A PROCESS FOR PREPARING TRIMETHYLHYDROQUINONE DIACETATE AND TRIMETHYLHYDROQUINONE

VERFAHREN ZUM HERSTELLEN VON TRIMETHYLHYDROQUINONEDIACETAT UND TRIMETHYLHYDROQUINON

PROCEDE POUR LA PREPARATION DE DIACETATE DE TRIMETHYLHYDROQUINONE ET DE TRIMETHYLHYDROQUINONE

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(56) References cited:
EP-A- 0 850 910
The invention relates to a process for preparing 2,3,5-trimethylhydroquinone diesters (TMHQ-DA) by the oxidatively aromatication of 2,6,6-trimethylcyclohexane-1,4-dione (dihydro-ketoisophorone = DH-KIP) by reaction with a sulfonating agent in the presence of an acylating agent and an acid catalyst which may be present in the reaction medium either in dissolved form or else as a heterogeneous solid catalyst. The trimethylhydroquinone diesters obtained may be converted directly to vitamin E acetate by reaction with phytol derivatives, in particular isophytol (IP) or else first be hydrolyzed in the presence of suitable catalysts to give trimethylhydroquinone (TMHQ) which can then be converted into vitamin E by condensation with isophytol derivatives followed by acylation to give vitamin E acetate.

2,3,5-trimethylhydroquinone and 2,3,5-trimethylhydroquinone diesters are very important intermediates in the synthesis of vitamin E and other chromane compounds which are pharmaceutically active substances and are used, inter alia, as antioxidants.

Vitamin E-acetate is used in the form of special formulations as an animal feedstuffs additive in addition to applications in the human sector.

To produce 2,3,5-trimethylhydroquinone diesters, 4-oxoisophorone (KIP) is normally used as the initial reactant which can be rearranged in the presence of strong acid catalysts and an acylating agent such as carboxylic anhydrides or acyl halides. The rearrangement of ketoisophorone (KIP) is described in US 4 247 720: Rearrangement in the gas phase under hydrogenating conditions, with maximum conversions of 30% a selectivity to give TMHQ of only 50% is achieved.

Bull. Korean Chem. Soc. 1991, 12, pages 253 et seq.: Rearrangement of KIP in 5% strength solution in acetonitrile with the addition of 5 equivalents of concentrated sulfuric acid. The TMHQ-DA yields are only 30%.

DE-OS 2 149 159: rearrangement of KIP in the presence of acetonitrile in a rearrangement catalyzed by proton or Lewis acids to give trimethylhydroquinone diacetate which is then saponified to give TMHQ. In order to achieve complete conversion, large excesses of acid have to be used, wherein the isolation yields (maximum 66%, with respect to the ketoisophorone used) are unsatisfactory because costly recrystallization procedures have to be used due to the presence of secondary products.

DE-OS 196 27 977: rearrangement of KIP in the presence of stoichiometric amounts of acetonitrile and catalytic amounts of various acids (trifluoromethanesulfonic acid, chlorosulfonic acid, oleum in various concentrations).

Other processes which describe basically the same procedure, that is the reaction of ketoisophorone with acetonitrile or acetic acid in the presence of a proton acid to give trimethylhydroquinone diacetate, are specified in EP 0 850 912 and EP 0 916 642 A1 and JP OS 11-49712 (Suyama et al., 23.2.99; rearrangement of KIP in the gas phase in the presence of a heterogeneous acid solid catalyst).

A common feature of all these processes is that the trimethylhydroquinone ester and the trimethylhydroquinone obtainable therefrom by hydrolysis, are prepared starting from a non-aromatic starting compound, that is 2,6,6-trimethyl-cyclohex-2-ene-1,4-dione. In this reaction, the initial reactant (KIP) already has the same oxidation state as the product, TMHQ-DA, which means that the reaction can be explained by a simple Wagner-Meerwein rearrangement. The diagram given below reproduces the reaction normally used to prepare TMHQ-DA:

![Diagram showing the process of preparing TMHQ-DA from DH-KIP]
The KIP enolester can be detected when following the course of reaction using gas chromatography, from which it is assumed that the enolester is the intermediate product of reaction.

