Patented May 28, 1940 2,202,437

UNITED STATES PATENT OFFICE

2,202,437

HIGHER ALIPHATIC LACTONES AND THE PROCESS OF MAKING THEM

Max Stoll, Geneva, Switzerland, assignor, by mesne assignments, to Firmenich & Cie., Geneva, Switzerland

No Drawing. Application May 25, 1934, Serial No. 727,583. In Switzerland July 17, 1933

12 Claims. (Cl. 260—344)

The present invention relates to a process for making higher aliphatic lactones from hydroxycarboxylic acids of the form OH.R.COOH, where R is an acyclic hydrocarbon group containing a chain of at least ten carbon atoms. This process consists in removing the elements of water from said acid at boiling temperature of the solution in use, the said acid being in a strongly diluted state.

The invention relates also to the lactones of hydroxycarboxylic acids of the above mentioned hydroxycarboxylic acids, these lactones being new products.

It is well known that higher lactones can be obtained by suitably oxidising higher carbocyclic ketones. It is also known that higher lactones are obtained if ω-halogen fatty acids are heated with metal oxides or the salts of ω-halogen fatty acids in indifferent solvents (German patent specification No. 449,217). As is apparent from the examples in the said German patent specification this prior process always involves lactonisation in the heterogeneous phase, that is to say, with undissolved salts, such as for example, copper and silver salts.

In contradistinction thereto it has been found that the higher lactones can be obtained with much better yields if the lactonisation (inner esterification) of the corresponding hydroxy acids or functional derivatives thereof is carried out in homogeneous strongly diluted solution or in the vapour phase. It is preferable to operate under conditions of some dilution so that the reactions taking part can proceed in the monomolecular form.

Under these new conditions, contrary to what is said in German specification No. 449,217, the lactonisation of free ω-hydroxycarboxylic acids can be successfully effected. Of course, corresponding to the esterification reactions chosen for the lactonisation, derivatives of the hydroxycarboxylic acids may also be used in place of the free acids, such as, for example, their salts, esters, halides, acid chlorides and so forth.

For effecting the lactonisation of the ω-hydroxycarboxylic acids chiefly all those esterification methods can be used which permit of operations being carried out in dilute homogeneous solution or in vapour form. Particularly favourable is that method in which the esterification is carried out with the aid of a solvent which forms an azeotropic mixture with the water formed by the water-splitting catalysts or by elevated temperatures, and which enables this mixture to be continuously removed from the reaction solution during the distillation.

The present method of carrying out the lactonisation is limited to those hydroxycarboxylic acids which possess a chain of eleven or more carbon atoms between their functional groups. It is immaterial whether the chain is branched or normal, whether it is saturated or unsaturated, or whether it still contains other substituted groups.

If operations are carried out in the vapour phase in the presence of esterifying catalysts only those derivatives of the ω-hydroxycarboxylic acids can be used which possess a certain stability at about 200° C., such as, for example, the formates or the carbonates of the hydroxycarboxylic acids. In order that the vaporisation takes place at the lowest possible temperature operations are carried out in the best possible vacuum. It is then preferable to dilute the vapours with other inert gases or vapours.

The present invention enables higher lactones to be prepared in a manner which is very simple technically and in outstanding yields. As compared with the methods heretofore known, therefore, which either had to commence with costly higher ketones or, in the case of direct lactonisation of the ω-hydroxycarboxylic acids, afforded very small yields, the process according to the present invention represents an important technical advance.

The lactones made according to this invention are intended for use in the perfume industry.

Example 1

A 0.1% solution of an ω-hydroxycarboxylic acid, e. g. 14-hydroxytetradecane-1-carboxylic acid, in petroleum ether or an aromatic hydrocarbon, is freed from small quantities of water by boiling. A solution of thionyl chloride in absolute benzene or some other hydrocarbon is then added. Approximately the theoretically necessary quantity is employed, or a slight excess. The reaction can be followed by the hydrogen chloride which is liberated. When about 60 to 70% of the amount of hydrogen chloride theoretically to be expected has been split off the experiment is stopped. The solutions are concentrated by evaporation, washed, and freed from unused acids and acid chloride by means of carbonate. The resulting oil is freed from resins with the aid of pentane or light petroleum ether, which dissolves the lactone, the resins remaining insoluble, and the lactone is finally distilled in a high vacuum. The lactone of 14-

hydroxytetradecane-1-carboxylic acid passes over as a colourless oil at 125–130° C. under a pressure of 0.35 mm.; at ordinary temperature the oil sets to a product resembling camphor. The yield amounts to at least 50%.

The reaction may also be carried out by adding the hydroxy acid to a diluted solution of thionyl chloride. In this case, however, the rate of addition of the hydroxy acid plays an important part. It must be regulated according to the hydrogen chloride evolved so that the concentration of the hydroxycarboxylic acid or of its chloride never exceeds 0.1%. This method of working mainly comes into consideration when it is desired to convert large quantities of hydroxycarboxylic acids in small volumes of solvent. Instead of thionyl chloride other analogously acting substances may, of course, also be used, such as, for example, phosphoroxychloride, etc.

