United States Patent Office 2,768,205 Patented Oct. 23, 1956

2,768,205

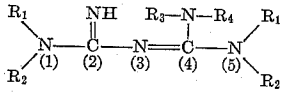
PREPARATION OF BIGUANIDES

Ingenuin Hechenbleikner, Adams, Mass., and Donald W. Kaiser, Hamden, Conn., assignors to American Cyanamid Company, New York, N. Y., a corporation of Maine

No Drawing. Application September 20, 1955, Serial No. 535,509

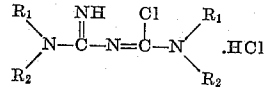
5 Claims. (Cl. 260—565)

The present invention relates to a method of preparing biguanides which are capable of representation by the generic formula



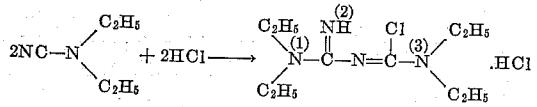
wherein R_1 stands for an alkyl radical having from 1 to 18 carbon atoms, R_2 stands for hydrogen or an alkyl radical having from 1 to 18 carbon atoms, and R_3 and R_4 stand for hydrogen, an aryl radical or an alkyl radical having from 1 to 18 carbon atoms.

In accordance with the present invention, the biguanide compounds may be readily prepared by reacting in an inert solvent an alkylguanylchloroformamidine hydrochloride of the formula



in which R_1 and R_2 have the meanings shown above, with a member of the group consisting of ammonia, a primary amine of the formula R_3NH_2 and a secondary amine of the formula R_3R_4NH wherein R_3 and R_4 represent an aryl radical or an alkyl radical having from 1 to 18 carbon atoms. If necessary or desirable, the hydrochloride salt of the biguanide thus obtained is easily converted to the free base by treatment with an alkali metal hydroxide.

Methods of preparing the alkylguanylchloroformamidine hydrochlorides employed in the present process are disclosed in copending application, Serial No. 358,549, filed May 29, 1953, now abandoned, by Hechenbleikner, one of the present inventors. For example, tetraethylguanylchloroformamidine hydrochloride is formed by reacting diethylcyanamide with hydrogen chloride at a temperature within the range of from 60° to 150° C. The reaction may be illustrated as follows:



Ninety grams of hydrogen chloride was passed into 196 g. of diethylcyanamide during a period of one hour. The diethylcyanamide was stirred rapidly during the addition of the hydrogen chloride gas, and the temperature rose gradually to 85° C. The mixture was then heated for thirty minutes and the temperature was maintained at about 150° C. The product (1,1,3,3-tetraethylguanylchloroformamidine hydrochloride) was a colorless crystalline solid which melted at 35°–40° C.

Other typical alkylguanylchloroformamidine hydrochlorides which may be employed in the present process are

1,3-dimethylguanylchloroformamidine hydrochloride
1,3-dipropylguanylchloroformamidine hydrochloride
1,3-dihexylguanylchloroformamidine hydrochloride
1,3-didecylguanylchloroformamidine hydrochloride
1,3-ditetradecylguanylchloroformamidine hydrochloride
1,3-dioctadecylguanylchloroformamidine hydrochloride
1,1,3,3-tetraisopropylguanylchloroformamidine hydrochloride
1,1,3,3-tetrabutylguanylchloroformamidine hydrochloride
1,1,3,3-tetraoctylguanylchloroformamidine hydrochloride
1,1,3,3-tetradecylguanylchloroformamidine hydrochloride
1,1,3,3-tetradodecylguanylchloroformamidine hydrochloride
1,1,3,3-tetraoctadecylguanylchloroformamidine hydrochloride

Amines typical of those capable of undergoing the reaction of the present invention are methylamine, dimethylamine, ethylamine, diethylamine, methylethylamine, methylisobutylamine, propylamine, dipropylamine, isopropylamine, ethylpropylamine, butylamine, dibutylamine, amylamine, hexylamine, 2-ethylhexylamine, octylamine, dioctylamine, decylamine, dodecylamine, octadecylamine, didodecylamine, dioctadecylamine, aniline, o-chloroaniline, p-bromoaniline, p-nitroaniline, N-methylaniline, N-ethylaniline, diphenylamine, N-methyl-α-naphthylamine, α-naphthylamine, β-naphthylamine, di-β-naphthylamine, o-anisidine, p-phenetidine, N-methyl-p-phenetidine, the toluidines and xylidines.