However, the ketoisophorone used for the synthesis is relatively expensive as a starting material. It is obtained using known processes by the oxygen oxidation of β-isophorone and the mixture obtained is then worked up by distillation.

To prepare TMHQ-DA, 2,2,6-trimethylcyclohexane-1,4-dione (DH-KIP = dihydro-KIP) is especially interesting, this being obtainable by oxidation, starting from β-isophorone, via β-isophorone epoxide and 4-hydroxyisophorone. The preparation of the aliphatic 1,4-diketone (DH-KIP) or its precursor 4-hydroxy-isophorone (HIP) is described, for example, in:

Journal Mol. Cat. 172, 427-435, (1997): epoxidation of β-isophorone with tert-butyl-hydroperoxide as oxidizing agent in the presence of a heterogeneous catalyst (SiO₂-TiO₂ solid catalyst), giving β-isophorone epoxide (β-IPO) and 4-hydroxy-isophorone (HIP).

Tetrahedron Lett., Suppl. 8, Part I, 1-7: oxidation of β-isophorone to β-IP epoxide by oxidation with metachlorobenzoic acid followed by isomerization in basic medium to give HIP which is rearranged to give DH-KIP (yield: 78%) in the presence of an apolar solvent and in the presence of catalytic amounts of p-toluenesulfonic acid.


DP 38 06 835: oxidation of β-IP by reaction with aqueous hydrogen peroxide in the presence of formic acid to give HIP with simultaneous back-isomerization of β-IP to alpha-isophorone.

The object of the invention is to find alternative aliphatic initial reactants for TMHQ-DA synthesis which are readily obtainable and to find a process for the efficient reaction of this alternative initial reactant to give TMHQ diesters.

The invention consists in particular of providing the use of dihydro-ketoisophorone (DH-KIP) as an alternative initial reactant for the synthesis of TMHQ-DA and an economically viable process for this reaction. It is intended that both the requisite oxidation reaction and also the rearrangement reaction involving aromatization can be performed in one process step.

Thus, the present invention is a process for preparing trimethylhydroquinone diesters of the general formula (2)
in which R represents an optionally substituted by halogen aliphatic, alicyclic or aromatic hydrocarbon group, or 2,3,5-trimethylhydroquinone of the general formula (3)

by reacting 2,2,6-trimethyl-cyclohexane-1,4-dione of the general formula (1)

with an acylating agent,
wherein the reaction is performed under oxidative conditions with a sulfonating agent and in the presence of a proton acid with a pKₐ value of 3 or less and/or a Lewis acid at a temperature between -50°C and 200°C, wherein the ratio between acylating agent and 2,2,6-trimethyl-cyclohexane-1,4-dione is at least 1.

[0016] The reaction of DH-KIP as an initial reactant in the preparation of TMHQ-DA has not hitherto been used because the saturated 1,4-diketone does not have the appropriate oxidation state to ensure successful reaction by a simple rearrangement to TMHQ-DA.

[0017] By means of the process according to the invention, it is now possible to use DH-KIP as an initial reactant for the synthesis of trimethylhydroquinone diesters and trimethylhydroquinone. The reaction according to the invention is shown in the following diagram:
As shown in the reaction scheme given above, the reaction also leads to trimethylpyrocatechol diacetate (TMBC-DA) and to 3,4,5-trimethylphenol acetate (TMP-Ac), in addition to trimethylhydroquinone diacetate, depending on the reaction conditions.

