

1

2,907,791

AMPHOTERIC SURFACE-ACTIVE ORGANIC COMPOUNDS

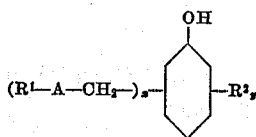
Adolf Schmitz and Gunther Cramer, Essen, Germany, assignors to The Goldschmidt A.G., Essen, Germany, a German company

No Drawing. Application May 16, 1955
Serial No. 508,768

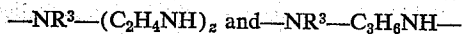
Claims priority, application Germany May 28, 1954

5 Claims. (Cl. 260—519)

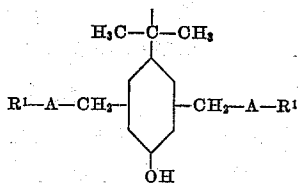
This invention relates to manufacture of amphoteric surface-active organic compounds; and it comprises a series of organic compounds having the general formula:



wherein x is an integer from 1 to 2, y ranges 0 to 3, but x plus y is not greater than 5, R^1 represents a substituent group selected from the class consisting of alkyl and aralkyl groups containing from 8 to 18 carbon atoms, A represents a divalent group selected from the class consisting of



z being an integer from 1 to 3 and R^3 representing a hydrogen substituent, and R^2 represents a substituent selected from the class consisting of methyl, halogen, carboxyl and the group



wherein A and R^1 have their former significances.

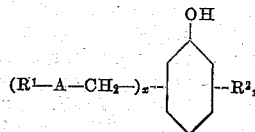
At the present time surface-active organic compounds are generally classified in accordance with the ion which contributes surface activity to the compounds. Thus anionic, cationic, nonionic and amphoteric surface-active compounds are recognized. Certain of the cationic and amphoteric compounds showing surface activity are also known to possess ability to kill pathogenic organisms, such as bacteria, fungi or rickettsia, and these compounds have come into use as disinfectants. Among the cationic compounds numerous quaternary ammonium compounds and quaternary phosphonium compounds have good bactericidal properties. In the amphoteric group of compounds derivatives of higher amino acids have achieved technical importance as disinfectants.

It has also long been known that certain phenols possess strong germicidal properties. Thus phenol itself, the cresols and the higher homologues of phenol, hydroxydiphenyl and benzylphenol all possess such properties. The germicidal effects are increased when the benzene nucleus contains in addition to the hydroxyl group certain other substituents, such as halogen atoms. It is also known that aliphatic substituents, containing from 5 to 6 carbon atoms for gram-negative, and 8 to 9 carbon atoms for gram-positive bacteria, increase the effectiveness of these phenol compounds.

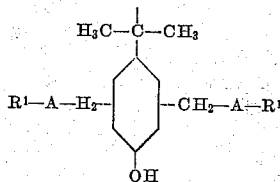
The present invention involves the discovery of a new group of amphoteric compounds which possess unexpectedly high germicidal properties and which ionize in

2

such fashion that the anion contains a phenol grouping while the cation contains at least two basic nitrogen atoms, one of which is attached to at least one high molecular organic group. These new compounds have the following general formula:

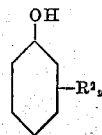


wherein x is an integer from 1 to 2, y ranges from 0 to 3, but x plus y is not greater than 5, R^1 represents a substituent group selected from the class consisting of alkyl and aralkyl groups containing from 8 to 18 carbon atoms, A represents a divalent group selected from the class consisting of $-NR^3-(C_2H_4NH)_z$ and R^3 representing a hydrogen substituent, and R^2 represents a substituent selected from the class consisting of methyl halogen, carboxyl and the group



wherein A and R^1 have their former significances.

These compounds can be produced in accordance with the present invention by reacting at elevated temperatures an amine of the formula R^1-A-H with formaldehyde and with a phenol having the formula:



wherein R^1 , R^2 , A and y have their former significances; the molecular proportions of amine and formaldehyde being about 1:1 while the molecular proportions of amine to phenol are from about 1:1 to 2:1, depending upon the number of R^1-A-CH_2- groups in the compound to be produced; and recovering the resulting amphoteric surface-active compound. The chemical reaction is usually exothermic but it is usually necessary to apply heat towards the end of the process in order to increase the yields. Aqueous formaldehyde can be used in the process and, if desired, an inert organic solvent can be added to the reaction zone.

