PREPARATION OF AMINOCARBOXYLIC ACIDS

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The present invention relates to an improved method for the preparation of organo-substituted aminocarboxylic acids containing more than one carboxylkyl group attached to the nitrogen atom.

More specifically, in the following description the term "organosubstituted aminocarboxylic acids containing more than one carboxylkyl group attached to the nitrogen atom" shall refer to N-substituted iminodialkanecarboxylic acids and salts of the formula:

\[ R-N-C_6H_4COOM \]

and N-substituted nitrotrialkane carboxylic acids and salts of the formula:

\[ R-N-C_6H_4(COOM) \]

where R is a hydrocarbon radical containing from 1 to 20 carbon atoms such as alkyl, aryl, cycloalkyl, alkaryl and aralkyl groups n is an integer of 1, 2 or 3 and M, M' and MM'' are chosen from the group comprising hydrogen, potassium and sodium. Examples of such compounds are N-lauryliminodiacetic acid, disodium N-octadecyl-β-iminodipropionate, N-phenyl-a-iminodisubtyric acid, monosodium N-tetradecyl-α-iminodipropionate and disodium N-methylnitrilotriacetate (disodium N,N-dicarboxymethylglycine methylester), betaine.

The preparation of such organo-substituted aminocarboxylic acids by reaction of primary or secondary amines with halogen-substituted Cs-C4 aliphatic mono- or polycarboxylic acids and salts thereof has been described in the art. This reaction is accompanied by the formation of a free inorganic halogen acid (HCl, HBr, HI or HF), which must be neutralized to prevent a competitive side reaction of the inorganic halogen acid with the amine. In accordance with the prior teachings of the art, neutralization of the inorganic halogen acids was effected by using sodium hydroxide in the form of aqueous solutions thereof of a suitable strength. However, the employment of aqueous caustic entails considerable disadvantages: When sodium hydroxide is employed in amounts and at concentrations adapted to prevent the inorganic halogen acid-amine side reaction, it causes hydrolysis of the salt of halogen-substituted aliphatic carboxylic acid and formation of a hydroxy-acid. For instance, hydrolysis of sodium chloroacetate results in the formation of glycolic acid. This entails considerable losses of a valuable reactant to undesirable end-products. In some cases, it has been observed, in fact, that the rate of hydrolysis of sodium chloroacetate actually approaches the rate of the reaction of formation in the desired organo-substituted aminocarboxylic acids, and thus necessitates the use of a large excess of sodium chloroacetate to obtain the desired aminocarboxylic acid product. In addition to the difficulties of ascertaining when the desired reaction is complete, mixtures of mono-, di-, and tricarboxymethyl derivatives of the amine are usually obtained.

I have found that these troublesome disadvantages can be substantially eliminated by carrying out the aforementioned reaction of an amine with a halogen-substituted Cs-C6 aliphatic acid, or its alkali metal salt, in the presence of sodium bicarbonate.

The attached drawing illustrates the advantages presented by the employment of sodium bicarbonate instead of sodium hydroxide. Curve A of the drawing shows the extent of hydrolysis of sodium chloroacetate as a function of time (in minutes) in the presence of aqueous sodium hydroxide. Curve B strikingly illustrates the almost complete absence of hydrolysis of sodium chloroacetate in the presence of aqueous sodium bicarbonate after two hours or more.

The amount of sodium bicarbonate required to neutralize the inorganic halogen acid formed in the reaction of the amine with the halogen-substituted aliphatic carboxylic acid, or its alkali metal salt, should be sufficient to maintain in the reaction mixture a pH of at least 7.0 during the reaction. Thus, in preparing monosodium N-alkyliminodiacetate from one mole of a primary amine and two moles of sodium chloroacetate, at least one mole of sodium bicarbonate is required. Likewise, in preparing monosodium N,N-dicarboxymethylalkylamine from one mole of a secondary amine with two moles of sodium chloroacetate, at least one mole of sodium bicarbonate is required. In the reaction of one mole of the primary amine with three moles of sodium chloroacetate, at least two moles of sodium bicarbonate are necessary. An excess of sodium bicarbonate in the reaction mixture may be used without any adverse effect on the pH in the range from 7.0 to 8.5 of the final reaction product.

When a diamine is employed in lieu of a monoamine, the number of moles of the halogen-substituted aliphatic acid, or of its alkali metal salt, and of sodium bicarbonate, will be necessarily doubled.

The temperature at which the amine is reacted with the halogen-substituted monocarboxylate and sodium bicarbonate to produce an organo-substituted aminocarboxylic acid in accordance with the present invention, lies in the range from 60 to 100° C., the preferred range being from 80 to 90° C. Even though an excess of sodium bicarbonate may be present in the reaction mixture, the pH will not be higher than 8.5, whereas the pH may be 11.0 and higher in the presence of even a slight excess of sodium hydroxide.