The invention provides a new process for preparing 2,3,5-trimethylhydroquinone diesters and trimethylhydroquinone by the rearrangement of 2,2,6-trimethylcyclohexane-1,4-dione (dihydroketoisophorone = DH-KIP) by reaction with an acylating agent in the presence of an acid proton-containing catalyst with a pKₐ value of 3 or less and/or a Lewis acid under oxidizing conditions. In the simplest case of the process according to the invention the catalyst acid used for rearrangement is also the oxidizing agent, in particular sulfuric acid or oleum. According to a further variant, however, the oxidative rearrangement of DH-KIP in the presence of an acylating agent may also be catalyzed by a non-oxidizing Brønsted or Lewis acid, wherein in this case a sulfonating agent such as, for example, sulfuric acid/oleum, must also be present.

The reaction takes place at temperatures of -50 - 200 °C, wherein the ratio of acylating agent to DH-KIP is at least 1:1. The reaction is preferably performed in the temperature interval between -20 and 120 °C. At higher temperatures the selectivity for TMHQ diester formation decreases in favour of the formation of secondary products such as trimethylphenol acetate and trimethylpyrocatechol diesters. At lower temperatures high product selectivity can be achieved but the rate of reaction decreases.

The TMHQ diester obtained at the end of reaction can be reacted directly with isophytol to give vitamin E acetate, after isolation and under suitable conditions. As an alternative to this procedure, the diester obtained as intermediate product is hydrolyzed to give trimethyl hydroquinone, with the addition of water to the reaction mixture.

The acylating agent used in the process is preferably a carboxylic anhydride, carboxylic acid halide, enolester, ketene or some other acylating agent known to a person skilled in the art. Carboxylic anhydrides with the general formula (4) given below are particularly preferably used:

\[
\text{(4)}
\]

wherein R and R’ are identical or different substituents and represent an optionally substituted aliphatic, alicyclic or aromatic group with 1 - 10 carbon atoms, which may optionally be halogenated.

In the context of the invention, acetic anhydride is particularly preferably used as an acylating agent. Another advantage of using acetic anhydride is the production of acetic acid during the reaction, which being a suitable phase-promoter for the subsequent hydrolysis reaction with water to give TMHQ. Other suitable acid anhydrides are the anhydrides of propionic acid, butyric acid, isobutyric acid, cyclohexanoic acid, benzoic acid or the anhydrides of mono- or polyhalogenated or polyhalogenated carboxylic acids. Chloroacetic acid and trifluoroacetic acid, for example, may be mentioned at this point. Cyclic anhydrides such as, for example, maleic anhydride or succinic anhydride are also suitable as acylating agents in the reaction. Also, there are no restrictions on the use of carboxylic acid halides, wherein good results are obtained in particular with the chlorides corresponding to the carboxylic acids listed above. The use of acetyl chloride as an acylating agent is particularly preferred.

The acylating agent should preferably be present in a molar ratio of at least 1:1 with respect to the DH-KIP used, preferably in a molar ratio of 1:1 to 1:10. The use of higher concentrations of acylating agent does not interfere with the reaction, but no further improvement in reaction is produced by these high dilutions. In this case, the excess acylating agent is used as a solvent which can be separated from the product and recycled in a simple manner by distillation after production of the TMHQ diester required as the target product.

When using carboxylic acid halides, the same data with regard to molar ratios apply as were mentioned in
the case of using anhydrides. The use of acetyl chloride, propionyl chloride and butyryl chloride may be mentioned, for example, for use as carboxylic acid chlorides. As an example of the use of enolesters, isopropenyl acetate and structurally related compounds of the following general formula (5) may be mentioned here:

![Diagram](image)

wherein \( R_1 \) to \( R_4 \) represent H atoms and hydrocarbon groups with 1 - 10 carbon atoms, or a 5 or 6-membered alicyclic hydrocarbon and \( R_5 \) represents an aliphatic, alicyclic or aromatic hydrocarbon groups, optionally substituted, with 1 to 10 carbon atoms.

