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3,795,704

## ANTI-MICROBIALY ACTIVE SURFACE-ACTIVE COMPOUNDS

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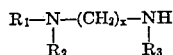
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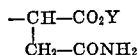
4 Claims

### ABSTRACT OF THE DISCLOSURE

Ampholytic compounds of the Formula I



in which  $R_1$  is a lipophilic group,  $x$  is 2 or 3, one of the radicals  $R_2$  and  $R_3$  stands for a moiety of the Formula II



and the other one stands for hydrogen or also for the moiety of the Formula II, and  $Y$  is hydrogen or an alkali metal ion, and the use of these ampholytic compounds as anti-microbially active surface-active substances.

The present invention relates to anti-microbially active compounds having surface-active properties. These compounds retain their anti-microbial action, i.e. their activity towards fungi, actinomycetes, bacteria and viruses, in the presence of surface-active cleansing compositions, especially textile cleansing compositions.

The known surface-active compounds which have good cleansing properties, in general, have no anti-microbial action. On the other hand, certain cationic compounds, for example quaternary ammonium compounds, which are active against certain bacteria types have only moderate cleansing properties. Hitherto, if the combating of bacteria and fungi was to be achieved simultaneously with cleansing, two separate treatments have generally been necessary, namely a normal washing step and a subsequent, separate treatment of the washed material with an anti-microbial agent in a suitable physical form, for example a solution or dispersion.

In many cases it would be more practical and effective if the cleansing composition and the anti-microbial agent could be used simultaneously or, if desired, if both effects could be combined in a single preparation. Attempts have already been made in this field; however, they have not provided satisfactory results. One reason for the past failures can be seen in the reciprocal action which occurs between most anti-microbial agents and the soap or synthetic surfactant. This incompatibility results either in a diminished cleansing efficiency of the surface-active agent or in the partial or complete inactivity of the anti-microbial agent or in both.

Striking examples of such a reciprocal action occur in preparations which contain anionic surface-active cleansing compounds, inclusively soaps and non-soap

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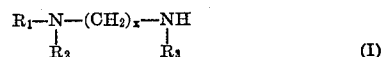
compounds, as well as the hitherto known anti-microbial agents. In these cases, the cleansing efficiency of the anionic cleansing composition is usually worse than when used alone and also the activity of the anti-microbial agents is substantially inferior than when used alone. A similar reciprocal action is also encountered in preparations which contain non-ionic cationic or amphoteric surface-active agents.

In recent times some anti-microbial agents which are compatible with certain cleansing compositions have been available (for example bromosalicyl anilide and carbanilide), which confers to soaps and synthetic cleansing compositions an inhibiting or destroying action towards gram positive bacteria, for example, *staphylococcus aureus*, *bact. ammoniagenes* and *lactobacillus casei*. On the other hand, suitable agents which would be compatible with soap and cleansing compositions and give them a considerable action also against the resistant gram negative bacteria, for example *escherichia coli*, *proteus mirabilis* and *pseudomonas aeruginosa*, and fungi, for example *candida albicans*, are still not available.

Until now no prediction has been possible as to how a given anti-microbial agent will behave in a washing preparation. Some of the numerous unknown factors which influence the behavior of the agent are, for example, the complex nature of the cleansing composition itself, the dirt present, the variety of the textiles to be cleaned, and the different ionogenic properties of the compounds.

Suitable anti-microbial agents are especially wanted for use in preparations of cleansing compositions intended for laundering purposes. For this purpose it is desirable that a residue of the disinfection agent remain on the textile after the laundering, so that a long-lasting action results. Therefore, for the laundering of textiles, anti-bacterial agents are desired which are applicable in washing solutions and remain behind on the textile, and thus prevent the reproduction of bacterial and/or fungi as well as the penetration of body odor into the textile. A similar treatment is especially advantageous with underwear, especially when the adhering anti-microbial agent is also active against-gram-negative bacteria. Anti-bacterial agents, which are compatible with soaps and synthetic cleansing compositions, are also used in deodorizing and cosmetic soaps. The latter application requires that the active compound has an adhesiveness to human skin, so that a residue of the agent remains behind on the skin after the washing-treatment and might thus inhibit the microbial population, which decompose sweat with the simultaneous formation of odor.

