United States Patent Office 2,837,532 Patented June 3, 1958

2,837,532

PROCESS FOR PRODUCTION OF GLUTAMIC ACID

Joseph L. Purvis, Cincinnati, Ohio, assignor to International Minerals & Chemical Corporation, a corporation of New York

No Drawing. Application February 28, 1956
Serial No. 568,198

11 Claims. (Cl. 260—326.3)

This invention is concerned with the preparation of alpha-hydroxy glutaric acid, the lactone of this acid, and alphahaloglutaric acid, and more particularly, with the preparation of these compounds from 3-halocyclopentene and the conversion of these compounds into glutamic acid.

Alpha-hydroxy glutaric acid, the lactone of this acid, and alpha-chloroglutaric acid are known compounds. Dehydrogenation of alpha-hydroxy glutaric acid produces alpha-ketoglutaric acid which can be converted to glutamic acid. The production of glutamic acid by this method, however, is commercially unfeasible due to the cost of raw materials and reagents and the cumbersome procedures involved. There has been a need for a commercially feasible method for producing alpha-hydroxy glutaric acid and particularly a method for converting these compounds to glutamic acid.

L-glutamic acid in the form of its monosodium salt is widely used as a seasoning material. Substantially all glutamic acid utilized commercially is recovered from naturally occurring materials such as proteins and sugar beet residues such as concentrated Steffen's filtrate. Heretofore, no commercially feasible process for synthesizing glutamic acid has been available.

One object of this invention is to provide a process for producing glutaric acid compounds from 3-halocyclopentenes.

Another object of this invention is to provide a process for producing alpha-hydroxy glutaric acid, alpha-hydroxy glutaric acid lactone or alpha-haloglutaric acid or a mixture of two or more of the compounds from 3-halocyclopentene.

Another object of this invention is to provide a process for producing alkyl substituted glutaric acid compounds from the corresponding alkyl substituted 3-halocyclopentene.

Another object of this invention is to provide a process for synthesizing DL-glutamic acid from 3-halocyclopentene.

It is a further object of this invention to provide a process for producing L-glutamic acid from alpha-hydroxy glutaric acid, alpha-hydroxy glutaric acid lactone, alpha-halogutaric acid or a mixture of two or more of these compounds.

In accordance with this invention, a 3-halocyclopentene such as 3-chlorocyclopentene or 3-bromocyclopentene is oxidized to either alpha-hydroxy glutaric acid, alpha-hydroxy glutaric acid lactone, alpha-haloglutaric acid or a mixture of two or more of these compounds. Alpha-hydroxy glutaric acid or the lactone of this acid or alpha-haloglutaric acid or a mixture of two or more of them may then be ammoniated to produce glutamic acid or a glutamic acid precursor compound. Hydrolysis of the glutamic acid precursor compound under either conventional acid or alkaline conditions results in the formation of DL-glutamic acid which may be resolved to produce L-glutamic acid.

The term "a halocyclopentene" as used herein refers

to unsubstituted halocyclopentenes such as chlorocyclopentene, bromocyclopentene, iodocyclopentene and fluorocyclopentene and also to substituted halocyclopentenes such as alkyl substituted halocyclopentenes, for example, halocyclopentenes in which one or more alkyl or other substituents is attached to a carbon atom in the cyclopentene ring. Representative alkyl substituent groups include lower alkyl groups, that is, alkyl groups containing less than about eight carbon atoms, for example, methyl, ethyl, propyl, isopropyl, butyl, etc. The term "halocyclopentene" refers to unsubstituted halocyclopentenes; namely, chlorocyclopentene, bromocyclopentene, iodocyclopentene or fluorocyclopentene.

Oxidation of a 3-halocyclopentene in accordance with this invention results in a glutaric acid compound corresponding to the starting material in the number of carbon atoms in the molecule. For example, an alkyl halocyclopentene will be converted to the corresponding alkyl substituted glutaric acid—an alkyl hydroxy glutaric acid or its lactone or an alkyl haloglutaric acid or a mixture of two or more of these glutaric acid compounds depending upon the reaction conditions used.