[0026] In the process according to the invention, rearrangement of the 1,4-dione has to be performed under oxidative conditions. In the simplest case, the catalyst acid used also takes on the function of the oxidizing agent. According to the invention, oxidizing acids with a pK\(_a\) value of 3 or less are suitable for rearranging DH-KIP to give TMHQ diesters, in particular sulfuric acid and oleum with a variety of SO\(_3\) concentrations.

[0027] Particularly suitable for the process according to the invention are sulfonating reagents, such as sulfuric acid or oleum with a variety of SO\(_3\) concentrations, but also mixtures of sulfuric acid with boric acid and oleum with boric acid. When using these reagents, the reaction takes place with sulfonation occurring in situ, wherein SO\(_2\) is given off in a subsequent step.

[0028] When using sulfuric acid, oleum and similar sulfonating reagents, additional non-oxidizing acid catalysts may also be added in order to accelerate the reaction. In principle, both proton acids and Lewis acids are suitable. Examples of Brønsted acids which can be used are mineral or organic acids with a pK\(_a\) value of 3 or less, including aliphatic or aromatic sulfonic acids such as para-toluenesulfonic acid, benzenesulfonic acid, methanesulfonic acid, ethanesulfonic acid, hydrohalic acids (HX; X = F, Cl, Br, I), phosphoric acid and aliphatic and aromatic phosphonic acids, haloacetic acids (XCH\(_2\)CO\(_2\)H; X = F, Cl, Br) or the corresponding polyhalogenated derivatives such as trichloroacetic acid or trifluoroacetic acid, nitrotetraphthalic acid or corresponding aryl carboxylic acids which are activated by electron-attracting substituents.

[0029] Particularly preferred proton acids which can be used in addition to the sulfonating reagents are catalyst systems which can also be used in order to accelerate the reaction. In principle, both proton acids and Lewis acids are suitable. Examples of Brønsted acids which can be used are mineral or organic acids with a pK\(_a\) value of 3 or less, including aliphatic or aromatic sulfonic acids such as para-toluenesulfonic acid, benzenesulfonic acid, methanesulfonic acid, ethanesulfonic acid, hydrohalic acids (HX; X = F, Cl, Br, I), phosphoric acid and aliphatic and aromatic phosphonic acids, haloacetic acids (XCH\(_2\)CO\(_2\)H; X = F, Cl, Br) or the corresponding polyhalogenated derivatives such as trichloroacetic acid or trifluoroacetic acid, nitrotetraphthalic acid or corresponding aryl carboxylic acids which are activated by electron-attracting substituents.

[0030] In another variant, the process is performed in the presence of a proton acid with a Hammett constant H\(_0\) < -11.9. Acids covered by this classification include the so-called superacids such as perchloric acid, halosulfonic acids (chlorosulfonic acid, fluorosulfonic acid, etc), perhaloalkanesulfonic acids such as, for example, perfluoroalkanesulfonic acids of the general formula (6):

\[
C_nF_{2n+1}SO_3H
\]  

wherein \( n \) may be 1-8.