An additional advantage secured through the application of sodium bicarbonate to neutralize the free inorganic acid formed in the production of organo-substituted aminocarboxylic acids, as described and claimed herein, consists in the ability to ascertain the end point of the reaction by the cessation of evolution of the CO₂ gas from the reaction vessel.

In the actual practice of the present invention instead of reacting an amine with a halogen-substituted Cs-C₄ aliphatic acid, an aqueous solution of an alkali metal salt of this acid is prepared first and then added to an aqueous solution of the amine and sodium bicarbonate containing, if necessary, a sufficient amount of an alcohol (either ethanol or isopropanol) as a solvent for the amine. The mixture is then agitated at 60 to 100° C., but preferably at 80 to 90° C., until no more CO₂ gas is evolved. Amines which may be employed for the reaction are those containing hydrocarbon substituents of 1 to 20 carbon atoms and at least one hydrogen attached to the amino-nitrogen; in other words, their number includes Cs-C₄ primary and secondary monoamines and diamines such as aliphatic, aromatic, cycloaliphatic and alky aromatic amines. Illustrative examples of monoamines are: octylamine, dodecylamine, stearylamine, phenylamine...
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(aniline), N-methylaniline, naphthylamine, p-methylaniline, dibenzylamine, etc. Primary and secondary alkyl amines containing from 8 to 18 carbon atoms in the alky chain are particularly suitable for the purpose. As the operative dianimes may be mentioned phenylenediamine, hexamethylenediamine, ethylenediamine, and the like.

The halogen-substituted C₂-C₄ aliphatic monocarboxylic acid to be employed for the preparation of the amino-carboxylic acids in accordance with the method of the present invention are preferably monohalogenated saturated C₂-C₄ aliphatic monocarboxylic acids such as halogenated acetic, propionic and butyric acids. Among the suitable fluoro-, chloro-, bromo-, and iodo-substituted C₂-C₄ aliphatic monocarboxylic acids, the chloro-substituted acids (acetic, propionic and butyric) are preferred, chloroacetic acid being generally employed because of its ready availability.

In the actual practice, it is more convenient to employ alkali metal salts of the aforesaid-halogen-substituted aliphatic acids, sodium chloroacetate being particularly suitable for the purpose. One may proceed by converting first the halogen-substituted aliphatic acid, such as chloroacetic, to its salt, as by neutralization with sodium hydroxide (provided a sufficiently low temperature is maintained to prevent hydrolysis), whereupon sodium bicarbonate can be employed to secure the desired organo-substituted aminocarboxylic acid from a suitable amine and an alkali metal salt such as CICH₂COONa with the minimum of hydrolysis taking place.

The following examples of the preparation of a representative N-alkyl-substituted iminodicarboxylic acid, namely, N-lauryldiglycine, further illustrate the improvement attained by employing the method of the present invention over the previous techniques of preparing organo-substituted aminocarboxylic acids which use sodium hydroxide as the neutralizing agent.

**Example 1**

1 mole of straight-chain dodecylamine (C₁₂H₂₅·NH₂) is caused to react for 3 hours at a temperature of 85°C. with 2 moles of sodium chloroacetate and 1 mole of 10% caustic soda solution. The resulting solution is found to contain sodium chloride and about equal amounts of N-laurylglycine and sodium N-lauryldiminoacetate.

**Example 2**

In this test carried out for 3 hours at 85°C., the same amounts of sodium chloroacetate and dodecylamine are employed; however, instead of caustic soda solution, sodium bicarbonate is the neutralizing agent. The final solution contains sodium chloride and amino-compounds, 90% by weight of which is constituted by sodium N-lauryldiminoacetate and less than 10% by weight of which is N-laurylglycine.

Similar advantages of sodium bicarbonate over sodium hydroxide in preventing hydrolysis, and securing a substantially unitary organo-substituted aminocarboxylic acid product rather than mixtures of several substituted amino-carboxylic acids, are observed in the tests of preparing other organo-substituted aminocarboxylic acids: e.g., N,-stearylaminodicarboxylic acid and sodium N,N-dicarboxymethylglycine methylester, betaine.

Among the various organo-substituted aminocarboxylic acids and their N-carboxyalkyl derivatives which can be produced according to the method of the present invention, N-alkyl aminocarboxylic acids characterized by the presence of straight alkyl chains containing from 8 to 18 carbon atoms are particularly attractive, because in addition to being amphoterically, they are surface-active and, therefore, lend themselves for the formulation of numerous washing (detergent), foam-improving, levelling and water-softening compositions, as well as for a number of other useful industrial applications.

It is to be understood that the above description and illustrative examples are not limitative of the invention, and that other specific embodiments thereof are to be included within the definitions of the following claims.

