United States Patent Office

10

1

3,419,562 QUATERNARY AMMONIUM ACINITRO COMPOUNDS

Reginald L. Wakeman, Philadelphia, Pa., and Joseph F. Coates, Washington, D.C., assignors to Millmaster Onyx Corporation, New York, N.Y., a corporation of 5 New York

No Drawing. Continuation-in-part of application Ser. No. 352,675, Mar. 17, 1964. This application July 7, 1966, Ser. No. 563,387

1 Claim. (Cl. 260-286)

This invention relates to the preparation of relatively water-insoluble, biocidally active compounds obtained by the reaction of water-soluble, biocidally active quaternary ammonium compounds with water-soluble salts of ali-15 phatic nitro compounds containing four to twenty-four carbon atoms.

This is a continuation-in-part of co-pending application Ser. No. 352,675, filed Mar. 17, 1964, now abandoned.

Nitro compounds which may be used in this invention 20correspond to the following formula:

RCH=N-0Z

where R and R^1 may be branched or straight chain ali- 25 phatic, alicyclic, aromatic, heterocyclic radicals or combinations thereof. In general, any nitro compound containing four to twenty-four carbon atoms in which the carbon atom bearing the nitro group also has at least one 30 hydrogen atom may be used. Tertiary nitro compounds such as 2-nitro-2-methyl propane may not be used. Examples of suitable nitro compounds which may be used include primary and secondary nitroparaffins containing four to twenty-four carbon atoms, nitro olefins, nitro alco-35 hols and their derivatives containing four to twenty-four carbon atoms, beta nitrostyrene, phenyl nitromethane and the like.

The compounds of this invention can be prepared by mixing an aqueous solution of a water-soluble salt of the 40 nitro compound with an aqueous solution of a quaternary ammonium salt having biocidally active properties. The two solutions are thoroughly mixed and are then allowed to stand until they separate into two distinct layers. The upper layer will normally contain the compound of the 45 present invention. Layer separation is conveniently effected by conducting the reaction in a separatory funnel and drawing off the desired layer. The product usually contains some water which can be removed by distillation or drying in a vacuum oven. The aqueous product 50 layer can, however, be used directly in any process where the entrapped water would not be harmful.

Many of the nitro compounds that can be used in this reaction are available commercially. The Commercial Solvents Corporation, for example, manufactures 2-nitro-551-butanol. Those not commercially available can be readily synthesized by well-known methods. For example, the preparation of a variety of nitro compounds is described by N. Kornblum in "Organic Reactions," volume 12, pages 101-156 (John Wiley 1962).

Typical examples of the quaternary ammonium compounds which may be used in this invention are the alkyl trimethyl ammonium chlorides, alkyl-benzyl trimethyl ammonium chlorides, alkyl dimethyl benzyl ammonium chlorides, alkyl dimethyl menaphthyl ammonium chlo-65 rides, alkyl dimethyl substituted-benzyl ammonium chlorides in which the benzyl radical is substituted with one or more side chains containing from one to five carbon atoms such, for example, as methyl, dimethyl, ethyl and the like and in which the carbon atoms may all be in the 70same or different side chains or in which the benzyl radical bears one, two or more halogen atoms such as chlo2

rine or bromine, alkyl pyridinium chlorides, alkyl isoquinolinium chlorides and bromides, alkyl lower-alkyl pyrrolidinium chlorides, alkyl lower-alkyl morpholinium chlorides in all of which the alkyl group may have from eight to twenty-two carbon atoms and the lower alkyl group may have from one to five carbon atoms and alkyl phenoxy ethoxy ethyl dimethyl-benzyl ammonium chloride in which the alkyl radical may be iso-ocyl or nonyl and in which the benzyl radical may, if desired, be substituted by a methyl radical. Various other analogs of these quaternaries may also be employed such, for example, as cetyl dimethyl ethyl ammonium bromide or oleyl dimethyl ethyl ammonium bromide.

