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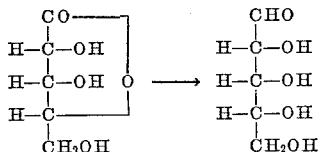
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PROCESS FOR PREPARING D-RIBOSE
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1 Claim. (Cl. 204—73)

This invention relates to improved process for preparing D-ribose by the electrolytic reduction of D-ribonolactone.

D-ribose is very important in the synthesis of vitamin B₂. It has been prepared commercially by the reduction of D-ribonolactone as shown by the following formulae.



Either chemical or electrolytic methods has been employed for this reduction. The chemical reduction was reported, e.g., in "Helvetica Chimica Acta" vol. 19, p. 189 (1936) in which sodium amalgam is used as a reducing agent. But, this method requires a considerable amount of mercury, and the preparation of amalgam is troublesome. Moreover, the control of the pH in the reaction mixture is difficult.

The electrolytic reduction is more advantageous than the chemical reduction. The electrolytic method heretofore reported employs mercury as the cathode, and an alkali metal salt of inorganic acid as the electrolyte which is capable of forming amalgam with mercury (e.g., "J. Chem. Soc." Japan, vol. 70, p. 310 (1950), Pat. Publ. No. 4359 (1950), Japan.) According to this method, the yield of D-ribose is higher than that of the chemical reduction while the amount of mercury required is smaller. (Usually 1/3—1/4 of the chemical reduction.) But, because the electrolyte is an alkali metal salt of inorganic acid, there remain such defects as follow.

In the course of electrolysis, an alkali metal ion discharges on the surface of cathode and forms amalgam with mercury continuously. The amalgam thus formed tends to react with water secondarily and produces an alkali metal hydroxide on the surface of cathode. As a result, the cathode is covered by a thin layer of alkaline solution during the electrolysis, even if the electrolytic solution itself is kept in a weakly acidic condition with addition of boric acid. On the other hand, D-ribonolactone is unstable in a strongly alkaline condition, and its lactone ring is cleaved to produce alkali metal ribonate which is no longer reduced. Accordingly, a part of D-ribonolactone is wasted by this unfavorable side-reaction, decreasing the yield of D-ribose.

We have found that the electrolytic reduction of D-ribonolactone may be improved by employing mineral acid-salts of primary, secondary or tertiary amines instead of alkali metal salts, as an electrolyte. According to this improved method, the yield of D-ribose may be increased, since the cleavage of D-ribonolactone may be substantially prevented.

According to our invention, said electrolysis may be carried out in a standard electrolytic cell, which, for example, consists of a glass beaker containing a small vol-

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ume porous cup, sheet anode being within the porous cup, and mercury or amalgamated metal cathode being placed in the bottom of the cell. The electrodes are set in a direct-current circuit having an ammeter and variable resistance, and the beaker placed in a cooling bath. The catholyte is placed in the cathode compartment between the porous cup which is the semi-permeable diaphragm and the beaker wall, and the anolyte within the porous cup. The reduction is effected with stirring and cooling until the reaction is substantially completed, as evidenced for example by the increased evolution of hydrogen.

"The semi-permeable diaphragm" of the electrolytic-reduction apparatus is one which permits hydrogen ions to pass from the anode compartment into the cathode compartment and permits the passage of anions (e.g., sulfate or chloride) from the cathode compartment to the anode compartment, but is sufficiently impermeable to prevent diffusion of the catholyte component to be reduced into the anode compartment. Various materials are suitable for use as semi-permeable diaphragms for the electrolytic reduction, and may be so used for the purpose of this invention; inter alia, unglazed porcelain, filters and notably Alundum.

The anode for the purpose of this invention may be of any of the materials commonly used for the electrolytic reduction. Thus the anode may be of lead, lead coated with lead dioxide, platinum and graphite. On the other hand, the cathode in this invention must be of mercury or amalgamated metal with mercury on its surface, for example, amalgamated lead, amalgamated silver, or amalgamated zinc, which have the hydrogen-overvoltage nearly equal to those of mercury.