Dicyclopentadienes are a convenient source material for the 3-halocyclopentenes employed in my invention. A suitable dicyclopentadiene is first heated to a temperature above 170° C., under which conditions it depolymerizes to the corresponding cyclopentadiene. Treatment of the cyclopentadiene with gaseous hydrogen halide, preferably hydrogen chloride at a temperature below about 0° C. and preferably between about —50° C. and —70° C., produces the corresponding 3-halocyclopentene, which may be separated from the reaction product mixture by distillation at subatmospheric pressures.

Oxidation of a 3-halocyclopentene to alpha-hydroxy glutaric acid, the lactone of this acid, alpha-haloglutaric acid or a mixture of two or more of these compounds in accordance with this invention is effected by treating the 3-halocyclopentene with an oxidizing agent preferably in a suitable solvent. Strong oxidizing agents such as nitric acid, potassium permanganate and alkali metal bichromates are preferred but other similar oxidizing agents may be utilized. Potassium bichromate is desirably used in conjunction with sulfuric acid but may also be used with acetic acid or similar acids. Oxidation with nitric acid is carried out in an aqueous medium. Permanganates, including alkali metal and alkaline earth metal permanganates, may be utilized in an acid, neutral or alkaline medium. The conditions for using the various oxidizing agents are conventional and the solvent used will depend upon the nature of the oxidizing agent. Oxidation with nitric acid, for example, is carried out in the presence of a catalyst such as vanadium in the form of an alkali metal vanadate and preferably at a temperature above about 50° C. Chromate and permanganate oxidations are preferably conducted at room temperature or below.

The oxidation reaction is continued until substantially all 3-halocyclopentene is reacted. Usually between about 0.5 and 10 hours are sufficient to complete the reaction, but under mild conditions longer periods may be required. The reaction product mixture comprises in addition to alpha-hydroxy glutaric acid, the lactone of this acid or alpha-chloroglutaric acid, also possibly some succinic acid and some oxalic acid. Recovery of the glutaric acid compounds from the mixture may be effected by extraction with a suitable solvent such as ether or by any other convenient procedure. The resulting ether solution may be evaporated to dryness leaving the glutaric acid compounds as a residue.

A mixture of alpha-hydroxy glutaric acid, the lactone of this acid and alpha-haloglutaric acid (preferably the

chloro or bromo derivative but permissibly the iodo and fluoro compounds) in aqueous media, upon standing at room temperature, spontaneously converts to substantially alpha-hydroxy glutaric acid lactone alone. By varying the conditions for oxidizing 3-halocyclopentene the resulting oxidation reaction product mixture will contain alpha-hydroxy glutaric acid, alpha-hydroxy glutaric acid lactone or alpha-haloglutaric acid as the predominant constituent. Since any of these compounds or their mixture may be ammoniated to glutamic acid or a glutamic acid precursor compound and this mixture hydrolyzed to glutamic acid, there is no particular need for producing any one of them as the sole decomposition product where glutamic acid is desired as the ultimate end product. Also in the case where alpha-hydroxy glutaric acid lactone is to be the end product there is no need to use special conditions to eliminate formation of alpha-haloglutaric acid simultaneously during the decomposition because an aqueous mixture of alpha-hydroxy glutaric acid, the lactone of this acid and alpha-haloglutaric acid upon standing at room temperature spontaneously changes to alpha-hydroxy glutaric acid lactone. After substantially complete conversion of the mixture to lactone, the latter may be recovered by simply evaporating the solution leaving the lactone as a residue.

Preparation of glutamic acid from alpha-hydroxy glutaric acid or its lactone or apha-haloglutaric acid or a mixture thereof may be carried out by treatment with ammonia at an elevated temperature. Best yields are obtained at temperatures above about 250° C. but temperatures as low as about 200° C. may be utilized if lower yields are acceptable. Preferably the ammonia treatment is carried out for between about one-half and about 30 hours at between about 250° C. and about 350° C. but shorter times and/or higher temperatures may be used.