Example 2

The reaction described in Example 1 may also be carried out in the presence of a tertiary base. For example, a diluted benzolic solution of 15-hydroxypentadecane-1-carboxylic acid is supplied to a diluted solution of thionyl chloride in benzene, the quantity of this latter solution being somewhat more than equimolecular, and this mixture is supplied to a hot reflux of a 0.1% benzene solution of dimethylaniline. The rate of supply must be regulated so that the hydroxy acid concentration does not exceed 0.1%. The conditions moreover may be widely varied, both as regards the reaction temperature, solvent, as well as the nature of the base. For working up purposes the reaction solution is washed with dilute hydrochloric acid and further worked as described in Example 1.

The yield amounts to at least 50%. The lactone of 15-hydroxypentadecane-1-carboxylic acid boils at 185–190° C. under a pressure of 15 mms.

Example 3

A 0.1% solution or suspension of concentrated sulphuric acid in benzene is boiled until no more water is separated. A diluted solution of an hydroxycarboxylic acid in benzene, e. g. 14-hydroxytetradecane-1-carboxylic acid is very slowlyisupplied to the reflux of the first-mentoned solution over a period of several days. The rate of supply must be regulated so that the concentration of hydroxycarbovylic acid is not much more than 0.001 molar. Better yields are obtained if the concentration is kept well below 0.001 molar. The esterification (but not the formation of the lactone) can conveniently be followed by means of the water distilling off. The product is worked up as described in Example 1; the yields amount to at least 70%.

Example 4

15-hydroxypentadecane-1-carboxylic acid,

$$CH_2OH\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot COOH$$

is gradually added, for example at a rate of 2 gms. per 24 hours, to the reflux of a boiling solution of 2 gms. of dry benzene sulphonic acid or toluene sulphonic acid in 12 litres of benzene, and the water which forms distilled off with benzene. The reaction solution is well washed with water and evaporated in a slight vacuum. The residue is treated with pentane in order to dissolve the lactone and frees it from traces of resin and unchanged acid. The filtrate is freed from pentane and rectified in a high vacuum.

The pure lactone is obtained in a yield of 90%. The reaction conditions may be varied within fairly wide limits without the yield being much under that just mentioned. For example, if the time taken for introducing the hydroxycarboxylic acid is shortened by a 6-fold amount, the catalyst concentration remaining the same, then the yield of lactone still always amounts to 70%. Other hydrocarbons may be used instead of benzene. The quantity and nature of the catalyst may also be varied. Further, the temperature may be raised with the aid of solvents of higher boiling point or by working under pressure.

On the other hand for all reaction combinations it is essential that the quantity of hydroxycarboxylic acid to be added during the reaction be regulated according to the quantity used up during the lactonisation, so that the maximum concentration allowable under the prevailing conditons is not exceeded.

Example 5

The formic acid ester of 14-hydroxytetradecane-1-carboxylic acid is very slowly led over a titanium dioxide catalyst heated to 200° to 300° C. in a vacuum. The distillate collected in the cooled receiver is freed from admixed acid by means of soda solution and is purified by vacuum distillation.

Example 6

Hexadecene Δ 7-01-16-carboxy 1 is lactonised under the conditions described in Example 4. The lactone which forms in almost quantitive yield is a new product and boils at 186°–190° C. under 15 mm. pressure; it has a density of

$$d_4^{20}=0.958$$

Example 7

ω-hydroxyundecane acid,

$$CH_2OH\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot CH_2\cdot COOH$$

is lactonised under the conditions given in Example 4. The ω-undecalactone, a new product, is obtained as a colourless musty smelling oil in a yield of at least 10%. It boils at 73–74° C. under 0.3 mm. pressure and upon saponification yields the ω-undecane acid of melting point 70° C.

Example 8

14-hydroxy-2-methylpentadecane-1-carboxylic acid is converted into its lactone as described in Example 4. The new lactone boils at 120-122° C. and a pressure of 0.3 mm. and has a density of

$$d_4^{20}=0.948$$

What I claim is:

1. A process for making higher aliphatic lactones from hydroxycarboxylic acids of the form OH.R.COOH, where R is an acyclic hydrocarbon group containing a chain of at least ten carbon atoms, consisting in removing the elements of water from the acid at boiling temperature of the solution in use, the acid being in a strongly diluted state recovering the mono-meric lactones from the reaction product by extraction with appropriate solvents and finally fractionally distilling the lactones.