The amines to be used in our process are primary amines having an alkyl or aralkyl group having from 8 to 18 carbon atoms and, in the case of secondary amines, an alkyl group containing from 8 to 18 carbon atoms, and which may contain from two to four $-NH-$ groups separated by ethylene or propylene groups. Specific examples are octyl amine, octyl-octadecyl amine, dodecylpropylene diamine, dodecyltriethylene triamine, octyldiethylene triamine, dodecylbenzyl triethylene tetramine, etc. The phenol to be employed may be phenol itself and phenols which are substituted with from 1 to 3 substituents, such as methyl groups, halogen groups, hydroxyl or carboxyl groups. Specific phenols found to be operative are phenol, o-, m- and p-cresol, p-chloro-m-cresol, p-chloro-m-xyleneol, p-hydroxy-benzoic acid, salicylic acid, etc. The formaldehyde can be employed in aqueous or alcoholic solution.

The novel compounds of the present invention are for the most part non-crystallizing hygroscopic oils, insoluble in water, which give neutral or alkaline reactions, depending on the number of acid or alkaline groups therein,

On the addition of acids or alkalis to their aqueous suspensions, however, there result clear solutions of good foaming quality.

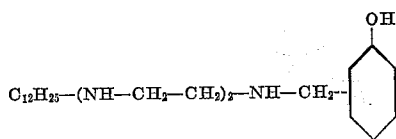
The bacteriological efficacy of our new compounds extends to gram-positive as well as gram-negative bacteria, this being an essential advantage over the cation-active surface-active compounds, and it exceeds that of the previously known amphoteric surface-active disinfectants 3 to 4 times. For instance, the compound of the following Example 8 reliably kills *Micrococcus aureus*, *Escherichia coli* and *Bacterium proteus vulg.* in a dilution of 1:8,000 after 10 minutes. Our compounds are also efficacious against *Mycobacterium tuberculosis*. Tubercle bacteria are killed by the compound of Example 9 in 0.1% solution after 30 minutes, in 0.05% solution after 60 minutes. In the presence of serum the efficacy is not appreciably impaired.

In practical use our compounds are usually transformed into their salts with organic or mineral acids and then dissolved in water to give solutions containing from 5 to 25% by weight of the salt. Some of the mineral acid salts are only slightly soluble in water and in these cases the salts of organic acids are used, for example the salts of formic, acetic and lactic acid can be employed. The salt solutions are usually diluted to a concentration of from about 0.05 to 2% before actual use which possess a considerably lower surface tension to water. A 0.1% solution of the acetate of the compound as per Example 10 has a surface tension of 32 dynes per centimeter. These solutions may have their pH values adjusted within the range of from about 4.5 to 8 without impairment of their effectiveness. This tolerance to pH change represents an important advantage over the surface-active amino acid derivatives which are used as disinfectants. Our compounds are also effective throughout a relative wide temperature range, being effective from about 15° to 75° C.

Solutions of our new compounds, because of their high bactericidal efficacy combined with their good detergent properties, are excellent for rough disinfection in hospitals, bathing establishments, wash rooms of industrial plants, toilets etc., as well as for disinfection of plants of the food industry, such as dairy operations, slaughterhouses, etc. In view of their high wetting and detergent effects these compounds represent an important advance in the field of germicidal and fungicidal agents having a cleaning action.

Our invention can be explained in greater detail by reference to the following specific examples which describe practical embodiments of our process of producing our novel amphoteric surface-active compounds.

Example 1.—Dodecyl-di-(aminoethyl)-aminomethylphenol

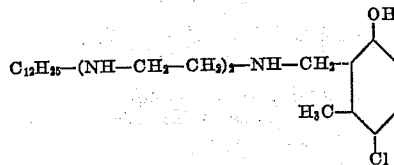


A mixture is made of 94 parts by weight of phenol, 271 parts by weight of dodecyl-diethylenetriamine and 81 parts by weight of a 37% formaldehyde solution, corresponding to 30 parts by weight of formaldehyde. The reaction occurs as in Example 1 with intense evolution of heat and is completed by heating for one hour on a boiling water bath. The resulting light-yellow syrupy liquid is soluble as a clear solution both in dilute bases and dilute organic acids, such as acetic acid and lactic acid.

Dodecyl-aminoethyl-aminomethyl phenol can be obtained by substituting 228 parts dodecyl-ethylene diamine for the 271 parts of dodecyl-diethylenetriamine used in the above process. Also dodecyl-aminopropyl-aminomethyl phenol can be obtained by substituting 242 parts

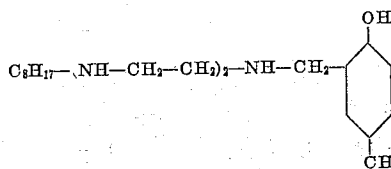
of dodecyl-propylene diamine for the 271 parts of dodecyl-diethylenetriamine used in the above process.

