbromide in a closed vessel at 90–100° C. during several hours. After the mixture is cold the reaction product is dissolved in nine times its quantity of distilled water. A 10% solution of dimethyl-diallyl-diocetyl- β -hydroxy-propylene-diammonium bromide is thus obtained.

Example 15.—184 parts by weight of N-diethyl-amino-ethyl-piperidine are heated with 442 parts by weight of decylbromide at 100° C. for 10 hours. After the mixture is cold the reaction product is dissolved in four times its quantity of water. A 20% solution of the N-(dimethyl-decyl-bromammoniumethyl)-decyl-piperidinium bromide of the formula



is thus obtained.

Example 16.—424 parts by weight of symmetrical dimethyl-didodecyl-ethylenediamine are heated with 252 parts by weight of dimethylsulfate at 80° C. for 6 hours. The symmetrical tetramethyl-didodecyl-ethylenediammonium-dimethosulfate is thus obtained.

Example 17.—100 parts by weight of tetramethyl-methylenediamine are heated with 498 parts by weight of dodecylbromide for 6 hours in a closed vessel to 90° C. Thus the tetramethyl-didodecyl-methylenediammoniumbromide is obtained which is readily soluble in water and alcohol.

When using instead of the tetramethyl-methylenediamine 158 parts by weight of tetramethyl-pentamethylenediamine the tetramethyl-didodecyl-pentamethylene-diammonium bromide is obtained. It is likewise readily soluble in water and alcohol.

We claim:—

1. Quaternary polyammonium compounds containing, attached to a quaternary nitrogen atom which is connected with another quaternary nitrogen atom by a lower aliphatic radical, at least one aliphatic hydrocarbon radical from 8 to 18 carbon atoms, and containing upon each quaternary nitrogen atom an anion selected from the group consisting of the hydroxyl anion and the anions of mineral and carboxylic acids, the excess valences of the nitrogen atoms being satisfied by radicals selected from the group consisting of alkyl, alkenyl and aralkyl radicals.

2. Quaternary polyammonium compounds containing, attached to each of the quaternary nitrogen atoms which are connected by a lower aliphatic radical, one aliphatic hydrocarbon radical from 8 to 18 carbon atoms, and containing upon each quaternary nitrogen atom an anion selected from the group consisting of the hydroxyl anion and the anions of mineral and carboxylic acids, the excess valences of the nitrogen atoms being satisfied by radicals selected from the group consisting of alkyl, alkenyl and aralkyl radicals.

3. Quaternary diammonium compounds containing, attached to a quaternary nitrogen atom which is connected with the other quaternary nitrogen atom by a lower aliphatic radical, at least one aliphatic hydrocarbon radical from 8 to 18 carbon atoms, and containing upon each quaternary nitrogen atom an anion selected from the group consisting of the hydroxyl anion and the

anions of mineral and carboxylic acids, the excess valences of the nitrogen atoms being satisfied by radicals selected from the group consisting of alkyl, alkenyl and aralkyl radicals.

4. Quaternary diammonium compounds containing, attached to each of the quaternary nitrogen atoms which are connected by a lower aliphatic radical, one aliphatic hydrocarbon radical from 8 to 18 carbon atoms, and containing upon each quaternary nitrogen atom an anion selected from the group consisting of the hydroxyl anion and the anions of mineral and carboxylic acids, the excess valences of the nitrogen atoms being satisfied by radicals selected from the group consisting of alkyl, alkenyl and aralkyl radicals.

5. Quaternary polyammonium compounds containing, attached to a quaternary nitrogen atom which is connected with another quaternary nitrogen atom by a lower aliphatic radical, at least one hydrocarbon radical from 8 to 18 carbon atoms, and containing upon each quaternary nitrogen atom an anion of a mineral acid, the excess valences of the nitrogen atoms being satisfied by radicals selected from the group consisting of alkyl, alkenyl and aralkyl radicals.

6. Quaternary diammonium compounds containing, attached to a quaternary nitrogen atom which is connected with the other quaternary nitrogen atom by a lower aliphatic radical, at least one aliphatic hydrocarbon radical from 8 to 18 carbon atoms, and containing upon each quaternary nitrogen atom an anion of a mineral acid, the excess valences of the nitrogen atoms being satisfied by radicals selected from the group consisting of alkyl, alkenyl and aralkyl radicals.

7. N.N.N'.N'-tetramethyl-N.N'-didodecyl- β -hydroxy-propylene-diammonium halides.

8. N.N.N'.N'-tetramethyl-N.N'-didodecyl- β -hydroxy-propylenediammonium bromide.

9. Quaternary diammonium compounds containing attached to each of the quaternary nitrogen atoms which are connected by a lower aliphatic radical one aliphatic hydrocarbon radical from 8 to 18 carbon atoms, two lower alkyl groups and an anion selected from the group consisting of the hydroxyl anion and the anions of mineral and carboxylic acids.

10. Quaternary diammonium compounds containing attached to each of the quaternary nitrogen atoms which are connected by a lower aliphatic radical one aliphatic hydrocarbon radical from 8 to 18 carbon atoms, two lower alkyl groups and an anion of a mineral acid.

11. Quaternary diammonium compounds containing attached to each of the quaternary nitrogen atoms which are connected by a lower aliphatic radical of 2 to 3 carbon atoms one aliphatic hydrocarbon radical from 8 to 18 carbon atoms, two lower alkyl groups and an anion selected from the group consisting of the hydroxyl anion and the anions of mineral and carboxylic acids.

12. Quaternary diammonium compounds containing attached to each of the quaternary nitrogen atoms which are connected by a lower aliphatic radical of 2 to 3 carbon atoms one aliphatic hydrocarbon radical from 8 to 18 carbon atoms, two lower alkyl groups and an anion of a mineral acid.

13. Quaternary diammonium compounds containing attached to each of the quaternary nitrogen atoms which are connected by a lower aliphatic radical of two to three carbon atoms one aliphatic hydrocarbon radical from 8 to 18 carbon

atoms, two lower alkyl and an anion of a hydrohalic acid.

14. Quaternary diammonium compounds containing attached to each of the quaternary nitrogen atoms which are connected by a lower aliphatic radical of 2 to 3 carbon atoms one dodecyl radical, two lower alkyl groups and an anion selected from the group consisting of the hydroxyl anion and the anions of mineral and carboxylic acids.

15. Quaternary diammonium compounds containing attached to each of the quaternary nitrogen atoms which are connected by a lower aliphatic radical of 2 to 3 carbon atoms one dodecyl radical, two lower alkyl groups and an anion of a hydrohalic acid.

16. Quaternary diammonium compounds containing attached to each of the quaternary nitro-

gen atoms which are connected by the β -hydroxypropylene radical one dodecyl radical, two lower alkyl groups and an anion selected from the group consisting of the hydroxyl anion and the anions of mineral and carboxylic acids.

17. Quaternary diammonium compounds containing attached to each of the quaternary nitrogen atoms which are connected by the β -hydroxypropylene radical one dodecyl radical, two lower alkyl groups and an anion of a hydrohalic acid.

18. N,N,N',N' -tetramethyl- N,N' -didodecyl- β -hydroxypropylene-diammonium compounds containing attached to each nitrogen atom an anion selected from the group consisting of the hydroxyl anion and the anions of mineral and carboxylic acids.

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