It has now been found that ampholytic compounds of the general Formula I



in which  $R_1$  stands for an alkyl or alkenyl radical having 8 to 18 carbon atoms, one of the radicals  $R_2$  and  $R_3$  stands for the moiety of the Formula II

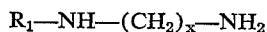


and the other one stands also for the radical of the Formula II or for hydrogen, and  $Y$  stands for hydrogen or an alkali metal ion, and  $x$  stands for 2 or 3, are excellent anti-microbially active surface-active substances that re-

tain their anti-microbial activity even in the presence of other surface-active washing and cleansing agents.

As lipophilic group  $R_1$  of the novel ampholytic compounds, there are mentioned saturated or olefinically unsaturated straight-chain or branched aliphatic hydrocarbon radicals which contain from 8 to 18, preferably from 12 to 18, carbon atoms.

The ampholytic compounds of the invention may be prepared by reacting a N-alkyl-alkylene diamine of the formula



in which  $R_1$  and  $x$  are defined as above, or a mixture of such a N-alkyl-alkylene diamine with a maleic acid semi-amide in an aqueous or aqueous alcoholic phase, advantageously at an elevated temperature to accelerate reaction. Salts of the maleic acid semi-amide may also be used for the reaction especially the alkali metal or ammonium salts, preferably the ammonium salt thereof, since this is easily obtainable and, upon reaction, sets free ammonia so that the ampholytic compound is obtained directly in the form of the inner salt. When alkali metal salts, for example the sodium or potassium salt, of the maleic acid semi-amide are used, the reaction with the diamine yields the compounds of the Formula I in the form of the corresponding alkali metal salts that can be converted, where required, into the inner salts by adding an acid until the pH-value of the equipotential point has been reached.

A special advantage of the ampholytic compounds of the present invention is that they retain their anti-microbial action even in the presence of anionic, cationic, and non-ionic surfactants and also in the presence of organic and inorganic builders. The ampholytic compounds of the invention can, therefore, be added to conventional washing agents and cleansing compositions as well as to soft-rinsing agents or can be used in conjunction with such agents.

Surface-active substances and builders, such as are used for the manufacture of washing agents and cleansing compositions together with the novel ampholytic compounds of the invention, are mentioned, for example, in Schwartz, Perry, Berch, "surface-active agents and detergents," volume II (1958), pages 25 to 138 and 288 to 317. The washing agents and cleansing compositions may further contain optical brightening agents, perborates and enzymes without impairing the anti-microbial action of the ampholytic compounds of the invention. In addition, other known additives and diluents, for example perfumes, fluorescence agents, foam-promoting or foam-depressing agents as well as auxiliaries preventing deposits, do not lessen the advantageous action of the ampholytic compounds of the invention.

The ampholytic compounds of the present invention are highly active and hence a small amount is sufficient to give the washing agent or cleansing composition an anti-microbial action. The amount of the ampholytic compounds added to the washing agent or cleaning composition may vary within wide limits. The amount used depends, primarily, upon the anti-microbial effect desired for the washing agent or cleansing composition. An amount of from 0.1 to 10%, calculated on the weight of the washing agent, cleansing composition or soft-rinsing agent is generally employed. The preferred range of concentration of the ampholytic compounds is, however, 0.5 to 5% by weight, calculated on the washing agent or cleansing composition. The upper limit of the amount of the ampholytic compounds of the invention is mainly dependent on economic considerations and, if necessary, upon the solubility properties. An increase in concentration augments, as is to be expected, the anti-microbial action of the washing agent or cleansing composition.