Example 2.—Dodecyl-di-(aminoethyl)-aminomethyl-p-chloro-m-cresol



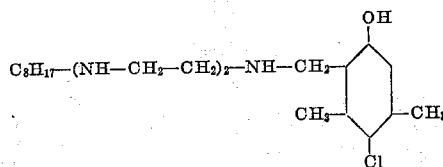
271 parts by weight of dodecyl-diethylenetriamine are condensed with 142 parts by weight of p-chloro-m-cresol and 30 parts by weight of formaldehyde as described in Example 1. After 1½ hours over the boiling water bath the reaction is terminated. The solubilities are the same as those described in Example 1.

Example 3.—Octyl-di-(aminoethyl)-aminomethyl-p-cresol



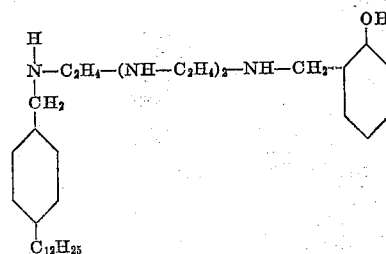
215 parts by weight of octyl-diethylenetriamine and 108 parts by weight of p-cresol are reacted, as described above, with 30 parts of formaldehyde. After heating on a boiling water bath for one hour there is formed an oily yellow liquid which is soluble in both dilute alkalis and acids.

Example 4.—Octyl-di-(aminoethyl)-aminomethyl-p-chloro-m-xenol



By reacting 215 parts by weight of octyl-diethylenetriamine, 156 parts by weight of p-chloro-m-xenol and 30 parts by weight of formaldehyde there results after 1½ hours at 100° C. a yellow liquid having the same solubility properties as the compounds described above.

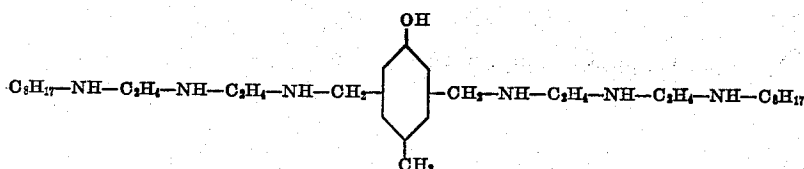
Example 5.—Manufacture of dodecylbenzyl-tri(aminoethyl)-aminomethyl phenol



404 parts by weight of dodecylbenzyl-triethylenetetramine, 94 parts by weight of phenol and 30 parts by weight of formaldehyde are reacted together as described above. The first reaction after addition of the formaldehyde heats the mixture to 80° C. After 1½ hours at 100° C. there results a yellow substance, which upon cooling is highly viscous and almost pulverizable, and which like the previous compounds can easily be dissolved in bases and dilute acids. Staphylococci are killed by a 0.1% solution of this compound in 1 minute.

5

Example 6.—Bis-[octyl-di-(aminoethyl)-aminomethyl]-*p*-cresol

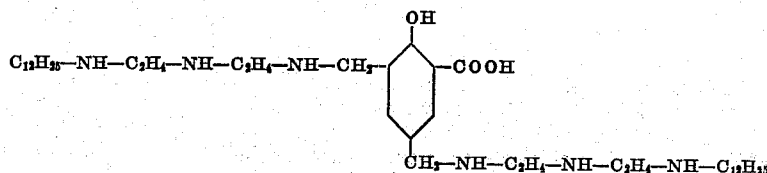


21.9 parts by weight of octyldiethylenetriamine, 5.4 parts by weight of *p*-cresol and 3 parts by weight of

used as a disinfecting-cleansing solution, preferably after dilution.