[0031] Solid catalysts which have advantages over homogeneously dissolved proton acids during the working up procedure, due to the ease of separation after the end of reaction, may also be used as acids. These solid catalysts include strongly acidic and superacidic ion exchangers, various acidic mixed oxides, zeolites (\( Y, X, A, \) or \( \beta \) type) and heteropolyacids (heteropolyacids which are composed, inter alia, from the elements P, Mo, V, W and Si). Acidic ion exchangers are, in particular, common ion exchangers in which the acidity is produced by -SO\(_3\)H groups on a suitable support (for example Amberlyst catalysts, or Deloxane; Degussa AG). The sulfonic acid groups may be bonded, inter alia, covalently to an organic or inorganic support material. Superacidic solid acids may also be used (for example those of the Nafion type, such as Nafion NR50 from Aldrich or Nafion H from Dupont), wherein the acidity here is produced by perfluoroalkanesulfonic acid groups which are bonded to various support materials. Insoluble sulfates
which are acidic under the reaction conditions, e.g. CaSO₄, Fe₂(SO₄)₃, CuSO₄, NiSO₄, (Al)₂(SO₄)₃, MnSO₄, BaSO₄, CoSO₄, ZnSO₄, (NH₄)₂SO₄ may also be used. Examples of acidic mixed oxides which may be mentioned at this point are SiO₂-Al₂O₃, SiO₂-TiO₂, TiO₂-ZrO₂, SiO₂-ZrO₂ and related compounds. Also suitable are zeolites, including ZSM-5, mordenite and acidic aluminium phosphate systems. Various Lewis acids and proton acids which have already been mentioned above, fixed to a support material, are also suitable as solid catalysts. Examples which may be mentioned here are SbF₅, TaF₅, BF₃, AlX₃ (X = Cl, Br, F), SbF₅-HF, SbF₅-FSO₃H, SbF₅-CF₃SO₃H, SO₄²⁻ and compounds with equivalent acidity. The previously specified compounds also include superacids which have a Hammett constant H₀ = < -11.9.

[0032] The solid catalyst may be used as a slurry or else, in an appropriate form, introduced into a fixed bed reactor.

[0033] The process may be performed in the presence of an organic solvent which behaves in an inert fashion under the reaction conditions. The concentration of reactants in the solvent has only a minor effect on the product mixture for the reaction and has an effect only on the ratio between trimethylhydroquinone diesters and the corresponding pyrocatechol diesters. The reaction is preferably performed without any solvent so that solvent distillation and separation from the product are not required.

[0034] If the rearrangement takes place in the presence of organic solvents, in particular aliphatic and cyclic esters, for example ethyl acetate, propyl acetate, butyl acetate, isobutyl acetate, gamma-butyrolactone, ethylene carbonate, their derivatives and homologues, aliphatic, alicyclic and aromatic hydrocarbons, for example pentane, hexane, heptane, octane and other homologues, benzene, toluene or xylene are used. Ketones are also suitable as solvents in the context of the invention, such as, for example, acetone, methyl-ethyl ketone, diethyl ketone or isophorone. Furthermore, aliphatic, aromatic or mixed ethers such as diethyl ether, methyl-tert-butyl ether may be used.

[0035] In one embodiment of the process, the trimethylhydroquinone diester being produced is crystallized directly from the carboxylic acid being produced during reaction, without needing to add another solvent. However, it is also possible to achieve isolation of the product (and thus the removal of secondary products such as trimethylphenol esters and pyrocatechol diesters) by adding a suitable solvent after distilling off the free carboxylic acid being produced. In another embodiment, the reaction is performed in one of the solvents mentioned and product isolation is performed by crystallization directly from the solvent for the reaction. The purity of the TMHQ DA isolated in this way corresponds to the product quality which is required for use as an initial reactant in vitamin E acetate synthesis.

[0036] In another embodiment, the TMHQ diacetate being produced is saponified without isolation by adding water to the crude mixture from reaction. The presence of the carboxylic acid produced during TMHQ-DA formation, in this case acetic acid, is advantageous because it acts as a phase promoter and ensures efficient hydrolysis of the diester. The same catalyst may be used as a saponification catalyst as the catalyst which has already been used for the oxidative rearrangement of DH-KIP. Free trimethylhydroquinone TMHQ is isolated in a manner known per se by crystallization from an appropriate medium. TMHQ may also be synthesized after the intermediate isolation of TMHQ-DA, wherein hydrolysis is then performed in the presence of a basic or acidic catalyst, optionally in the presence of a phase-promoting compound such as, for example, acetic acid, n-butanol or n-butylic acetate. It is also possible to convert TMHQ-DA into TMHQ by hydrolysis under pressure in the presence of a catalyst.

[0037] The following examples further illustrate the invention.