The ampholytic compounds of the present invention can be incorporated into soaps, washing or cleansing preparations according to any method provided an even distribution in the entire mass is guaranteed. In doing so

the good compatibility of the ampholytic compounds with the above-mentioned soaps and non-soapy washing agents or cleansing compositions in the form of, for example, bars, liquids, flakes and granules becomes apparent. Even under the influence of sun-light the ampholytic compounds of the invention do not cause any decoloration of the soaps, washing agents or cleansing compositions. In this respect, the ampholytic compounds of the invention are superior to the known anti-microbial additives based on bisphenolic compounds.

A further advantage associated with the use of the ampholytic compounds of the present invention is that they are substantively absorbed by fabrics comprising, for example, wool or cotton during washing or rinsing with a washing or rinsing agent containing a compound of the invention. Thereby, the textiles obtain a long-lasting anti-microbial protection.

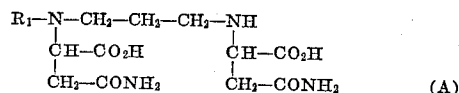
The anti-microbial action on textiles is tested by the textiles protection test. This test essentially comprises first washing a sample with a known washing liquor and subsequently treating it in an aqueous solution with a soft-rinsing agent which contains the anti-microbially active agent, drying the sample and placing it on a nutrient agar, to which the bacteria used for the test have been added. After a short time the samples are removed and the agar plates incubated at 37° C. for 24 hours. Due to the anti-bacterial action, no growth of bacteria is observed on the bearing surfaces and their surroundings.

The ampholytic compounds of the present invention cover such a broad range of action that they may be used, for example, as disinfection agents, and more especially, for medicinal and hygienic purposes. Their use in soaps and cleansing compositions, for example heavy duty of fine washing agents and soft-rinsing agents, is of special interest since their anti-bacterial action is retained in the presence of such agents. This favorable behavior of the ampholytic compounds of the invention renders possible the combination of a washing agent, cleansing composition or rinsing agent and an anti-microbially active agent in one preparation.

The following examples serve to illustrate the invention, the parts and percentages being by weight unless stated otherwise.

#### EXAMPLE 1

(A) A solution of 52.8 parts of the ammonium salt of maleic acid semi-amide (prepared from maleic acid anhydride and gaseous ammonia in chloroform) in 200 parts of water is stirred at 92° C. for 2.5 hours with 53 parts of coco fat propylene diamine (having a content of basic nitrogen of 10.6%). During the reaction ammonia develops. The liquid is concentrated under reduced pressure (in a rotary evaporator) by distilling off water. The pasty residue is dried in vacuo at a temperature of about 50° C. The compound of the formula



in which  $R_1$  stands for an alkyl group of 8 to 18 carbon atoms, corresponding to the chain distribution of the coco fatty acid, is obtained as a yellowish solid substance which can be ground to a fine powder.

The acid number is 230 (calc. 227) and the content of basic nitrogen is 6.1% (calc. 5.66%).

The pH-value of the 1%-solution in water is 5.5 (by potentiometry).

When 54.7 parts of the sodium salt of maleic acid semi-amide are used for the reaction under the same conditions instead of 52.8 parts of the ammonium salt of maleic acid semi-amide, the above-mentioned Compound (A) is obtained not in the form of the inner salt but as the sodium salt.

(B) A mixture of 132 parts of the ammonium salt of maleic acid semi-amide, 274 parts of coco fat propylene



TABLE III.—BACTERICIDAL CONCENTRATION

	Type of germ				
	<i>Staph. aureus</i> , γ/ml.	<i>E. coli</i> 055, γ/ml.	<i>Proteus mirab.</i> , mg./ml.	<i>Ps. aeruginosa</i> , mg./ml.	<i>Cand. albicans</i> mg./ml.
Product A:					
5'-----	350	350	>10	1.25	1.25
15'-----	350	160	5	1.350	1.625
Comparison I:					
5'-----	(?)	(?)	(?)	(?)	(?)
15'-----	(?)	(?)	(?)	(?)	(?)
Comparison II:					
5'-----	156	(?)	(?)	(?)	1.25
15'-----	156	(?)	(?)	16	1.350

<sup>1</sup> γ/ml. <sup>2</sup> Ineffective.