In general, the quaternary ammonium compounds useful in this invention are those wherein there is at least one alkyl group of 8 to 22 carbon atoms attached to the quaternary ammonium nitrogen and which has a phenol coefficient of at least 100 with respect to both Staphylococcus aureus and Salmonella typhosa at 20° C. These include the higher alkyl quaternary ammonium hydroxides, halides (chlorides and bromides), sulfates, methosulfates and the like possessing the following formula:



where R is an alkyl or alkaralkyl radical containing from eight to twenty-two carbon atoms or an alkyl phenoxy ethoxy ethyl radical in which R is an alkyl radical containing from eight to nine carbon atoms and in which the phenyl radical may be substituted by a methyl group; R' and R" are methyl or ethyl radicals or members of a heterocyclic ring system such as pyridine, isoquinoline, pyrrolidine and morpholine; R''' is a methyl radical or a benzyl group or a substituted-benzyl group such, for example, as a monochlorobenzyl radical or a dichlorobenzyl radical or mixture thereof or a methyl benzyl, dimethyl benzyl, ethyl benzyl, diethyl benzyl, isopropyl benzyl, tertiary butyl benzyl, isoamyl benzyl or another benzyl radical containing from one to five carbon atoms as side chains, either as a single side chain or a multiplicity of side chains including mixtures thereof or a menaphthyl group or hydrogenated menaphthyl group. When R' and R' are members of a morpholine or pyrrolidine ring, R''' is a methyl, ethyl, propyl or butyl group. When R'and R" are members of an unsaturated heterocyclic ring such as pyridine or isoquinoline, R''' is the same radical as R". X in the above formula corresponds to a halide radical such as chloride, bromide or iodide or to any other water-soluble anion such as methosulfate.

After thorough mixing in the manner previously described, the organic product layer is separated from the aqueous layer (as with a separatory funnel) since two distinct phases are formed. Separation may be facilitated by the addition of an organic solvent immiscible with water. The product layer may be washed with water to remove any residual by-product salt or unreacted materials. The solvent, if any, may be evaporated and the product air or vacuum dried to a paste, wax, oil or solid.

It is not necessary to use an aqueous medium. Any solvent or solvent mixture in which the starting materials are soluble will be satisfactory. Non-aqueous solvents facilitate the separation of by-product inorganic salt and reduce the need for vacuum drying to get an anhydrous product. When a non-aqueous medium is employed, it is usually necessary to add a small amount of water to facilitate ionic reaction.

An alternative method for the preparation of compounds especially applicable to the treatment of fabric, ropes, net, woven and non-woven fabric and reticulated

or convoluted materials, involves a two-step process. In the first step, the material is passed through a bath containing the anionic moiety. Excess solution is removed by methods well known to those skilled in the art. The treated material is then passed through a second bath 5 wherein the concentration of quaternary ammonium compound is such that the material pickup will result in an equivalent amount of quaternary ammonium compound reacting with the anionic moiety, depositing the product in the most intimate way on the surface and in the interstices, convolutions and reticulations of the material.

The method of adjustment of solution concentration to achieve the required pickup is well known to those skilled in the art. The order of treatment may be reversed without affecting the biological activity or durability of the product on the material. The products of this invention may be formulated as water dispersions by dissolving them in a water-miscible organic solvent such as acetone or methanol and diluting with water or by dissolving them in emulsifiable oils such, for example, as sulfonated castor oil or pine oil and diluting with water. In preparing aqueous dispersions, emulsifying agents such, for example, as ethylene oxide condensates of alkyl phenols may be used with or without organic solvents.

It is surprising that the compounds of this invention 25 exhibit high microbiocidal activty despite their relative insolubility in water. Because of their unusual combination of physical and microbiological properties, they can be used to impart laundry-resistant anti-microbial characteristics to textiles. They can also be used as the active 30 agent in anti-mildew finishes for testiles which are resistant to leaching with water.