2. A process for making higher aliphatic lactones from hydroxycarboxylic acids of the form OH.R.COOH, where R is an acyclic hydrocarbon group containing a chain of at least ten carbon atoms, consisting in removing the elements of water from the acid at boiling temperature of the solution in use, the acid being in the form of a highly diluted solution recovering the mono-

meric lactones from the reaction product by extraction with appropriate solvents and finally fractionally distilling the lactones.

3. A process for making higher aliphatic lactones from a hydroxycarboxylic acid of the formula OH.R.COOH, where R is an acyclic hydrocarbon group containing a chain of at least ten carbon atoms, consisting in removing the elements of water from the acid in an inert liquid solution in the presence of water-eliminating catalysts at boiling temperature of the solution in use, the acid being in a strongly diluted state recovering the mono-meric lactones from the reaction product by extraction with appropriate solvents and finally fractionally distilling the lactones.

4. A process for making higher aliphatic lactones from a hydroxycarboxylic acid of the formula OH.R.COOH, where R is an acyclic hydrocarbon group containing a chain of at least ten carbon atoms, consisting in removing the elements of water from the acid in an inert liquid solution at boiling temperature of the solution in use in the presence of a water-eliminating catalyst and in large quantities of a solvent, the water eliminated by said catalyst and the solvent forming an azeotropic mixture recovering the mono-meric lactones from the reaction product by extraction with appropriate solvents and finally fractionally distilling the lactones.

5. A process for making a higher aliphatic lactone from a hydroxycarboxylic acid of the form OH.R.COOH, where R is an acyclic hydrocarbon group containing a carbon chain of at least ten carbon atoms consisting in adding at least the stoichiometric quantity of thionyl chloride to the acid and allowing the interaction to take place in anhydrous non-aqueous solution, stopping the reaction when about 70% of the theoretical quantity of hydrogen chloride has been evolved, concentrating and washing the solution, neutralising the acid substances contained in the solution, separating lactones from resins by means of a lactone solvent, and separating the lactone from the solution by vacuum distillation.

6. A process for making a higher aliphatic lactone from a hydroxycarboxylic acid of the form OH.R.COOH, where R is an acyclic hydrocarbon group containing a carbon chain of at least ten carbon atoms consisting in adding at least the stoichiometric quantity of thionyl chloride to the acid and allowing the interaction to take place in anhydrous non-aqueous solution supplying the mixture to a hot reflux of a diluted non-aqueous solution of dimethylaniline at a rate which keeps the hydroxy acid concentration below 0.1%, washing the reaction solution with hydrochloric acid, neutralising the acid substances contained in the solution, separating lactones from resins by means of a lactone solvent, and separating the lactone from the solution by vacuum distillation.

7. A process for making the lactone from hydroxycarboxylic acid of the form OH.R.COOH, where R is an acyclic hydrocarbon group containing a carbon chain of at least ten carbon atoms consisting in slowly adding said acid to the reflux of a boiling benzene solution of benzene sulphonic acid, distilling off the water-benzene mixture which forms, washing the solution with water, evaporating the solution in a slight vacuum, extracting the lactones from the resins by means of a lactone solvent, and finally rectifying the lactone by vacuum distillation.

8. A process for making the lactone of hexadecene-Δ-7-ol-16-carboxy 1 consisting in slowly adding said acid to the reflux of a boiling benzene solution of benzene sulphonic acid, distilling off the water-benzene mixture which forms, washing the solution with water, evaporating the solution in a slight vacuum, extracting the lactone from the resins by means of a lactone-solvent, and finally rectifying the lactone by vacuum distillation.

9. A process for making the lactone of 14-hydroxy-2-methylpentadecane-1-carboxylic acid consisting in gradually adding said acid to the reflux of a boiling benzene solution of benzene sulphonic acid, distilling off the water-benzene mixture which forms, washing the solution with water, evaporating the solution in a slight vacuum, extracting the lactone from the resins by means of a lactone solvent and finally rectifying the lactone by vacuum distillation.

10. As a new product the lactone of ω-hydroxy-undecane-acid forming a colourless musty smelling oil boiling at 73 to 74 degrees Centigrade under 0.3 mm pressure and upon saponification yielding the ω-undecane acid of melting point 70 degrees Centigrade.

11. A method of preparing the lactone of ω-hydroxy pentadecanoic acid which comprises heating ω-hydroxy pentadecanoic acid in the presence of a larger amount of an insert liquid which is a solvent for the reacting material recovering the mono-meric lactones from the reaction product by extraction with appropriate solvents and finally fractionally distilling the lactones.

12. A process for making the lactone from hydroxy-carboxylic acid of the formula OH.R.COOH, where R is an acyclic hydrocarbon group containing a carbon chain of at least ten carbon atoms consisting in slowly adding said acid to the reflux of a boiling hydrocarbon solution of benzene sulphonic acid, distilling off the water-benzene mixture which forms recovering the mono-meric lactones from the reaction product by extraction with appropriate solvents and finally fractionally distilling the lactones.

MAX STOLL.