The results were obtained in a series dilution test, which was performed in agreement with the procedure of "Richtlinien fuer die Pruefung chemischer Desinfektionsmittel" (Gustav-Fischer Verlag, Stuttgart, Germany (1959)), edited by the German Society for Hygiene and Microbiology. In these tests, the minimal inhibition concentration (MIC) has been determined. This is the minimal concentration ascertained in the pure dilution test, in the weight unit per cubic centimeter of the test solution of an anti-microbially active substance, at which no increase of the examined organisms could be observed.

The bactericidal activity (bactericidal concentration) was also tested in germ suspension tests according to the criteria indicated above. The results of these tests are represented in Table III.

## EXAMPLE 2

A synthetic heavy-duty detergent, which has a granular builder, consists of the following components:

- 8.00% of the sodium salt of secondary alkanesulfonic acid (average molecular weight 328), prepared by sulfoxidation of a mixture of n-paraffins with 13 to 18 carbon atoms,
- 5.00% of an addition product of 15 mols of ethylene oxide to 1 mol of tallow-fatty alcohol
- 3.00% of sodium soap
- 37.00% of sodiumtripolyphosphate
- 7.00% of sodium metasilicate
- 3.00% of magnesium silicate
- 4.00% of carboxymethyl cellulose
- 0.30% of an optical brightener
- 0.15% of perfume oil
- 20.00% of sodium-perborate
- the remainder, to 100 percent of water
- 0.1 percent or 0.01 percent of Product A

were added to said detergent mixture for obtention of the anti-microbial effect desired.

In solutions of 0.3 g. per liter of the pure detergent mixture (without the disinfection component), the minimum inhibition concentration of the ampholytic compounds of the invention was determined according to the above-specified method and compared with the MIC-values found for the detergent alone. It appeared that the heavy-duty detergent practically did not impair the anti-microbial activity of the ampholytic Compound A. The results of the tests are compiled in Table IV.

TABLE IV

[Minimum inhibition concentration (γ/ml.) in the presence of heavy-duty detergents]

Type of germ	Product A alone	Detergent alone	Product A in detergent solution of 0.3 g./l.
<i>Str. faecalis</i> -----	78.2	1,250	156
<i>E. coli</i> -----	156	1,250	313

The same tests were performed on heavy-duty detergents of the above-mentioned composition which, how-

ever, contains instead of 8.0% of the secondary sodium salt of alkane-sulfonic acid:

- (a) 8.00% of a mixture of equal parts of the sodium salts of an α-olefin sulfonate having 15 to 18 carbon atoms and of the secondary alkane-sulfonate, and
- (b) 8.00% of the sodium salt of dodecyl-benzene-sulfonic acid.

In both cases, no impairment of the anti-microbial activity of the ampholytic compounds of the invention by the detergents was ascertained.

## EXAMPLE 3

A high-duty detergent consists of the following components:

- 10.00% of an addition product of 8 mols of ethylene oxide on 1 mol of coco fatty acid,
- 10.00% of an addition product of 5 mols of ethylene oxide on 1 mol of isotridecyl alcohol,
- 40.00% of sodium tripolyphosphate,
- 5.00% of sodium silicate,
- 10.00% of calcined sodium carbonate,
- 2.00% of carboxymethyl cellulose, and
- the remainder to 100% of sodium sulfate.

To render the detergent antimicrobially active, an ampholytic compound of the invention, for example Product A, may be added in an amount depending on the effect desired.

In solutions of 5 g. per liter of the pure high-duty detergent, the minimum inhibition concentration for Product A was determined in a manner analogous to Example 2 and compared with the values ascertained for the detergent alone and for Product A alone. The results obtained are compiled in Table V.

TABLE V

[Minimum inhibition concentration (γ/ml.)]

Type of germ	Product A	High-duty detergent	Product A in high-duty detergent solution of 5 g./l.
<i>Str. faecalis</i> -----	78.2 γ/ml.	5 mg./ml.	19.6 γ/ml.
<i>E. coli</i> 055-----	156 γ/ml.	Ineffective.	313 γ/ml.

