United States Patent Office 3,029,273 Patented Apr. 10, 1962

3,029,273

NITROALKYL DIHALOCARBANILATES

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No Drawing. Filed Sept. 29, 1958, Ser. No. 763,797
7 Claims. (Cl. 260—471)

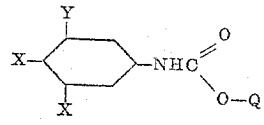
The invention relates to new and useful compounds and to the process of making the same.

The invention also relates to certain compositions comprising (1) a cleansing compound such as soap or other organic cleansing detergent including either anionic or non-ionic surface active detergents and mixtures thereof; and (2) an antiseptic amount and more specifically a bacteriostatic amount of these new compounds.

Numerous compounds are known in the art which will serve as effective antiseptics or bacteriostats. However, it has also been observed in compositions containing these compounds combined with a detergent, that the latter tends to destroy or greatly vitiate this antiseptic or bacteriostatic effect. In addition to such compounds not losing this antiseptic or bacteriostatic activity in the presence of a detergent, these compounds should not be toxic, should not irritate the human skin, should not impart any color or odor to the detergent, and should have affinity for the skin whereby a small amount will remain and exert an antiseptic and bacteriostatic effect.

It is, therefore, an object of this invention to provide new compounds which have utility as antiseptics and particularly exhibit bacteriostatic properties. A further object is to provide new compositions, which when mixed with a detergent, retain their antiseptic or bacteriostatic properties. A further object is to provide new antiseptic compounds which are non-irritating when combined with detergents and do not impart any color or odor thereto. A still further object is to provide antiseptic and bacteriostatic compositions for controlling the growth of bacteria such as *Micrococcus pyogenes* var. *aureus* on surfaces containing the same. Additional objects will be evident from the description that follows.

The new compounds of this invention may be represented by the general formula



where X is a halogen selected from the group consisting of chlorine and bromine, Y is a member selected from the group consisting of hydrogen, chlorine and bromine and Q is a mono-nitroalkyl radical having from 3 to 8 carbon atoms. Representative of the compounds of this invention are 1-(2-nitrobutyl) 3,4-dichlorocarbanilate, 1-(2-nitro-2-methylpropyl) 3,4-dichlorocarbanilate, 4-(3-nitroheptyl) 3,4-dichlorocarbanilate, 3-(2-nitro-2-methylhexyl) 3,4-dichlorocarbanilate, 1(2-nitroamyl) 3,4-dichlorocarbanilate, 4-(5-nitrooctyl) 3,4-dichlorocarbanilate, 1-(3-nitrohexyl) 3,4-dichlorocarbanilate, 1-(2-nitropropyl) 3,4-dichlorocarbanilate, 1-(2-nitrobutyl) 3,4-dibromocarbanilate, 1-(2-nitro-2-methylpropyl) 3,4,5-trichlorocarbanilate, 4-(3-nitroheptyl) 3,4-dibromocarbanilate, 4-(5-nitrooctyl) 3,4-dibromocarbanilate, 3-(2-nitro-2-methylhexyl) 3,4,5-trichlorocarbanilate, and the like.

In general the process of making the new compounds of this invention involves the reaction of a polyhalophenylisocyanate with the desired nitroalcohol, which latter type of compound is well known as a class of chemical compounds. The following examples are illustrative of the process.

EXAMPLE I

1-(2-Nitrobutyl) 3,4-Dichlorocarbanilate

A mixture of 18.8 g. (0.1 mole) 3,4-dichlorophenylisocyanate and 11.9 g. (0.1 mole) 2-nitro-1-butanol is gently warmed in a flask of 45–50°. An exothermic reaction sets in and the temperature is held at 60–65° using an ice bath. The contents of the flask solidify upon completion of the reaction. Recrystallization of the product from 60% ethanol gives fine colorless needles (M.P. 121.4–122.1° C.) yield: 88.6% of theory. Analysis percent N=calculated 9.12; found 9.07.