In the present process the optimum reaction temperature varies somewhat with the specific reactants employed, but in most reactions a temperature within the range of from about 10° C. to about 90° C. is preferred. Compounds which may be employed as solvents in the process are benzene, toluene, acetonitrile, tetrahydrofurane, dioxane, water and the lower aliphatic monohydric alcohols such as the methyl, ethyl, propyl and butyl alcohols.

The invention is further illustrated, but not limited, by the following examples:

EXAMPLE 1

1,1,5,5-tetramethylbiguanide

A solution of 21.3 g. of tetramethylguanylchloroformamidine hydrochloride in 50 cc. of water was added slowly with stirring to 50 cc. of 28.6% aqueous ammonia. The temperature of the mixture rose rapidly to 65° C. The reaction mixture was then allowed to stand in an evaporating vessel at room temperature for 72 hours. The solid residue was leached with boiling isopropanol. Evaporation of the filtrate gave 17 g. (88% yield) of the 1,1,5,5-tetramethylbiguanide hydrochloride which melted at 212–215° C. The free base was formed by treating the hydrochloride salt with sodium hydroxide in aqueous solution.

EXAMPLE 2

1,1,5,5-tetraethylbiguanide

A solution of 13.4 g. of tetraethylguanylchloroformamidine hydrochloride in 50 cc. of methanol was added to 25 cc. of 28.6% aqueous ammonia at 5° C. The temperature of the mixture rose quickly to 40° C. After standing at room temperature for one hour, the reaction mixture was poured into 200 cc. of water, and then made alkaline by the addition of sodium hydroxide. The precipitated biguanide was separated by filtration and recrystallized from hexane. The white crystalline product melted at 79–80° C.

EXAMPLE 3

1,5-di-t-butylbiguanide

26.9 g. of 1,3-di-t-butylguanylchloroformamidine hydrochloride was added slowly with stirring to 50 cc. of 28.6% aqueous ammonia at 5–10° C. After standing at room temperature for one hour, the reaction mixture was

filtered to recover the precipitated 1,5-di-t-butylbiguanide hydrochloride. After recrystallization from ethanol the hydrochloride salt melted at 230° C. The free base melted at 179–180° C.

EXAMPLE 4

1,5-di-t-butyl-4-amylbiguanide

10 g. of 1,3-di-t-butylguanylchloroformamidine hydrochloride was added slowly with stirring to a solution of 10 g. of n-amylamine in 20 cc. of acetonitrile maintained at about 5° C. After standing at room temperature for two hours, the reaction mixture was poured into 100 cc. of water and filtered to recover the precipitated 1,5-di-t-butyl-4-amylbiguanide hydrochloride. After recrystallization from ethanol the hydrochloride salt melted at 245–246° C. The free base was formed by treating the hydrochloride salt with potassium hydroxide in aqueous solution.

EXAMPLE 5

1,1,4,4,5,5-hexamethylbiguanide

213 g. of tetramethylguanylchloroformamidine hydrochloride was added slowly with stirring to 250 g. of a 40% aqueous solution of dimethylamine. The temperature of the mixture rose rapidly to about 40° C. After standing for 15 minutes, solid sodium hydroxide was added and the liquid separated into two phases. The organic phase was separated, dried over solid sodium hydroxide, and distilled under reduced pressure. The product, a colorless liquid, distilled at 115–117° C./1.0 mm.