6

Example 8.—Bis[dodecyl-di-(aminoethyl)-aminomethyl]-salicylic acid

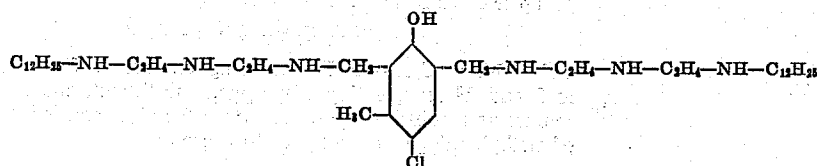


54.2 parts by weight of dodecyl-diethylenetriamine are heated with 13.8 parts by weight of salicylic acid on a boiling waterbath with mechanical agitation until a clear solution is obtained. The mixture is then cooled to 40° C. and then 20 parts by weight of a 30% aqueous solution of formaldehyde are added. This causes the temperature to rise to about 70° C. After the first reaction has died down, heating is continued on a boiling waterbath for another two hours. A yellow-brown viscous oil is formed which is readily soluble in dilute acids and alkali-

formaldehyde, as a 37% aqueous solution, are reacted together as above. The reaction product is a viscous yellowish liquid of distinctly amphoteric properties. On admixture of an aqueous suspension with concentrated hydrochloric acid the hexachloride is formed as a colorless, fine-crystalline precipitate, having the analysis:

$C_{33}H_{72}ON_6Cl_6$ (mol. wt. 781).—Found: Cl, 27.5%; N, 10.7%. Calculated: Cl, 27.3%; N, 10.75%.

Example 7.—Bis[dodecyl-di-(aminoethyl)-aminomethyl]-*p*-chloro-*m*-cresol



17.75 parts by weight of *p*-chloro-*m*-cresol, 69.5 parts by weight of dodecyldiethylenetriamine and 8 parts by weight of formaldehyde as a 37% aqueous solution are reacted together as described under Example 1. This results in a viscous oil readily soluble in acids and alkalis from which a fine-crystalline hexachloride can be obtained with concentrated hydrochloric acid. This hexachloride has the analysis:

$C_{41}H_{87}ON_6Cl_7$ (mol. wt. 927.5).—Found: Ionogenic

Cl, 23.9%; total Cl, 26.86%; N, 9.75%. Calculated: Ionogenic Cl, 23.0%; total Cl, 26.80%; N, 9.06%.

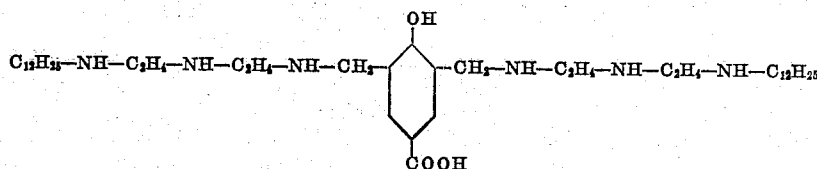
68.5 parts by weight of the almost pure reaction product are stirred up with 18.4 parts by weight of an approximately 80% lactic acid without addition of a solvent, whereupon an intensive heat of neutralization develops. After cooling, the still oily product is stirred into 740 cc. of water to form a 10% clear solution. This can be

lies. From a 50% alcohol solution a fine-crystalline hexachloride can be isolated after adding concentrated hydrochloric acid. This has the analysis:

$C_{41}H_{86}O_3N_6O_6$ (mol. wt. 923).—Found: Cl, 23.1%. Calculated: Cl, 23.1%.

25.16 parts by weight of the almost pure product are dissolved with a mixture of 65.6 cc. of N/2 HCl and 409 cc. of water with gentle heating. The concentration of this solution is 5%. It is an excellent cleansing and disinfecting agent.

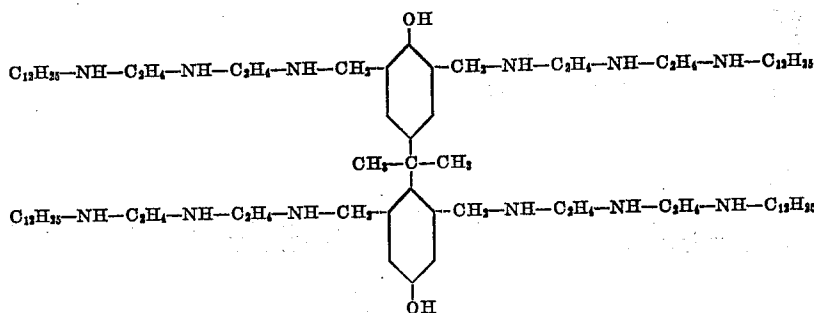
Example 9.—Bis-(dodecyl-diethylenetriaminomethyl)-*p*-hydroxybenzoic acid



27.8 parts by weight of dodecyldiethylenetriamine are reacted with 6.9 parts by weight of *p*-oxybenzoic acid and 3 parts by weight of formaldehyde are added, as described in Example 7, to form a yellow viscous paste. On treating a 50% alcohol solution of this with concentrated hydrochloric acid while cooling with ice, a fine-crystalline almost colorless hexachloride is formed having the analysis:

$C_{41}H_{86}O_3N_6Cl_6$ (mol. wt. 923).—Found: Cl, 22.7%; N, 0.07%. Calculated: Cl, 23.1%; N, 9.1%.