1. A method of preparing organo-substituted amino-carboxylic acids having more than one carbonyl group and at least one hydrocarbon substituent with 1 to 20 carbon atoms attached to the amino-nitrogen atom, which comprises reacting an amine containing at least one hydrocarbon substituent having from 1 to 20 carbon atoms with at least one hydrogen attached to the amino-nitrogen atom with an alkali metal salt of a monohalogen-substituted C₂-C₄ aliphatic monocarboxylic acid in the presence of sodium bicarbonate in an amount sufficient to neutralize the free inorganic halogen acid formed in the reaction.

2. A method of preparing organo-substituted amino-carboxylic acids having more than one carbonyl group and at least one hydrocarbon substituent with 1 to 20 carbon atoms attached to the amino-nitrogen atom, which comprises reacting an amine containing at least one hydrocarbon substituent having from 1 to 20 carbon atoms with at least one hydrogen attached to the amino-nitrogen atom with an alkali metal salt of a monohalogen-substituted C₂-C₄ aliphatic monocarboxylic acid in the presence of sodium bicarbonate in an amount sufficient to maintain a pH in the range of 7.0 to 8.5 in the reaction mixture throughout the reaction.

3. A method of preparing organo-substituted amino-carboxylic acids having more than one carbonyl group and one hydrocarbon substituent having from 1 to 20 carbon atoms attached to the amino-nitrogen atom, which comprises reacting a primary amine having one hydrocarbon substituent of 1 to 20 carbon atoms attached to the amino-nitrogen atom with an alkali metal salt of a monohalogen-substituted C₂-C₄ aliphatic monocarboxylic acid in the presence of sodium bicarbonate in an amount equal to at least 0.5 mol per each mol of said alkali metal salt and sufficient to neutralize the free inorganic halogen acid formed in the reaction.

4. A method of preparing organo-substituted amino-carboxylic acids having two hydrocarbon substituents containing each from 1 to 20 carbon atoms and attached to the amino-nitrogen atom and, further, having more than one carbonyl group attached to said nitrogen atom, said method comprising reacting a secondary amine having two hydrocarbon substituents from 1 to 20 carbon atoms attached to the amino-nitrogen atom, with an alkali metal salt of a monohalogen-substituted C₂-C₄ aliphatic monocarboxylic acid and sodium bicarbonate in an amount equal to at least 0.5 mol per each mol of said alkali metal salt and sufficient to neutralize the free inorganic halogen acid formed in the reaction.

5. A method of preparing organo-substituted amino-carboxylic acids having two hydrocarbon substituents containing each from 1 to 20 carbon atoms and attached to the amino-nitrogen atom and, further, having more than one carbonyl group attached to said nitrogen atom, said method comprising reacting a secondary amine having two hydrocarbon substituents from 1 to 20 carbon atoms attached to the amino-nitrogen atom, with an alkali metal salt of a monohalogen-substituted C₂-C₄ aliphatic monocarboxylic acid in the presence of sodium bicarbonate in a manner sufficient to maintain a pH in the range of 7.0 to 8.5 in the reaction product mixture throughout the reaction.

6. A method of preparing organo-substituted amino-carboxylic acids having more than one carbonyl group and at least one alkyl substituent with 8 to 18 carbon atoms attached to the amino-nitrogen atom, which comprises reacting a primary alkyl amine containing from 8 to 18 carbon atoms in the alkyl chain with an alkali metal salt of a halogen-substituted saturated C₂-C₄ aliphatic monocarboxylic acid in the presence of sodium bicar-
bonate in an amount sufficient to neutralize the free inorganic halogen acid formed in the reaction to maintain a pH in the range of 7.0 to 8.5 in the reaction product mixture throughout the reaction.

7. A method of preparing organo-substituted amino-carboxylic acids having more than one carboxyl group attached to the amino-nitrogen atom and, further, having two alkyl substituents containing each from 8 to 18 carbon atoms attached to said nitrogen atom, said method comprising reacting a secondary alkyl amine containing from 8 to 18 carbon atoms in the alkyl chains attached to the amino-nitrogen atom, with an alkali metal salt of a monohalogen-substituted C₈-C₁₈ aliphatic monocarboxylic acid in the presence of sodium bicarbonate in an amount sufficient to neutralize the free inorganic halogen acid formed in the reaction to maintain a pH in the range of 7.0 to 8.5 in the reaction product mixture throughout the reaction.

8. A method of preparing N-alkyl-substituted amino-carboxylic acids having more than one carboxyl group and at least one C₆-C₁₄ straight-chain alkyl substituent attached to the amino-nitrogen atom, which comprises reacting an amine containing at least one C₆-C₁₄ straight-chain alkyl chain and at least one hydrogen attached to the amino-nitrogen atom with a sodium salt of a monohalogen-substituted saturated aliphatic monocarboxylic acid containing from 2 to 4 carbon atoms in the presence of sodium bicarbonate in an amount sufficient to neutralize the free inorganic halogen acid formed in the reaction to maintain a pH in the range of 7.0 to 8.5 in the reaction product mixture throughout the reaction.

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