EXAMPLE II

1-(2-Nitrobutyl) 3,4-Dibromocarbanilate

Employing the procedure of Example I but using 27.7 g. (0.1 mole) 3,4-dibromophenylisocyanate in place of the 3,4-dichlorophenylisocyanate, 1-(2-nitrobutyl) 3,4-dibromocarbanilate is obtained in good yields.

EXAMPLE III

1-(2-Methyl-2-Nitropropyl) 3,4-Dichlorocarbanilate

Following the procedure of Example I but using 18.8 g. (0.1 mole) 3,4-dichlorophenylisocyanate and 11.9 g. (0.1 mole) 2-methyl-2-nitro-1-propanol, small colorless needles of 1-(2-methyl-2-nitropropyl) 3,4-dichlorocarbanilate are recrystallized from 60% ethanol (M.P. 114.2–115.1° C.) yield: 98.0% theory. Analysis percent Cl: calculated 23.08; found 22.91.

EXAMPLE IV

3-(2-Methyl-2-Nitrohexyl) Butyl(3,4-Dichlorocarbanilate)

Following the procedure of Example I but using 16.1 g. (0.1 mole) 2-nitro-2-methyl-3-hexanol as the alcohol, small white granules of 3-(2-methyl-2-nitrohexyl) butyl 3,4-dichlorocarbanilate are recrystallized from 90% ethanol (M.P. 98.3–99.2° C.) yield 99.2% theory. Analysis percent Cl: Calculated 20.30; found 20.99.

EXAMPLE V

4-(3-Nitroheptyl) 3,4-Dichlorocarbanilate

Following the procedure of Example I but using 16.1 g. (0.1 mole) 3-nitro-4-heptanol, small white granules of 4-(3-nitroheptyl) 3,4-dichlorocarbanilate are recrystallized from heptane (M.P. 114.8–115.5° C.) yield: 80.0% theory. Analysis percent Cl: calculated 20.30; found 20.46.

EXAMPLE VI

4-(5-Nitrooctyl) 3,4-Dichlorocarbanilate

Following the procedure of Example I but using 17.5 g. (0.1 mole) 5-nitro-4-octanol as the alcohol, white granules of 4-(5-nitrooctyl) 3,4-dichlorocarbanilate are obtained in good yields.

EXAMPLE VII

1-(2-Nitrobutyl) 3,4,5-Trichlorocarbanilate

Employing the procedure of Example I but using 22.4 g. (0.1 mole) 3,4,5-trichlorophenylisocyanate in place of the 3,4-dichlorophenylisocyanate, 1-(2-nitrobutyl) 3,4,5-trichlorocarbanilate is obtained in good yield.

From the above examples it will be noted that in a preferred method of preparing the new compounds of this invention, substantially equimolecular proportions of a polyhalophenylisocyanate and the appropriate mono-nitroalcohol are mixed and gently heated usually in the range of 45° to 50° C. An exothermic reaction sets in and it has been found desirable to maintain the reaction temperature around 60° C. to 65° C. by means of an ice bath during the reaction period of about ½ to 1 hour.

Upon completion of the reaction, the desired nitroalkyl polyhalocarbanilate is then recrystallized from an appropriate solvent such as ethanol. However, depending on the particular alcohol used, the mixture of polyhalophenylisocyanate and the nitroalcohol will react in certain instances at room temperature of about 20° C. to temperatures up to 80° C. with reaction periods up to 4 hours. In addition other solvents may be used for recrystallization of the product such as xylene, benzene, heptane, and the like.

The compounds of this invention having the general formula given above have been found to have excellent antiseptic properties and more particularly exhibit bacteriostatic properties when mixed with cleansing compounds or detergents in cleansing compositions. The term "detergent" as used in this patent application has reference to any of the following classes of cleansing compounds and mixtures thereof: soaps and other anionic surface active detergents plus non-ionic surface active detergents.