EXAMPLE 6

1,1,5,5-tetramethyl-4-phenylbiguanide

A mixture of 21.3 g. (0.1 mol) of tetramethylguanylchloroformamidine hydrochloride, 18.6 g. (0.2 mol) of aniline and 100 cc. of acetonitrile was heated for 10 minutes at reflux. The clear solution upon cooling to room temperature deposited 32 g. of solid material which was dissolved in 100 cc. of water and made basic with ammonia. The aniline which separated was extracted with benzene and the aqueous layer was made alkaline by the addition of sodium hydroxide. The precipitated biguanide (20 g.) was separated by filtration and recrystallized from cyclohexane. The white crystalline product melted at 89–90° C.

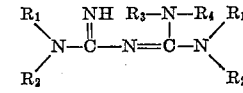
The biguanides prepared by the method of the present invention are useful as tarnish inhibitors in detergent compositions utilized in the washing of household utensils such as tableware or "silverware" consisting of German silver and like alloys. The quantity of the tarnish inhibitor to be used is generally less than 1% by weight of the detergent composition, and preferably from .05 to .5%. The biguanides of Examples 2, 4, 5 and 6 above were tested as tarnish inhibitors by the following method: alloy bars (65% copper, 18% nickel, 17% zinc) ⅛" x ½" x 2½" in size were cleaned with approximately 0.7 N nitric acid, rinsed with water and then acetone. A commercial detergent composition consisting of approximately 50% sodium tripolyphosphate, 25–30% alkyl-aryl sulfonate, 12–19% sodium sulfate and 3–4% sodium silicate was employed. The alloy bar was immersed in 25 cc. of detergent solution (2.5 g. of

detergent per 1500 cc. of water) containing 0.4% of the biguanide compound (based on the weight of the detergent). The temperature of the detergent solution was maintained at 43° C. and the period of immersion was 7 minutes. The bar was removed from the solution, rinsed with water and acetone, and stored under toluene for observation of tarnish film. A blank test with the detergent solution gave a heavy tarnish film on the alloy bar, whereas tarnishing was substantially diminished with the detergent solutions containing the biguanide compounds.

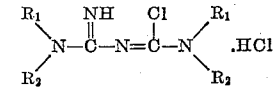
While the invention has been described with particular reference to specific embodiments, it is to be understood that it is not to be limited thereto but is to be construed broadly and restricted solely by the scope of the appended claims.

We claim:

1. A method of preparing a biguanide of the formula



wherein R_1 represents an alkyl radical having from 1 to 18 carbon atoms, R_2 represents a member of the group consisting of hydrogen and R_1, and R_3 and R_4 are selected from the group consisting of hydrogen, an aryl radical and an alkyl radical having from 1 to 18 carbon atoms, which comprises reacting in an inert solvent an alkylguanylchloroformamidine hydrochloride of the formula



in which R_1 and R_2 have the above meanings, with a member of the group consisting of ammonia, a primary amine of the formula R_3NH_2 and a secondary amine of the formula R_3R_4NH wherein R_3 and R_4 represent members of the group consisting of an aryl radical and an alkyl radical having from 1 to 18 carbon atoms, and recovering the thus-formed biguanide from the reaction mixture.

2. The method of claim 1 in which the reaction is carried out at a temperature within the range of from about 10° C. to about 90° C.

3. The method which comprises reacting tetraethylguanylchloroformamidine hydrochloride with ammonia in an inert solvent at a temperature within the range of from 10° C. to 90° C., and recovering 1,1,5,5-tetraethylbiguanide from the reaction mixture.

4. The method which comprises reacting tetramethylguanylchloroformamidine hydrochloride with dimethylamine in an inert solvent at a temperature within the range of from 10° C. to 90° C., and recovering 1,1,4,4,5,5-hexamethylbiguanide from the reaction mixture.

5. The method which comprises reacting tetramethylguanylchloroformamidine hydrochloride with aniline in an inert solvent at a temperature within the range of from 10° C. to 90° C., and recovering 1,1,5,5-tetramethyl-4-phenylbiguanide from the reaction mixture.

No references cited.