United States Patent Office 3,024,283 Patented Mar. 6, 1962

3,024,283

PRODUCTION OF QUATERNARY AMMONIUM COMPOUNDS

Lincoln D. Metcalfe, Riverdale, and Milton A. Mitz, Chicago, Ill., assignors, by mesne assignments, to Armour and Company, Chicago, Ill., a corporation of Delaware

No Drawing. Filed Apr. 1, 1958, Ser. No. 725,488
5 Claims. (Cl. 260—567.6)

This invention relates to the production of quaternary ammonium compounds and more particularly to the production of such compounds by means of ion exchangers.

Quaternary ammonium compounds are highly versatile materials finding use as wetting, foaming, and emulsifying agents, chemical sterilizing and sanitizing agents, softening agents and dyeing aids, and anti-static agents, to name a few. The production of these compounds employing conventional chemical methods generally requires a lengthy reaction time and is accompanied by the formation of interfering agents which either prevent the desired reaction from going to completion or result in a contaminated final product. This is evidenced, for example, in the preparation of quaternary ammonium acetate from the corresponding chloride wherein a portion of the chloride remains unreacted due to the formation of interfering agents. The quantitative purification of the desired acetate involves several chemical steps which ultimately result in a refined product in substantially reduced yields.

Applicant has discovered a process for quantitatively and selectively producing quaternary ammonium compounds which to a large extent overcomes the disadvantages encountered in conventional methods and which can be advantageously adapted to large scale manufacturing at a realistic cost and with facility of operation. In its most general aspect the invention involves contacting a cationic fragment of a quaternary ammonium compound with a cationic exchange polymer and eluting the fixed cationic fragment from the exchange polymer with a substantially non-aqueous solvent medium containing an anionic fragment of an ionizable compound to obtain the quaternary ammonium reaction product of the cationic and anionic fragments. This method presents almost unlimited possibilities for producing a wide variety of quaternary ammonium compounds in addition to providing means for interchanging selectively one anionic fragment for another to achieve a desired end product. Yields are quantitative, resulting in substantially 100% recovery.

In another of its aspects, this inventive procedure enables the separation and purification of quaternary ammonium compounds from undesirable impurities, and, in still another modification, provides means for assaying quaternary ammonium compounds, trimethyloctadecylammonium stearate in particular, incorporated in regulated amounts in such materials, for example, as animal feeds.

It is therefore the primary object of this invention to provide a highly efficient, commercially practical process for the quantitative production of quaternary ammonium compounds.

It is another object of this invention to provide a process for selectively interchanging anionic fragments of quaternary ammonium derivatives to produce a desired end product.

A further object of this invention is to provide a method for purifying quaternary ammonium compounds.

A still further object of this invention is to provide a process for assaying the quaternary ammonium compound content of materials in which such compounds are incorporated.

Other objects and advantages will become apparent as the specification proceeds.

In the preferred practice of this invention, any insoluble, open chain, high molecular weight polymer containing acidic, that is, cationic exchange groups, may be employed. For the purpose of this invention, "open chain" means a polymer of the fibrous type in which the ion exchange groups are exposed as opposed to spherical particles of ion exchange resins wherein the ion exchange groups are positioned in a matrix. The material for this cationic exchanger may be derived from a polysaccharide of vegetable, animal or bacterial origin, which can be either the structural or nutrient type. Thus, the material for this cation exchange polysaccharide may be a suitable derivative of such vegetable nutrient polysaccharides as starches, e.g. amylose and amlopectin, and inulins; such vegetable structural polysaccharides as celluloses, e.g. alpha cellulose, xylans, pectins and algins; such animal polysaccharides as glycogens, chitins and mucopolysaccharides, e.g. chondroitin sulfuric acid, heparin and hyaluronic acid; and such bacterial polysaccharides as levans and dextrans. An especially desirable polysaccharide cationic exchanger can be derived from such alpha celluloses as paper, cotton, wood pulp, cotton cloth, etc.

The cationic exchange groups contained in these open chain, high molecular polymers may be any radical or group capable of reacting with an ionizable substance to fix cations on the exchangers. Examples of these preferred cellulose cation exchangers are oxidized cellulose, carboxymethyl cellulose (CMC), cellulose phosphate, and cellulose citrate. The oxidized cellulose and carboxymethyl cellulose are available commercially, while cellulose citrate can be prepared by esterifying an alpha cellulose with citric acid.