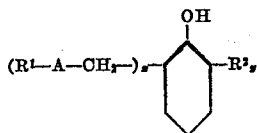
Example 10.—2,2-bis-[p-hydroxy-m,m-di(dodecyl-diethylenetriaminomethyl)-phenyl]-propane



22.8 parts by weight of 2,2-bis-(4,4'-dioxy-diphenyl)-propane are mixed with 110.1 parts by weight of dodecyl-diethylene-triamine and with 32.6 parts by weight of a 37% aqueous formaldehyde solution. After the initial reaction has died down, which reaction is accompanied by intensive evolution of heat, the product is heated on a boiling waterbath for 1 hour. There is formed a very viscous yellow oil which dissolves only slightly in water but readily in acids and alkalis. With concentrated hydrochloric acid there is formed a crystalline, slightly soluble salt which it was possible to identify as dodeca-chloride. This has the analysis:

$C_{83}H_{176}O_2N_{12}Cl_{12}$ (mol. wt. 1798).—Found: Cl, 23.3%; N, 9.2%. Calculated: Cl, 23.65%; N, 9.33%.

It is believed to be within the skill of the art, with the assistance of the above examples, to produce any of the specific compounds which fall within the scope of the general formula



since it is only necessary to react a phenol, substituted with from 0 to 3 of the groups R^2y , with formaldehyde and with an amine of the formula R^1-A-H at elevated temperatures, with the molar proportions of the amine and formaldehyde being 1:1 and the molar proportions of the amine and the phenol ranging from 1:1 to 3:1, depending upon the number of R^1-A-CH_2- substituents desired in the compound and, of course, taking into consideration the number of positions available for substitution in the phenol nucleus. Thus x plus y can never equal more than 5.

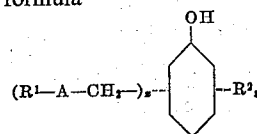
While we have described what we consider to be the most advantageous embodiments of our process and products it is evident, of course, that various modifications can be made in the specific procedures which have been described without departing from the purview of this invention. Thus the several components of the chemical reaction which is involved in the production of our compounds can be dissolved or suspended in an inert organic solvent if desired but it is usually more convenient to employ water as the reaction medium since formaldehyde is readily available in aqueous solution. Compounds having different R^1-A-CH_2- substituents can be produced by using a mixture of different amines in place of a single amine. It is convenient to conduct the chemi-

cal reaction of our process at temperatures below the boiling point of the reaction medium but higher tempera-

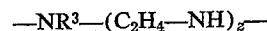
tures can be employed and superatmospheric pressures can be used if desired. Other modifications of our process which fall within the scope of the following claims will be immediately evident to those skilled in the art.

What we claim is:

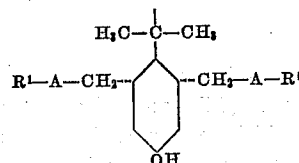
1. Amphoteric surface-active organic compounds having the general formula



wherein x is an integer from 1 to 2, y ranges from 0 to 3, R^1 represents a substituent group selected from the class consisting of alkyl and aralkyl groups containing from 8 to 18 carbon atoms, A represents a divalent group selected from the class consisting of



and $-NR^3-C_3H_6-NH-$, z being an integer from 1 to 3 and R^3 representing a hydrogen substituent, and R^2 represents a substituent selected from the class consisting of methyl, halogen, carboxyl and the group



wherein A and R^1 have their former significances.

2. As a new amphoteric surface-active compound bis[dodecyl-di(aminoethyl)-aminomethyl]-salicylic acid.

3. As a new amphoteric surface-active compound dodecyl-di-(aminoethyl)-aminomethyl-p-chloro-m-cresol.

4. As a new amphoteric surface-active compound octyl-di-(aminoethyl)-aminomethyl-p-cresol.

5. As a new amphoteric surface-active compound octyl-di-(aminoethyl)-aminomethyl-p-chloro-m-xyleneol.

References Cited in the file of this patent

UNITED STATES PATENTS

2,098,869	Harmon et al.	Nov. 9, 1937
2,260,967	Bruson	Oct. 28, 1941
2,363,134	McCleary	Nov. 21, 1944

OTHER REFERENCES

Bovet et al.: Chem. Abstracts 42, 982f (1948).