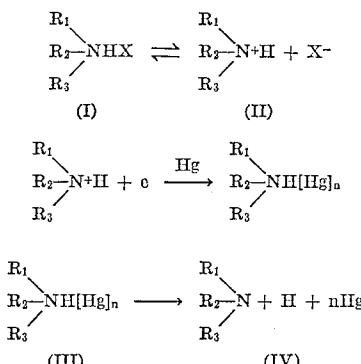
The anolyte for the purpose of this invention may be of the compositions commonly used for the electrolytic reduction, e.g., aqueous solutions of various concentrations of strong inorganic acids such as sulfuric, hydrochloric, or phosphoric acids. Preferably, the anolyte is sulfuric acid in a concentration of about 0.5% to about 80%, notably a concentration of about 10%.

The catholyte for the purpose of this invention is a non-alkaline aqueous solution of D-ribonolactone, i.e., a solution which contains D-ribonolactone, a sufficient amount of acid to make the solution non-alkaline and a mineral acid-salt of primary, secondary or tertiary amine. It is most preferable to maintain the catholyte at a pH of 3 to 5. For this purpose, dilute hydrochloric acid, dilute sulfuric acid, boric acid, phosphoric acid, etc. may be preferably used. Among them, boric acid and phosphoric acid are particularly suitable for this purpose.

Examples of suitable mineral acid-salts of amines for this purpose are the sulfate, nitrate, hydrochloride or phosphate of the following amines; monoalkyl amine e.g., methylamine, ethylamine, propylamine, butylamine, amylamine, hexylamine, heptylamine, octylamine; *ω*-hydroxymonoalkylamine e.g., ethanolamine, propanolamine; di- or tri-alkylamine e.g., dimethylamine, diethylamine, trimethylamine; cycloalkylamine e.g., cyclohexylamine, lower phenylalkyl amine e.g., benzylamine, phenethylamine.

In the electrolysis, the salts of amines (I) illustrated below act as protonized amine ions (II) which may form amalgams of protonized amines (III) with mercury on the surface of cathode, and act similarly to those of alkali metal. The amalgams thus formed are unstable even at room temperature and degrade rapidly producing nascent hydrogen which is utilized for the reduction of D-ribonolactone. (Ref.: J.C.S. 1954, p. 760.)

The electrolytic reaction of this invention may be illustrated by the following equations, wherein R_1 represents hydrogen, alkyl, ω -hydroxyalkyl, lower phenyl-alkyl or cycloalkyl radicals, R_2 and R_3 represent hydrogen or alkyl radicals, and X represents residue of mineral acid.



Protonized amine on the surface of cathode does not affect ribonolactone so much as an alkali hydroxide due to its weak alkalinity. Accordingly, D-ribonolactone is utilized efficiently to produce D-ribose.

Suitable concentration of the amine salt in the catholyte is not so high, because the amine salt is used as the source of protonized amine ion for the purpose of giving electric conductivity to the solution. Usually about 5% is most suitable for best results.

The electrolysis may be effected at various amperages; e.g., 0.5 ampere and 15 amperes, and preferably 1 to 4 ampere/dm.² of the cathode at various temperatures in which D-ribonolactone hardly decompose in the catholyte (e.g., between about 10 to about 40° C.). Higher amperages require more efficient cooling of the electrolytic-reduction cell. The above mentioned temperature, voltage, amperage and current density are not critical in the process of this invention.

When the current is passed through the cell, protonized amine ions migrate to the cathode and discharge and nascent hydrogen is produced consequently, which reduces D-ribonolactone to D-ribose. As the catholyte tends to become alkaline during the electrolysis, dilute acid is added during the electrolysis to maintain the catholyte in non-alkalinity preferably at a pH from about 3 to 5.

According to the method described above, the yield of D-ribose is apparently higher than those of prior meth-

The following examples will further illustrate this invention.

EXAMPLE 1

20 ml. of mercury purified by distillation was placed as the cathode in the bottom of a 300 ml. glass electrolytic cell having a 36 cm.² base. A platinum plate having an area of 10 cm.² is used as the anode and the plate is set in a diaphragm made of unglazed porcelain. 30 ml. of 10% sulfuric acid was used as the anolyte. A solution dissolving 3.3 g. of D-ribonolactone, 4 g. of methylamine sulfate, 3 g. of boric acid in 80 ml. of distilled water was used as the catholyte. A stirrer and the thermometer were placed in the cell and the cell was cooled with ice water from outside. Then, the electrolysis was carried out with vigorous stirring under such condition that the temperature of catholyte is at 10-30° C., the current is one ampere, and the current density of the cathode is 2.8 ampere/dm.². When the content of D-ribose (assayed as reducing sugar) in the catholyte reached the maximum after about three hours, the electrolysis was stopped, and the catholyte was separated. The solution was adjusted to litmus alkalinity with 10% sodium hydroxide, subsequently it was neutralized with 10% sulfuric acid, and concentrated at a temperature lower than 40° C. at a reduced pressure. The residue was extracted with hot methanol, and the extract was concentrated to a syrup containing D-ribose. A small quantity of D-ribose crystals were seeded into the syrup, then 2.8 g. of white crystals of D-ribose was precipitated. The product showed M.P. 80-83° C., which was not depressed when mixed with an authentic sample of D-ribose.