The cationic exchanger employed for the purposes of this invention should demonstrate the following properties from a practical consideration: (1) it should not be soluble in a substantially non-aqueous solvent selected as a medium for the reaction; (2) it should not be destructive or detrimental to the ionizable solute in the solvent medium; and (3) it should not react with the solvent to the exclusion of the ionizable solute.

The cationic fragment having utility for the purpose of this invention may be derived from any quaternary ammonium compound and can contain saturated or unsaturated groups. Also, the quaternary ammonium compound can contain an aromatic group, such as the benzyl group, and thus the cationic fragment can be obtained from such compounds as alkylbenzyldimethylammonium halides. In addition, such naturally occurring mixtures where the quaternary ammonium compound is prepared from a natural fatty acid source may be used. For example, trimethyl"coco"ammonium chloride, dimethyldi"tallow"ammonium chloride, trimethyl"soya" ammonium chloride, etc., are suitable sources for the cationic fragment. The cationic fragment may also be derived from primary, secondary and tertiary amines, such as alkylamines, dialkylamines, dimethylalkylamines, bis(2-hydroxyethyl)alkylamines and N-alkyl-1,3-propanediamines. Further, polyamines, such as N-dodecyltrimethylenediamine and cyclic nitrogen compounds such as 1-alkylpyridinium halides, e.g. octadecylpyrididinum chloride, can be employed to derive the cationic fragment.

Contact between the cationic fragment and the cationic exchanger may be effected in a batch or column operation. For example, the exchanger may be packed into a vertically positioned cylinder, then a suitable substantially non-aqueous solvent medium containing the cationic

fragment may be passed through the exchanger to fix the fragment on the exchanger.

The anionic fragment that may be employed in this invention can be derived from any ionizable compound capable of electrolytic dissociation in a substantially non-aqueous solvent medium and preferably exhibiting stronger acidic properties than the cationic exchanger. This encompasses a large and diversified group of compounds and includes, in addition to the more common compounds displaying these preferred characteristics, such compounds as the lower fatty acids, i.e. acetic, propionic, and butyric acid, and any anionic polyelectrolyte, such as, for example, polysulfonic acids, non-polymeric polysulfonic acids, polysulfuric esters, polycarboxylic acids, polysaccharinic acids, polyphosphoric acids, polyphosphoric esters, and polysilicate.

The term "substantially non-aqueous medium" refers to a solvent or mixture of solvents substantially free from water. Although the solvent included in the medium may be water-immiscible, better ion exchange can be obtained in a substantially non-aqueous, water miscible solvent medium. Thus, in the process of this invention the non-aqueous medium may consist of a non-aqueous solvent or a mixture of water and a non-aqueous solvent. It is preferred, however, that the amount of water employed in such a mixture not exceed 50% of the total volume.

The solvents having utility for the purpose of this invention may be an inorganic solvent such as liquid ammonia, liquid sulfur dioxide, liquid hydrogen fluoride, liquid nitrogen, liquid helium, etc. However, better results can be obtained when the medium includes an organic solvent of either the aliphatic or aromatic type. Thus, the medium may contain an aliphatic, oxygen-containing solvent such as ketones, e.g. acetone, methylethyl ketone, methylisobutyl ketone and diethyl ketone; aldehydes, e.g. propionaldehyde and butyraldehyde; acids, e.g. caproic and pelargonic; esters, e.g. alkyl acetates, propionates and caproates; acid anhydrides, e.g. acetic anhydride; esters, e.g. ethyl propyl and butyl; monohydric alcohols, e.g. methanol, ethanol, propanol, butanol, pentanol and hexanol; polyhydric alcohols, e.g. ethylene glycol and propylene glycol. Also, this organic solvent may be hydrocarbon, such as a paraffin, e.g. pentane, hexane, heptane and decane; and olefin, e.g. heptene, octene, decene, tridecene and pentadecene; or an aromatic hydrocarbon, e.g. benzene, toluene and napthalene. Another group of suitable organic solvents are the halogen-containing organic solvents; i.e. chlorine, fluorine, bromine and iodine derivatives of organic radicals, such as propyl, butyl, amyl, heptyl, nonyl, ethylidene, propylidene, ethylene; e.g. chloroform, carbon tetrachloride and ethylene chloride. Still another group of suitable organic solvents are the nitrogen-containing organic solvents, such as nitro compounds, e.g. nitroethylene; amides, e.g. formamide and diethyl formamide; nitriles; and primary, secondary and tertiary amines. A further group of suitable organic solvents are the sulfur-containing solvents, such as mercaptans, e.g. ethylmercaptan; alkyl sulfoxides, e.g. dimethyl sulfoxide; and thioesters.