Although the compounds have low water solubility, they are compatible with various organic solvents, plasticizers and high molecular weight compounds. Consequently, they may be incorporated as anti-microbial agents in synthetic resins and plastics. The compounds are compatible with natural and synthetic rubber latices. Therefore, they may be used to prepare bacteriostatic films and molded objects deposited from such latices.

The compounds can be incorporated into cutting and grinding fluids without precipitation. Also, they blend well with non-ionic and anionic surface active agents. In such compositions they retain their microbiological activity.

The compounds of this invention also possess effective $_{45}$ antistatic properties and may be incorporated in or used as a coating upon any product that is subject to static electricity. For example, they may be used to coat or impregnate wood, paper, ceramics, natural or synthetic polymers, etc. They may be coated upon the surface of $_{50}$ such products or intermixed with the components of a molded, cast or extruded product.

It will be understood that the properties of the products described herein will vary depending upon the nature of the cationic quaternary ammonium compound 55 used in their preparation as well as the anionic compound reacted therewith.

The chemical, physical and biological properties of the products of our invention make them especially appropriate for the following applications when suitably in- $_{60}$ corporated in active amounts in an appropriate vehicle, binder, medium or substrate:

(1) Mildewproofing, fabric, canvas, ropes, textiles, awnings, sails, tenting and other woven and non-woven reticulated materials.

(2) Paint mildewstats.

(3) Jet plane fuel additive to control growth of microorganisms.

(4) Odor preservative agents for clothes and shoes.
(5) Mildew retardant and odor suppressant for shoes 70 and other leather products.

(6) Topical antiseptics.

(7) Antidandruff agents.

(8) Disinfection agents for hair and gut of man and beast.

(9) Bacteriostatic furniture dressing.

(10) Surface finishes for stone, plaster, tile, cement, brick and other inorganic building materials to retard growth of micoorganisms, fungi, mold and algae.

(11) Wool preservative.

(12) Plant and tree spray to combat fungi.

(13) Antimycotic agents for soap wrappers.

(14) Self-sanitizing brushes.

(15) Mildewproofing agent in and on plastic and film. (16) Mildewproofing of cellulosics, cardboard, fibre-

board, paper and cordage.

(17) Contact biostat for application to film, waxes and cloth to preserve cheese, meats and vegetables and other food products.

15 (18) Algal inhibition, especially on surfaces and in solution where low foaming is desirable.

(19) Paper pulp slime control.

(20) Sanitizing agent for rug, carpet, curtains.

(21) Egg preservation.

(22) Adhesive preservation.

(23) Preservation of latex paints.

(24) Preservation of metal-working compounds.

(25) Additives for soap and for both anionic and nonionic detergents in liquid, bar, powder, bead, solution and other forms to impart bacteriostatic and fungistatic

properties thereto. (26) Antistatic coatings and impregnants.

The microbiocidal activity of our compounds has been

evaluated for microbiological stasis by the Standard Tube
30 Dilution Test, the technique for which is common knowledge to those skilled in the art. A Difco Bacto CSMA Broth #0826 was used in the study. This test is used to determine the lowest concentration of microbiologically active compounds which will inhibit the growth
35 of the organism in question. For a wide range of applications, the inhibition of growth rather than outright kill is satisfactory.

Briefly put, the Tube Dilution Test consists in placing 9 cc. of the CSMA Broth in a test tube which is then sterilized in an autoclave. One cc. solution of the microbiologically active compound at an appropriate concentration is added to the test tube which is then inoculated with 0.1 cc. of a twenty-four hour old culture of the organism under study. The test tube is then incubated 45 at 37° C. for forty-eight hours and observed for bacterial growth.

The same procedure is followed for fungi. In such tests, however, the tubes are incubated for fourteen days at a temperature suitable for optimum fungal growth, usually 25° C.