Prior to ammonia treatment, any sulfuric acid in the solution containing the glutaric acid compound is preferably either neutralized or removed. If sulfuric acid is utilized in the oxidation, the sulfate ions in the reaction product mixture may be precipitated as barium sulfate by treatment with BaO or hydroxide, for example, and removed by filtration. Other inorganic ions may be similarly separated as their insoluble salts.

Ammoniation may be carried out using either aqueous or anhydrous ammonia. Ammonium carbonate may be employed as a catalyst where aqueous ammonia is employed but excellent results are also obtained in the absence of such a catalyst. Prior to ammoniation it is desirable to remove any acids present in order to minimize the amount of ammonia required. Lower fatty acids may be removed by evaporation.

The quantity of ammonia either in the aqueous or anhydrous form is not critical and may be varied widely. It is only necessary that sufficient ammonia be utilized to completely react with alpha-hydroxy glutaric acid lactone or alpha-haloglutaric acid or a mixture thereof as the case may be.

The product of the ammoniation reaction is glutamic acid or a glutamic acid precursor compound which is thought to be the ammonium salt of 2-oxo-5-pyrrolidine carboxylic acid. The precursor is readily converted to glutamic acid by hydrolysis under the same conditions which convert 2-oxo-5-pyrrolidine carboxylic acid to glutamic acid. Glutamic acid is recovered from the hydrolyzate by crystallization at its isoelectric point.

The following examples illustrate specific embodiments of this invention. All parts and percentages are by weight unless otherwise indicated.

Example I

Potassium permanganate in the amount of 50 parts was dissolved in 1000 parts water and the solution cooled to about 9° C. At this temperature, 10 parts of 3-chlorocyclopentene was added to the solution dropwise over a period of 15 minutes and the resulting mixture agitated for about one hour. The reaction product mixture was filtered to remove insoluble solids. Analysis of the filtrate showed the presence of apha-chloroglutaric acid and alpha-hydroxy glutaric acid lactone. These glutaric acid compounds are recovered from the reaction product mixture by acidification of the reaction mixture followed by extraction with ethyl ether. Evaporation of the resulting ether solution leaves the glutaric acid compounds as a residue.

Example II

3-chlorocyclopentene in the amount of 20.2 parts was added to 250 parts of a 50% aqueous nitric acid solution containing 0.05 part of sodium vanadate. Addition of the 3-chlorocyclopentene took place at 59° C. over a period of three and one-half hours. The reaction mixture was allowed to cool to about 30° C. over a period of one-half hour and then filtered to remove insoluble solids. A 20% aqueous sodium hydroxide solution in the amount of 65 parts was added to 50 parts of the filtrate in order to adjust the pH to about 1. The adjusted filtrate was then filtered. Analysis of the resulting filtrate showed the presence of alpha-hydroxy glutaric acid lactone and alpha-chloroglutaric acid along with succinic acid. The glutaric acid compounds are separated from this reaction product mixture by extraction with ethyl ether. Evaporation of the resulting ether solution leaves the glutaric acid compounds as residue. Purification of the glutaric acid compounds may be effected by conventional procedures.

Example III

A mixture of alpha-hydroxy glutaric acid lactone, alpha-hydroxy glutaric acid and alpha-chloroglutaric acid produced in the amount of 51.2 parts was dissolved in 450 parts of 28% aqueous ammonia and heated at 200° C. in an autoclave under autogenous pressure for about twelve hours. Aqueous ammonia was then evaporated from the reaction product mixture and the residue admixed with 208 parts of 20% hydrochloric acid and hydrolyzed for four hours. The hydrolyzate was evaporated to dryness, dissolved in 200 parts of H_2O and treated with sodium hydroxide to adjust the pH to about 3.2. Glutamic acid was crystallized from the resulting solution. The glutamic acid thus recovered was identified as DL-glutamic acid and obtained in an amount corresponding to a 15.7% yield. L-glutamic acid was produced from the DL-glutamic acid by resolution in accordance with conventional procedures.

Example IV

Following the procedure of Example III, but using a temperature of 300° C. and a reaction time of three hours, a yield of DL-glutamic acid in the amount of 75.1% of the theoretical was obtained.