For the production of quaternary ammonium compounds in accordance with this method, it is preferred that the substantially non-aqueous solvent medium containing the anionic fragment have a pH of between about 0.1 and about 5.0. This preferred range has been demonstrated to be sufficient to displace the cationic fragment fixed on the ion exchanger and thus permit the desired cationic-anionic reaction product to form.

In the preferred practice of this invention a suitable solvent medium containing the cationic fragment of a quaternary ammonium compound is contacted with the special cationic exchange polymer to fix the fragment thereon. An eluant comprising a substantially non-aqueous solvent medium having a pH in the preferred range and containing a pre-selected anionic fragment is then passed through the exchanger and the eluate collected. Washings may be necessary to insure complete elution. The solvent containing the desired cationic-anionic reaction product is then removed by conventional methods, for example, evaporation.

The method of this invention can also be adapted to the purification of quaternary ammonium compounds. Thus, their separation from substances displaying no cationic activity can be effected by placing the material containing the desired quaternary ammonium compound into solution with a suitable solvent and then contacting it with the cationic exchanger. The cationic fragment of the quaternary ammonium compound is preferentially fixed onto the exchanger while the impurities pass through. One or more washings eliminates all of the undesired contaminants. Thereafter, elution with a suitable solvent medium containing the appropriate anionic fragment quantitatively reforms the quaternary ammonium compound in a pure state, the refined compound comprising the reaction product of the cationic fragment of the starting material and the substituted but equivalent anionic fragment carried by the eluant.

As a further modification of this invention, there is provided a convenient and accurate method for assaying the quaternary ammonium compound content of materials such as, for example, animal feeds. The quantity of trimethyloctadecylammonium stearate, a growth promotant employed in animal feeds, is subject to federal administrative control. Heretofore there has been no facile and accurate method for determining the amount of this substance contained in a unit weight of animal feed. The process of this invention has provided means for effecting such an assay. In the preferred practice of this method a measured quantity of the feed is placed in an extractor with a suitable solvent. The extract is then contacted with the cationic exchange polymer. An eluant comprising a substantially non-aqueous solvent medium having a suitable pH and containing a preselected anionic fragment, is passed through the exchanger to obtain the reaction product of the cationic trimethyloctadecylammonium fragment and the preselected anionic fragment. A sample is taken of the eluate and by conventional methods such as titration or colorimetry the quantity of quaternary ammonium compound in the feed can be determined. This assay process can, obviously, be employed in conjunction with materials other than animal feeds.

The cationic exchanger employed in accordance with the process of this invention can be regenerated after each completed operation by washing with water to desorb any contaminating eluting substances. It is thus possible to utilize the same exchanger indefinitely resulting in substantial savings in materials and labor.

This invention can be further illustrated by the following specific examples:

EXAMPLE I

The production of various quaternary ammonium compounds (QAC) employing different starting materials and different cellulose cation exchangers was effected in the following manner:

A solution of the starting material in alcohol was passed through a column of the cationic exchanger. The column was washed with 25 ml. of 3A alcohol and then with 25 ml. of distilled water. The column was then washed with a solution of an acid in 3A alcohol until the acid wash coming off the column no longer gave a test for quaternary ammonium compound (QAC). The acid solution was tested for the starting anion, the final anion, and the quaternary ammonium cation by standard chemical analysis tests. The new QAC was recovered from the solution and weighed.