The invention is illustrated by, but not restricted to, the following examples:

EXAMPLE I

A 10% aqueous solution of the sodium salt of nitrocyclohexane, which may be made by reacting cyclohexane with dilute nitric acid and which is also available commercially from the Aldrich Chemical Co., Inc. Milwaukee, Wis., was prepared, and 130 grams of this solution 60 was placed in a separatory funnel. To this solution was added 350 grams of a 10% solution of lauryl isoquinolinium bromide (Onyx Chemical Corporation's "Isothan Q-75") and 100 ml. of benzene. The funnel was shaken and then layer separated and dried first on a steam bath and then in a vacuum oven to give 38 grams (99% yield) of a dark red syrup of lauryl isoquinolinium nitrocyclohexane enolate.

EXAMPLE II

An additional 130 grams of the nitrocyclohexane solution described in Example I was placed in a separatory funnel and 320 grams of a 10% solution of alkyl dimethyl ethylbenzyl ammonium chloride (Onyx Chemical 75 Corporation's "BTC-471"; alkyl distribution: C₁₂, 50%; 5

 $C_{14},\,30\%\,;\,C_{16},\,17\%\,;\,C_{18},\,3\%\,)$ was added along with 100 ml. of benzene. The funnel was shaken and the benzene layer separated and dried to give 37 grams (89% yield) of a yellow paste of alkyl dimethyl ethylbenzyl ammonium nitrocyclohexane enolate.

EXAMPLE III

160 grams of a 10% solution of the potassium salt of 1-nitrododecane, which may be prepared similarly to the nitrocyclohexane of Example 1, was placed in a 1 liter 10 separatory funnel together with 260 grams of a 10% solution of the quaternary ammonium compound shown in Example II. After 100 ml. of benzene was added, the funnel was well shaken. Layer separation was allowed to occur and the benzene layer separated and dried to 15 give 35 grams (97% yield) of an orange paste of alkyl dimethyl ethylbenzyl ammonium nitrododecane enolate.

To an additional 100 grams of the nitrododecane solution was added a chemically equivalent amount of alkyl dimethyl benzyl ammonium chloride (Onyx Chemical 20 Corporation's "BTC-824"; alkyl distribution: C14, 60%; C_{16} , 30%; C_{12} , 5%; C_{18} , 5%). Benzene was added and the solutions mixed. The product was worked up as above to give 149 grams (100% yield) of a yellow paste of alkyl dimethyl benzyl ammonium nitrododecane enolate. 25

Using the quaternary ammonium compound of Example I, a dark red viscous liquid of lauryl isoquinolinium nitrododecane enolate, in 98% yield, was obtained from 1-nitrododecane.

EXAMPLE IV

To 1 mol of undecenyl alcohol containing 0.5 cc. of pyridine and kept in an ice-salt mixture, there was added slowly, with stirring, 2 mols of thionyl chloride. The mix-ture was heated at 130°-140° C. until evolution of sulfur 35dioxide ceased. The excess of thionyl chloride was distilled off under diminished pressure and the residue was washed first with saturated aqueous sodium chloride solution, then with 10% aqueous sodium carbonate solution, and, finally, again with the sodium chloride solu-tion. The oil was taken up in ether, the solution was 40 dried and distilled under reduced pressure to yield 83% of 10-undecene 1-chloride. This product was reacted with silver nitrite in the manner described in "The Journal of the American Chemical Society," vol. 51, page 279 45(1929), to obtain 1-nitro-10-undecene. This product was then brominated in the standard manner to obtain 1nitro-10,11-dibromoundecane, which was then dehydrobrominated by the action of caustic potash to potassium salt of 1-nitro-10,11-undecyne.

50Stoichiometric amounts of the 1-nitro-10,11-undecyne and "BTC-471 (disclosed in Example II) were reacted in the same manner, and using the same procedures as in Example II, to yield a dark, viscous product identified as alkyl dimethyl ethyl-benzyl ammonium 1-acinitroundecyne.