Example V

Following the procedure of Example III, but using a temperature of 400° C. and a reaction time of 30 minutes, a yield of glutamic acid in the amount of 49.1% of the theoretical was obtained.

Having thus fully described and illustrated the character of the instant invention, what is desired to be secured by Letters Patent is:

1. A process for preparing an alpha-amino dicarboxylic acid which comprises heating ammonia at a temperature above about 200° C. with a glutaric acid compound selected from the group consisting of alpha-chloroglutaric acid, alpha-hydroxyglutaric acid, alpha-hydroxyglutaric acid lactone, and the alkyl-substituted homologues thereof wherein the alkyl substituent contains less than eight carbon atoms until the reaction of ammonia therewith is substantially complete, hydrolyzing any amino acid precursor compounds therein, and recovering said alpha-amino dicarboxylic acid therefrom.

2. The process of claim 1 in which the ammonia treatment is at a temperature above about 250° C.

3. The process of claim 2 in which ammonia is in the form of aqueous ammonia.

4. The process of claim 2 in which the ammonia is in the form of anhydrous ammonia.

5. The process of claim 3 in which the reaction with aqueous ammonia is catalyzed with ammonium carbonate.

6. The process of claim 1 in which the ammonia treatment is at a temperature between about 250 and about 350° C.

7. A process for preparing glutamic acid which comprises commingling ammonia with a glutaric acid compound selected from the group consisting of alpha-chloroglutaric acid, alpha-hydroxyglutaric acid, and alpha-hydroxyglutaric acid lactone in a proportion sufficient to react with substantially all of said glutaric acid compound, heating the resulting mixture to a temperature between about 250 and about 350° C. for a period of about 0.5 to about 30 hours, subjecting the ammoniation product to hydrolysis in the presence of sodium hydroxide, and recovering glutamic acid from the hydrolyzate.

8. In a process for preparing an alpha-amino dicarboxylic acid wherein a 3-halocyclopentene having at most one ring-substituted alkyl group of less than eight carbon atoms is treated with a strong oxidizing agent under oxidizing conditions and the oxidation product is treated with ammonia, the improvement which comprises carrying out said treatment with ammonia at a temperature above about 200° C. until the reaction is substantially complete, hydrolyzing any amino acid precursor compounds in the reaction product, and recovering said alpha-amino dicarboxylic acid therefrom.

9. In a process for preparing glutamic acid wherein 3-chlorocyclopentene is treated with a strong oxidizing agent under oxidizing conditions to produce a mixture of alpha-chloroglutaric acid, alpha-hydroxyglutaric acid, and alpha-hydroxyglutaric acid lactone, and the oxidation product is treated with ammonia, the improvement which comprises carrying out said treatment with ammonia at a temperature between about 250 and about 350° C. until the reaction is substantially complete, hydrolyzing any glutamic acid precursor compounds contained in the ammoniation product and recovering glutamic acid therefrom.

10. A process for preparing glutamic acid which comprises heating ammonia at a temperature above about 200° C. with a glutaric acid compound selected from the group consisting of alpha-chloroglutaric acid, alpha-hydroxyglutaric acid, and alpha-hydroxyglutaric acid lactone until the reaction of ammonia therewith is substantially complete, subjecting the reaction product to hydrolysis under conditions conventional for hydrolysis of glutamic acid precursor compounds and recovering glutamic acid from the hydrolyzate.

11. A process for preparing the ammonium salt of 2-oxo-5-pyrrolidine carboxylic acid which comprises heating ammonia at a temperature above about 200° C. with a glutaric acid compound selected from the group consisting of alpha-haloglutaric acid, alpha-hydroxyglutaric acid, and alpha-hydroxyglutaric acid lactone until the reaction of ammonia therewith is substantially complete.

References Cited in the file of this patent

UNITED STATES PATENTS

2,285,601	McAllister	June 9, 1942
2,478,047	Johnson	Aug. 2, 1949
2,525,794	Gresham et al.	Oct. 17, 1950
2,791,606	Novak et al.	May 7, 1957

OTHER REFERENCES

Moreschi: Chem. Abs., vol. 9 (1915), p. 1326.