The materials used and the products formed are set out in the accompanying table:

Production of Quaternary Ammonium Compounds (QAC) Using Cellulose Ion-Exchangers

Starting QAC	Cellulose column	Acid solution used for recovery	QAC recovered from column	Tests on recovered QAC soln.		
				QAC cation	Starting anion	Final anion
1. Trimethyloctadecylammonium chloride—115 mg.	Phosphorylated	10% acetic acid in 3A alcohol.	Trimethyloctadecylammonium acetate—120 mg.	(+)	(−)	(+)
2. Trimethyloctadecylammonium chloride.	do	10% citric acid in 3A alcohol.	Trimethyloctadecylammonium citrate.	(+)	(−)	(+)
3. Trimethyloctadecylammonium chloride.	do	0.5 N. H_2SO_4 in 3A alcohol.	Trimethyloctadecylammonium sulfate.	(+)	(−)	(+)
4. Trimethyloctadecylammonium chloride.	do	0.5 N. HNO_3 in 3A alcohol.	Trimethyloctadecylammonium nitrate.	(+)	(−)	(+)
5. Trimethyloctadecylammonium stearate.	do	1 N. HCl in 3A alcohol	Trimethyloctadecylammonium chloride.	(+)	(−)	(+)
6. Trimethyloctadecylammonium laurate.	do	do	do	(+)	(−)	(+)
7. Trimethylhexadecylammonium laurate.	do	do	Trimethylhexadecylammonium chloride.	(+)	(−)	(+)
8. Trimethyloctadecylammonium stearate.	Oxidized	do	Trimethyloctadecylammonium chloride.	(+)	(−)	(+)
9. Trimethyloctadecylammonium chloride.	do	10% acetic acid in 3A alcohol.	Trimethyloctadecylammonium acetate.	(+)	(−)	(+)
10. Trimethyloctadecylammonium citrate.	do	1 N. HCl in 3A alcohol	Trimethyloctadecylammonium chloride.	(+)	(−)	(+)
11. Trimethyloctadecylammonium pelargonate.	Phosphorylated	do	do	(+)	(−)	(+)
12. Trimethylhexadecylammonium palmitate.	do	do	do	(+)	(−)	(+)
13. Trimethyloctadecylammonium stearate.	Citrate	do	do	(+)	(−)	(+)
14. Trimethyloctadecylammonium stearate.	CMC	do	do	(+)	(−)	(+)
15. Dimethyldioctadecylammonium chloride.	CMC	10% acetic acid in 3A alcohol.	Dimethyldioctadecylammonium acetate.	(+)	(−)	(+)
16. Trimethyl-"Coco"-ammonium tartrate.	Oxidized	1 N. HCl in 3A alcohol	Trimethyl-"Coco"-ammonium chloride.	(+)	(−)	(+)
17. Trimethyldodecylammonium chloride.	do	10% acetic acid in 3A alcohol.	Trimethyldodecylammonium acetate.	(+)	(−)	(+)

EXAMPLE II

The quantitative recovery of quaternary ammonium compounds from solutions containing them was demonstrated in the following manner:

A sample of a QAC dissolved in isopropyl alcohol was placed on a cellulose column. The solution contained from 100 to 500 micrograms QAC. The column was washed with 20 ml. of 3A alcohol followed by 20 ml. of distilled water. Then the column was washed with 5 ml. alcoholic 1 N. HCl. This acid fraction was collected with 10 ml. of distilled wash water. The acid fraction was analyzed for QAC by the Colorimetric Method of Wilson. A number of quaternaries were analyzed in this manner.

Analysis of Various QAC Solutions

Compound	Cellulose column	Micrograms QAC	
		Added	Recovered
Trimethyloctadecylammonium pelargonate	Phosphorylated	179.5	177
Trimethylhexadecylammonium laurate	do	320	324
Trimethyloctadecylammmonium laurate	do	425	420
Trimethyloctadecylammonium stearate.	do	400	420
Trimethyloctadecylammonium chloride.	Oxidized	250	250
Do	Citrate	114	112
Do	CMC	500	500

EXAMPLE III

The purification of quaternary ammonium compounds containing several impurities was effected in the following way:

A cellulose column was made of 1 gram of phosphorylated cellulose in a glass tube. A sample of a QAC containing impurities was then passed through the column. The column was washed with 20 ml. of 3A alcohol followed by 28 ml. of distilled water. These washings were discarded. An eluant of 10 ml. of 1 N. alcoholic hydrochloric acid was then passed through the column and collected. This was followed by a washing with 10 ml. of 3A alcohol which was collected and added to the acid wash. The alcohol was evaporated and the sample recovered weighed. The results are set out below.