EXAMPLE V

A 10% solution of the sodium salt of 2-nitro-1-butanol was prepared and reacted with a chemically equivalent amount of a 10% solution of lauryl isoquinolinium bro-60 mide. Extraction with benzene and drying yield a 100% yield of a red-brown paste of lauryl isoquinolinium 2nitro-1-butanol enolate.

EXAMPLE VI

Using the general procedure and the quaternary ammonium compounds of Examples I-V, the potassium salt of beta nitrostyrene was reacted with lauryl isoquinolinium bromide (red paste-98% yield), alkyl dimethyl benzyl ammonium chloride (orange paste-61% yield) and 70 alkyl dimethyl ethylbenzyl ammonium chloride (orange solid-98% yield).

(S.t.) and Aspergillus niger (A.n.). Zones were obtained as shown in Table I.

TABLE I			
Beta nitrostyrene reaction-product	Zones of inhibition, mm.		
W1011	S.a.	S.t.	A.n.
Alkyl dimethyl ethylbenzyl ammonium chloride	10.8	4.2	15.8
ride	28.26	7.0	26.24

EXAMPLE VII

Two of the quaternary-nitro aliphatic reaction products were run against Desulfovibrio desulfuricans according to the procedure outlined in the report of the American Petroleum Institute Subcommittee on Biological Analysis of Injection Waters To Be Used for Water Flood Purposes (March 17, 1958).

Reaction product of lauryl ethylbenzyl dimethyl ammonium chloride with—	Bacteriostatic level vs. Desulfovibrio desulfuri- cans (p.p.m.) at—
Sodium nitrocyclohexane	5.0
Potassium 1-nitrododecane	7.5

EXAMPLE VIII

Using the Standard Tube Dilution Test described above, the following bacteriostatic levels were determined (S.a.=Staphylococcus aureus; S.t.=Salmonella typhosa; A.n.=Aspergillus niger):

	Bacteriostatic dilution level vs.		
Product form	S.a.	S.t.	A.n.
Example I	105	104	103
Example II	105	105	105
Example IV	107	105	104

Obviously, many modifications and variations of the present invention are possible in the light of the above teachings. It is, therefore, to be understood that, within the scope of the appended claims, the invention may be practiced otherwise than as specifically described.

The invention claimed is:

1. A quaternary ammonium compound having a quaternary cation selected from the group consisting of alkyl dimethyl benzyl ammonium, alkyl dimethyl ethylbenzyl ammonium and alkyl isoquinolinium, wherein the alkyl, in each instance, has 12 to 18 carbon atoms, and having an anion selected from the group consisting of mono-acinitrocyclohexane, 1-acinitrododecane, 2-acinitro-1-butanol, beta-acinitrostyrene and 1-nitro-10,11-undecyne.

References Cited

UNITED STATES PATENTS

2,335,384	11/1943	Bousquet 167-22
2,700,683	1/1955	Tesoro et al 260-567.6
2,700,684	1/1955	Tesoro et al 260-567.6
3,054,749	9/1962	Bennett et al 167-22
3,097,132	7/1963	Weigand et al 167-33
3,223,704	12/1965	Shibe et al 260-286 XR

OTHER REFERENCES

Schwartz, "Surface Active Agents," vol. II, Interscience, 1958, p. 222 relied on.

ALEX MAZEL, Primary Examiner.

D. G. DAUS, Assistant Examiner.

U.S. Cl. X.R.

Solid=9870 yield).260-290, 247, 632, 644, 326.85, 567.6, 645, 501; 8-The latter two derivatives were subjected to the Agar260-290, 247, 632, 644, 326.85, 567.6, 645, 501; 8-Plate Test to determine zones of inhibition of growth<math>116.2, 128; 99-161, 222; 252-8.55, 8.57, 51, 107, 175;against Staphylococcus aureus (S.a.), Salmonella typhosa 75162-8; 106-3, 15; 167-13, 33, 38.5, 43, 42, 58, 30, 87

30