The term soap is employed in its popular meaning and refers to cleansing compounds usually made by the action of an alkali or fat or fatty acids, e.g., the sodium or potassium salts of either saturated or unsaturated fatty acids. By way of example each of the compounds described in Examples I, III, IV and V above were separately incorporated in a neutral high grade white soap (a mixture of 80 percent sodium soap and 20 percent potassium soap produced from a 70 percent tallow and 30 percent oil glyceride blend in accordance with U.S. Patent 2,295,594) in a weight ratio of two parts to 100 parts by weight soap. Aliquots of each were added to a Saboraud's dextrose agar medium so as to give concentrations of the compounds in the agar as set forth in Table I below. The agar in each case was then poured into a petri dish, allowed to harden, and then innoculated with a standard culture of the bacterium *Micrococcus pyrogenes* var. *aureus* of standard resistance. The incubation in each instance was made simultaneously at 37° C. for 48 hours. The extent of growth is noted below:

TABLE I

Concentration, parts per	10T[1]	100T	1M[2]	5M	10M	50M
Group A:						
1-(2-nitrobutyl)3,4 - dichlorocarbanilate	−	−	−	−	−	+
1-(2 - methyl-2-nitropropyl)3,4-dichlorocarbanilate	−	−	−	+	------	------
4-(3-nitroheptyl)3,4-dichlorocarbanilate	−	−	−	+	------	------
3-(2-methyl-2-nitrohexyl)3,4-4-dichlorocarbanilate	−	−	−	+	------	------
Group B:						
2-nitrobutyl 2-nitrocarbanilate	−	+	------	----	------	------
2-nitrobutyl 4-nitrocarbanilate	−	+	------	----	------	------
2-nitrobutyl 2-chlorocarbanilate	−	+	------	----	------	------
2-nitrobutyl 3-chlorocarbanilate	−	+	------	----	------	------

Legend:
[1]T=thousand
[2]M=million
+=growth
−=no growth

The Group B compounds were included in the above table to point up the importance of the placement and number of chlorine and nitro substituents in the molecule of the carbanilate compounds of this invention.

It is to be understood that the use of the nitroalkyl dichlorocarbanilates with soap, as set forth in the above table, is merely illustrative and that these compounds may also be used with other soaps and other anionic surface active and non-ionic surface active organic detergents and have proven equally effective therein. Other alkali metal soaps of higher fatty acids of animal or vegetable origin may be used such as stearic, lauric, palmitic, oleic, linoleic, ricinoleic, and the like, including mixtures thereof obtained from tallow, lard, coconut oil, palm oil, castor oil, olive oil, hydrogenated fish and cottonseed oils and the like.

The organic anionic detergents of this invention include in addition to the alkali metal fatty acid soaps the well known surface active alkali metal sulfonates and sulfates. Representative of these are the long chain alkyl aryl sulfonates, i.e. those wherein the alkali radical is straight or branched in structure and contains from 8 to 22 carbon atoms, but preferably 10 to 16 carbon atoms, examples of which are octyl, decyl, dodecyl, keryl, pentadecyl, hexadecyl, octadecyl, mixed long chain alkyls derived from long chain fatty materials such as the lauryl radical, cracked paraffin wax olefins, polymers of lower mono-olefins such as propylene tetramer and the like, and wherein the aryl radical is derived from benzene, toluene, xylene phenol, the cresols, naphthalene, and the like. Specific examples of such comprise sodium decyl benzene sulfonate, sodium dodecyl benzene sulfonate, sodium lauryl benzene sulfonate and sodium hexadecyl benzene sulfonate. Further descriptive information regarding these compounds may be found in U.S. Patent 2,264,737.

Other sulfonate surface-active agents are also contemplated, e.g. the long chain alkyl sulfonates such as sodium hexadecane sulfonate and sodium octadecane sulfonate.

The well known sulfate detergents having 12 to 26 carbon atoms and particularly those having an alkyl radical of about 8 to 22 carbon atoms may be employed as anionic detergent bases in accordance with this invention. Such detergents include the sulfuric acid esters of polyhydric alcohols incompletely esterified with fatty acids, e.g. sodium coconut oil monoglyceride mono-sulfate, sodium tallow diglyceride mono-sulfate, the pure and mixed higher alkyl sulfates such as sodium lauryl sulfate and sodium cetyl sulfate.