EXAMPLE 2

The electrolysis was carried out under the same conditions as in Example 1 with the exception that 4 g. of methylamine sulfate was replaced by 5 g. of ethylamine sulfate, the electrolyzing current is 1.5 ampere and the current density of the cathode is 4.2 ampere/dm.². After two hours, the content of D-ribose in the catholyte reached the maximum, and the electrolysis was stopped. The catholyte was treated similarly to Example 1 and 2.9 g. of the crystalline D-ribose was obtained.

The electrolysis was carried out under the same conditions as in Example 1 with the exceptions which are tabulated in Table 1. After the content of D-ribose in the catholyte reached the maximum, the electrolysis was stopped, and the catholyte was treated similarly to Example 1. The results are tabulated in Table 1.

TABLE 1

| Example | Catholyte | | Electrolysis | | | Yield of D-ribose, g. |
|---------|---------------------------------|---------------------------|-------------------------------|-------------------------|--|-----------------------|
| | Salt of amine | Content of boric acid, g. | Temperature of catholyte, °C. | Electrolysis time, hrs. | | |
| 3..... | Ethylamine sulfate, 5 g..... | 3 | 10-40 | 3 | | 2.9 |
| 4..... | Benzylamine sulfate, 5.9 g..... | 3 | 10-40 | 3 | | 3.1 |
| 5..... | Hexylamine sulfate, 5 g..... | 2 | 20-40 | 2 | | 3.3 |
| 6..... | Heptylamine sulfate, 5.5 g..... | 2 | 10-40 | 2 | | 3.3 |
| 7..... | Amylamine sulfate, 4.5 g..... | 1.5 | 10-30 | 3 | | 3.1 |

ods. Although the amalgamated metals could not be used advantageously in the prior methods, they may be used as the cathode in this invention. In this case, the necessary amount of mercury for carrying out the electrolytic reduction of D-ribonolactone is only one hundredth as much as the case of mercury cathode. The amine is not susceptible to any unfavorable changes throughout the electrolysis, and may be easily recovered from the reaction mixture by distillation after separating the crystalline D-ribose and adjusting the pH to a strong alkalinity.

EXAMPLE 3

A silver sheet having an area of 30 cm.² was amalgamated on its surface by soaking in dilute nitric acid and exposing its metallic surface subsequently to mercury. The electrolysis was carried out under the same conditions as in Example 1 with the exceptions that mercury cathode was replaced by the amalgamated silver sheet prepared above and 4 g. of methylamine sulfate was replaced by 5 g. of ethylamine sulfate, and the current density of cathode is 3.3 ampere/dm.². After three hours,

the content of D-ribose in the catholyte reached the maximum, then the electrolysis was stopped. The catholyte was treated similarly to Example 1 and 2.7 g. of the crystalline D-ribose was obtained.

What we claim is:

1. The process for preparing D-ribose, which essentially comprises charging an electrolytic cell, having anodic and cathodic compartments separated by a semi-permeable diaphragm, with a non-alkaline, aqueous solution in which D-ribonolactone and a salt of an amine selected from the group consisting of mineral acid-salts of monoalkylamine, dialkylamine, trialkylamine, ω -hydroxymonoalkylamine, cycloalkylamine and lower phenylalkylamines are dissolved as the catholyte, and as the anolyte an aqueous solution of a strong inorganic acid, said acid being substantially non-reactive with the anode material, and said cathode being mercury or amalgamated metal with mercury on its surface, passing

an electric current between the anode and the cathode in the respective compartments while adding acid to the catholyte until D-ribonolactone is substantially converted into D-ribose, the electrolysis being effected below such 5 a temperature that D-ribonolactone decomposes in the catholyte, and recovering D-ribose from the catholyte.

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