Sample 1.—Trimethyloctadecylammonium Chloride

Impurities—Isopropyl alcohol, sodium chloride, tertiary amine, acid amide, fatty acid, nitrile.

Weight added to column	mg.	150
Sample recovered from column	mg.	142
Assay of recovered sample	percent	99.7

Sample 2.—Tris-2-Hydroxyethyloctadecylammonium Chloride

Impurities—Isopropyl alcohol, ethylene glycol, ethylenechlorohydrin, tertiary amine, acid amide, fatty acid, nitrile.

Weight added to column	mg.	150
Sample recovered from column	mg.	145
Assay of recovered sample	percent	99.6

EXAMPLE IV

The trimethyloctadecylammonium stearate content in animal feed was assayed by titration as follows:

A 550 mm. Pyrex glass column of 20 mm. internal diameter was fitted with a stopcock to shut off the flow of emerging liquid. A 50–50 mixture by weight of cellulose and Supercel was thoroughly mixed and placed in the column to a depth of 60 to 80 mm. on a glass-wool plug. A device for placing a head of air on the above column was made by making a pressure flask from a suction flask containing a glass tube into which mercury could be forced by an aspirator bulb. The mercury in the tube sustains a small but sufficient air pressure on the column.

A feed sample containing from 0.5 to 1 mg. of trimethyloctadecylammonium stearate (QAC) was extracted with 30 ml. of chloroform in a continuous extractor such as a Soxhlet or Butt extractor for one hour. The chloroform solution was passed through an oxidized cellulose, cellulose citrate, or a low-capacity CMC column prepared as described above. The column was washed free of chloroform and other foreign material with 3A alco-

hol. These washings were discarded. The QAC was removed from the column with 10 ml. of 1 N alcoholic hydrochloric acid followed by 40 ml. of distilled water. These washings were collected and transferred to a 250 ml. separatory funnel. 0.5 ml. of 0.1% dichlorofluorescein and 10 ml. of chloroform were added to the funnel. After vigorous shaking for about one minute the layers were allowed to separate. The chloroform layer was drawn off into a 20 x 150 mm. test tube. 0.5 ml. of distilled water and several drops of 0.5 N NaOH solution were added to the tube. The tube was stoppered and shaken vigorously. The layers were allowed to separate. A red or pink color in the lower layer indicated QAC was present. The solution was treated with a pre-prepared standard sodium lauryl sulfate, shaking vigorously after each 0.1 to 0.2 ml. addition allowing the layers to separate. This was continued until the chloroform layer was colorless. The solution was made acid with 0.5 N HCl, shaken well, then made basic with 0.5 N. NaOH and again shaken well. Titration was continued until the chloroform layer was again colorless. This acid-base step was repeated again. This step split any QAC that was in the stearate form and made it titratable. 10 ml. more chloroform was added to the separatory funnel and the extraction and titration repeated. The 10 ml. chloroform extraction was repeated until there was no longer any pink color extracted from the solution in the separatory funnel. Two extractions were sufficient for complete removal of QAC for titration.

Calculation:

$$\text{Percent QAC} = \frac{(\text{Moles of sodium lauryl sulfate/ml.})(\text{ml. tit.})(\text{mol. wt.})(100)}{\text{grams of sample taken}}$$

EXAMPLE V

The trimethyloctadecylammonium stearate content in animal feed was assayed by colorimetric means as follows:

At least five grams of a feed sample were weighed into a piece of fluted filter paper, and extracted for 3 hours, in a Butt extractor, by percolation with 30 ml. of chloroform. 5 ml. of 3A alcohol were added and the extract solution passed through an oxidized cellulose column aided by either pressure or vacuum, at a rate of 40–60 drops a minute. The extraction flask was washed 3 times with small portions of 3A alcohol and the washings passed through the column. An aliquot that gave 0.2 to 0.5 mg. of the QAC was taken and passed through the oxidized cellulose column. The column was washed with 5 ml. of anhydrous 3A alcohol and then with 5 ml. of 50–50 3A alcohol and water, and again with 5 ml. of distilled water. All these washings were discarded. A test tube or small beaker was placed under the column and the column eluted with 5 ml. of 1 N alcoholic HCl. The column was then washed with 20 ml. of distilled water. The alcoholic eluate and aqueous washings were combined in a 250 ml. separatory funnel. 50 ml. of chloroform were pipetted into the funnel and then 1 ml. of bromophenol blue indicator was added. The funnel was shaken for one minute, and the layers allowed to separate. The lower chloroform layer was transferred into a second separatory funnel containing 10 ml. of 1% carbonate solution. The funnel was shaken for 15 seconds and again the layers were allowed to separate. The lower (chloroform) layer was blue indicating that the QAC was present in the sample. This layer was transferred to a 250 ml. glass-stoppered Erlenmeyer flask containing 0.5 g. of anhydrous granulated sodium sulfate, and allowed to stand for 30 minutes. The optical density of the solution was read on the Coleman Jr. spectrophotometer using chloroform as a blank. The reading obtained was compared with a previously prepared calibration curve made from known solutions to determine the amount of trimethyloctadecylammonium stearate present.

While in the foregoing specification various modifications of this invention have been set forth and specific details thereof elaborated for purpose of illustration, it will be apparent to those skilled in the art that this invention is susceptible to other embodiments and that many of these details may be varied without departing from the basic concept and spirit of the invention.

We claim:

1. A process for the production of a long-chain quaternary ammonium compound comprising the steps of adsorbing on an insoluble polysaccharide cationic exchanger the cationic fragment of a long-chain quaternary ammonium compound by treating said exchanger with a substantially non-aqueous solvent solution of said quaternary ammonium compound, passing through said exchanger a substantially non-aqueous eluant solution of an ionizable compound having a preselected anionic fragment, said eluant solution being at a pH between about 0.1 to about 5.0, to cause a reaction between said cationic and anionic fragment to form a long-chain quaternary ammonium compound, and recovering in the eluate the quaternary ammonium compound thus formed.

2. A process for the production of a long-chain quaternary ammonium compound comprising the steps of adsorbing an oxidized cellulose the cationic fragment of a long-chain quaternary ammonium compound by treating the oxidized cellulose with a substantially non-aqueous solvent solution of said quaternary ammonium compound, passing through said exchanger a substantially non-aqueous eluant solution of an ionizable compound having a preselected anionic fragment, said eluant solution being at a pH between about 0.1 to about 5.0, to cause a reaction between said cationic and anionic fragment to form a long-chain quaternary ammonium compound, and recovering in the eluate the quaternary ammonium compound thus formed.

3. A process for the production of a long-chain quaternary ammonium compound comprising the steps of adsorbing on carboxymethyl cellulose the cationic fragment of a long-chain quaternary ammonium compound by treating the carboxymethyl cellulose with a substantially non-aqueous solvent solution of said quaternary ammonium compound, passing through said exchanger a substantially non-aqueous eluant solution of an ionizable compound having a preselected anionic fragment, said eluant solution being at a pH between about 0.1 to about 5.0, to cause a reaction between said cationic and anionic fragment to form a long-chain quaternary ammonium compound, and recovering in the eluate the quaternary ammonium compound thus formed.

4. A process for the production of a long-chain quaternary ammonium compound comprising the steps of adsorbing on phosphorylated cellulose the cationic fragment of a long-chain quaternary ammonium compound by treating the phosphorylated cellulose with a substantially non-aqueous solvent solution of said quaternary ammonium compound, passing through said exchanger a substantially non-aqueous eluant solution of an ionizable compound having a preselected anionic fragment, said eluant solution being at a pH between about 0.1 to about 5.0, to cause a reaction between said cationic and anionic fragment to form a long-chain quaternary ammonium compound, and recovering in the eluate the quaternary ammonium compound thus formed.

5. In a process for the purification of a long-chain quaternary ammonium compound, the steps of treating an insoluble polysaccharide cationic exchanger with a substantially non-aqueous solution of a long-chain quaternary ammonium compound and non-cationic active impurities to adsorb said cationic fragment on said exchanger, passing through said exchanger a substantially non-aqueous eluant solution of an ionizable compound, said eluant solution having a pH between about 0.1 to

about 5.0, to cause a reaction between said cationic and anionic fragments to reform in a pure state the starting quaternary ammonium compound, and recovering in the eluate said quaternary ammonium compounds.

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