Additional anionic surface active sulfonates and sulfates contemplated by this invention are the sulfated and sulfonated alkyl acid amides such as Igepon T

$$(C_{17}H_{33}CO.NHCH_2CH_2SO_3NA)$$

the sulfated and sulfonated esters such as Igepon AP ($RCOOCH_2SO_3Na$ where R is an alkyl radical containing from 12 to 18 carbon atoms), sodium salt of the bisulfate of a dialkyl dicarboxylate, sodium salt of the sulfonic acid derivative of a dialkyl dicarboxylate, sodium sulfosuccinic esters such as

$$NaOOCCH_2CH(SO_3Na)CONHC_{18}H_{27}$$

and the like.

In addition to the organic anionic detergents, the non-ionic surface-active agents containing the desired nitroalkyl dichlorocarbanilate derivatives provide effective bacteriostatic cleaning compositions. The non-ionic surface active agents contemplated are viscous liquid to wax-like water-soluble surface-active substances containing a polyglycol ether group of the structure

$$R-(\underset{\underset{R_1}{|}}{CH}-\underset{\underset{R_2}{|}}{CH}-O)_nH$$

wherein R_1 and R_2 are hydrogen or short chain alkyl, where n is an integer greater than 3, and where R is a residue of a monomeric organic compound having an active hydrogen, e.g. alcohols, phenols, amides, primary amines, secondary amines, carboxylic acids, etc. These non-ionic detergents are well known (note U.S. 1,970,578 and U.S. 2,213,477) and may be typified by the polyalkylene oxide derivatives (i.e. polyethylene oxide, polypropylene oxide, polybutylene oxide) of water-insoluble higher fatty acids, such as lauric, oleic, palmitic and stearic acid and the like or mixtures thereof, such as the mixtures of fatty acids, obtained from animal and vegetable fats and oils or by oxidation of petroleum fractions such as paraffin wax. They may also be exemplified by the polyalkylene oxide derivatives of such water-insoluble organic hydroxy compounds as higher aliphatic alcohols

(i.e. the alcohols corresponding to the fatty acids specified above or mixtures thereof), oil or phenols, particularly alkyl phenols containing at least six alkyl carbon atoms such as isooctyl-, di-tertiary butyl-, triisopropyl-, nonyl-, dodecyl-, octadecyl- phenols or naphthols, or higher alkyl alcohols, such as benzyl alcohol, cinnamyl alcohol. They may also be exemplified by the polyalkylene oxide derivatives of such amines as stearyl, lauryl, dicyclohexyl, dibutyl amine and the like. A particularly useful nonionic detergent is that obtained by condensing one mol of tall oil with 5 to 15 mols of ethylene oxide (see U.S. 2,550,691).

The nitroalkyl dichlorocarbanilates are also useful in preparing bacteriostatic cleansing compositions compounded from mixtures of detergents plus other ingredients as illustrated by the following compositions:

Composition A:	Parts by weight
Triethanol amine lauryl sulfate	60
Methyl cellulose	2
Propylene glycol	4
Potassium stearate	6
Water	130
1-(2-nitrobutyl)3,4-dichlorocarbanilate	1

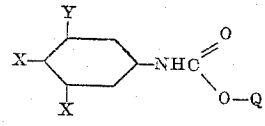
Composition B:	Parts by weight
Tall oil-ethylene oxide condensation product (1 mol tall oil-11 mols ethylene oxide)	20
Sodium dodecyl benzene sulfonate	80
Carboxy methyl cellulose, sodium	4
Sodium tripolyphosphate	80
Sodium sulfate	200
1-(2-nitrobutyl) 3,4-dichlorocarbanilate	1