The results show that the addition of an ampholytic compound of the invention imparts an excellent anti-microbial activity to the high-duty detergent, the action of the ampholytic compound being even increased, in some cases, by the components of the high-duty detergent.

## EXAMPLE 4

A soft-rinsing agent has the following composition:

- 6.0% of distearyl-dimethyl-ammonium chloride,
- 0.5% of an addition product of 12 mols of ethylene oxide on 1 mol of oleyl alcohol,
- 0.5% of optical brighteners,
- 0.05% of perfume oil, and
- the remainder to 100% water.

By addition of an ampholytic compound of the invention, e.g. Product A, this said soft-rinsing agent obtained an excellent anti-microbial action.

In the same manner as in Example 3, in solutions of 0.3 g. per liter of the pure soft-rinsing agent the minimum inhibition concentration of the ampholytic compound of the invention was determined and compared with the values ascertained for the soft-rinsing agent alone and the ampholytic agent singly. The results are represented in Table VI. They show that the anti-microbial action is not impaired by the components of the soft-rinsing agent.

TABLE VI.—Minimum inhibition concentration

Type of germ	Product A	Soft-rinsing agent alone	Product A in soft-rinsing agent solution of 0.3 g./l.
<i>Str. faecalis</i> .....	80 γ/ml.....	1.25 mg./ml..	156 γ/ml.

## EXAMPLE 5

A liquid foot-washing agent of following composition is prepared:

30% of an addition product of 10 mols of ethylene oxide on 1 mol of coco fatty alcohol,  
0.2% of perfume and dyestuffs,  
1% of Product A, and  
remainder to 100% water.

Due to the fungicidal activity of the ampholytic compound, the foot-washing agent shows excellent action against foot fungi. The anti-microbial action of the ampholytic compound is not impaired by the remaining components of the foot-washing agent.

## EXAMPLE 6

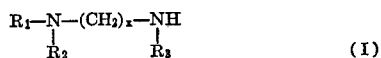
A high-duty detergent containing the compounds of the invention as the washing-active and anti-microbially active substance, has the following composition:

12% of Product A,  
8% of an addition product of 8 mols of ethylene oxide on 1 mol of coco fatty alcohol,  
40% of sodium tripolyphosphate,  
5% of sodium silicate,  
10% of calcined sodium carbonate,  
2% of carboxymethyl cellulose and  
23% of sodium sulfate.

A detergent of this composition showed very good washing effects on wool, polyamide, polyester and other fibers and reduced the germ content of the washing liquor.

What we claim is:

1. A compound of the Formula I



in which  $R_1$  stands for an alkyl or alkenyl radical having 8 to 18 carbon atoms,  $x$  for the integer 2 or 3, and  $R_2$

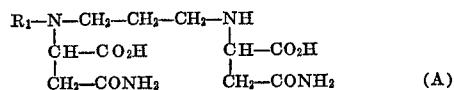
and  $R_3$  each stands for a hydrogen atom or the radical of the Formula II



and in which at least one of the radicals  $R_2$  and  $R_3$  stands for the radical of the Formula II, and  $Y$  stands for a hydrogen atom or an alkali metal ion.

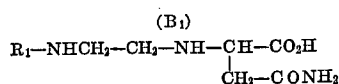
2. The compound of claim 1, wherein  $R_1$  stands for an alkyl or alkenyl radical having 12 to 18 carbon atoms.

3. A compound of the formula

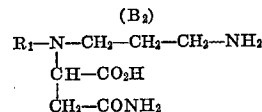


in which  $R_1$  stands for an alkyl radical having 8 to 18 carbon atoms.

4. A mixture of the compounds of the formula



and



in which  $R_1$  stands for an alkyl radical having 8 to 18 carbon atoms, the mixture being in a weight ratio of 72 parts  $B_1$  to 28 parts  $B_2$ .

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VIVIAN GARNER, Primary Examiner

U.S. Cl. X.R.

252-106, 525, 544; 260-534 E