The nitroalkyl dichlorocarbanilates of this invention may be employed in cosmetic compositions ordinarily used to beautify, cleanse or protect the skin in any amount sufficient to inhibit the growth of or to kill bacteria, specifically *Micrococcus pyogenes* var. *aurenus*, normally present on the skin. Relatively small amounts of the nitroalkyl dichlorocarbanilates of this invention in cosmetics, particularly those having as a base an anionic or non-ionic organic detergent base composition or combination of said detergents, have been found to yield effective bacteriostatic compositions. With respect to cosmetics having an anionic or non-ionic detergent base amounts as low as 0.1% to 1% by weight based upon the total weight of the organic detergent may be employed. It is preferred in detergent cleansing compositions having an anionic detergent base or non-ionic detergent base to employ these nitroalkyl dichlorocarbanilates in amounts in the order of 1% to 3% by weight based on the total weight of detergent. While larger amounts up to 10% and even 50% by weight of the detergent base may be employed, the upper limit will be determined by practical considerations as well as by the particular cosmetic composition involved, i.e. whether the composition is to be used for cleansing purposes in the sense of a toilet soap or as a shaving cream or as a shampoo, etc. In cleansing compositions in the sense of a toilet soap containing an anionic organic detergent base (e.g. an alkali metal fatty acid detergent soap alone or in admixture with another anionic organic detergent such as the aforedescribed sodium alkyl aryl sulfonate detergents) or non-ionic detergent base, the amount of nitroalkyl dichlorocarbanilates of this invention ordinarily will not exceed 10% by weight of the detergent base. However, in shampoos, shaving creams, and the like, employing an anionic organic detergent base or non-ionic detergent base the amounts of nitroalkyl dichlorocarbanilates of this invention may be present to the extent of 50% by weight based on the total detergent base content. Various colors, antioxidants, perfumes, water-softeners, salts such as silicates, chlorides, carbonates, phosphates and sulfates of alkali metals and the like builders, sodium carboxy methyl cellulose, the low molecular weight alcohols such as methanol, ethanol, isopropanol, ethylene glycol, and the like, may be included where desirable.

While this invention has been described with respect to certain embodiments, it is not so limited and it is to be understood that variations and modifications thereof obvious to those skilled in the art may be made without departing from the spirit or scope of this invention.

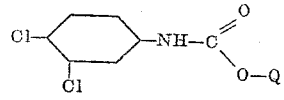
What is claimed is:

1. A compound of the formula



where X is a halogen selected from the group consisting of chlorine and bromine, Y is a member selected from the group consisting of hydrogen, chlorine and bromine, and Q is mononitroalkyl having from 3 to 8 carbon atoms.

2. A compound of the formula



where Q is mononitroalkyl having from 3 to 8 carbon atoms.

3. 1-(2-nitrobutyl) 3,4-dichlorocarbanilate.

4. 1-(2-methyl-2-nitropropyl) 3,4-dichlorocarbanilate.

5. 3-(2-methyl-2-nitrohexyl) hexyl 3,4-dichlorocarbanilate.

6. 4-(3-nitroheptyl) 3,4-dichlorocarbanilate.

7. 4-(5-nitrooctyl) 3,4-dichlorocarbanilate.

References Cited in the file of this patent

UNITED STATES PATENTS

2,487,799	Gump	Nov. 15, 1949
2,535,077	Kunz et al.	Dec. 26, 1950
2,734,911	Strain	Feb. 14, 1956
2,789,129	Bissinger	Apr. 16, 1957
2,850,524	Mowry et al.	Sept. 2, 1958
2,858,328	Beaver et al.	Oct. 28, 1958

UNITED STATES PATENT OFFICE
CERTIFICATE OF CORRECTION

Patent No. 3,029,273 April 10, 1962

David J. Beaver et al.

It is hereby certified that error appears in the above numbered patent requiring correction and that the said Letters Patent should read as corrected below.

Column 2, EXAMPLE IV, in the heading, line 33, strike out "Butyl", in italics; column 2, line 37, strike out "butyl"; column 3, TABLE I, column 1, lines 9 and 10 thereof, for "4-4-dichlorocarbanilate" read -- 4-dichlorocarbanilate --; column 5, line 37, for "aurenus", in italics, read -- aureus --, in italics ; column 6, line 45, strike out "hexyl".

Signed and sealed this 28th day of August 1962.

(SEAL)
Attest:

ESTON G. JOHNSON
Attesting Officer

DAVID L. LADD
Commissioner of Patents