Example 1

Reaction of DH-KIP with acetonhydride/acetic acid in the presence of sulfuric acid

[0038] 0.6 gram (g (10 mmol)) of acetic acid are added to 1.54 g of dihydro-ketoisophorone (DH-KIP) and a suspension is formed by stirring. To this suspension is added, with stirring at room temperature, 10.21 g of acetonhydride (100 mmol). To this colourless solution is added, using an injection pump and over the course of 10 minutes, concentrated 96% sulfuric acid (721 µl; 13 mmol; 130 mol.% w.r.t. to DH-KIP). The continuous evolution of SO₂ is observed during the time of addition. After completion of sulfuric acid addition, the mixture is heated for 3 hours at 100°C, then cooled to 20°C, wherein crystals separate out. For complete crystallization, 5 ml of water are added to the suspension and crystallization takes place at 20°C. The crystals are washed with a little cold acetic acid and colourless crystals are obtained which are identified as pure trimethylhydroquinone diacetate after drying under vacuum at 55°C. The conversion of DH-KIP is quantitative.

<table>
<thead>
<tr>
<th>Yield</th>
<th>1.95 g (82.5% of theoretical)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purity</td>
<td>99.3% (HPLC)</td>
</tr>
</tbody>
</table>
Example 2

Reaction of DH-KIP with acetanhydride in the presence of sulfuric acid

[0039] 1.54 g (10 mmol) of DH-KIP are placed in a three-necked bulb and concentrated 96% sulfuric acid (13 mmol) and 5.1 g of acetanhydride (50 mmol) are added one after the other, with cooling by an external water bath so that the temperature does not exceed 30°C. Then the mixture is stirred for 3 hours at 30°C. After quantitative GC analysis of the reaction mixture obtained in this way the following results are obtained:

<table>
<thead>
<tr>
<th>Conversion of DH-KIP</th>
<th>99.14%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yield of TMHQ-DA</td>
<td>93.6% (i.e. selectivity:94.4%)</td>
</tr>
<tr>
<td>Yield of TMBC-DA</td>
<td>4.6% (i.e. selectivity:4.6%)</td>
</tr>
</tbody>
</table>

Example 3

Reaction of DH-KIP with acetanhydride in the presence of sulfuric acid at 50°C

[0040] 1.54 g (10 mmol) of DH-KIP and concentrated 96% sulfuric acid (13 mmol) are initially introduced into a three-necked bulb at 50°C and 5.1 g of acetanhydride (50 mmol) are added thereto, wherein the temperature is held at 50°C by regulating the rate of addition. Then the mixture is stirred for 3 hours at 50°C. Following quantitative GC analysis of the reaction mixture obtained in this way, the following results are obtained:

<table>
<thead>
<tr>
<th>Conversion of DH-KIP</th>
<th>100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yield of TMHQ-DA</td>
<td>91.2% (i.e. selectivity:91.2%)</td>
</tr>
<tr>
<td>Yield of TMBC-DA</td>
<td>5.2% (i.e. selectivity:5.2%)</td>
</tr>
</tbody>
</table>

Example 4

Reaction of DH-KIP to give TMHQ-DA with acetanhydride/acetic acid in the presence of sulfuric acid and then hydrolysis to give TMHQ

[0041] 15.4 g of DH-KIP (100 mmol) were dissolved in 20 g (0.33 mol) of acetic acid at room temperature and the solution was cooled to 5°C with stirring. Then, over the course of 10 minutes, 13.3 g (130 mmol) of concentrated 96% sulfuric acid were added. The clear solution was then heated to 50°C and 102.1 g of acetanhydride (1 mol) were added via an injection pump over the course of 0.5 hours. Finally, the mixture was stirred for 2 hours at 50°C. Quantification of the reaction solution using GC provided the following results:

<table>
<thead>
<tr>
<th>Conversion of DH-KIP</th>
<th>100%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yield of TMHQ-DA</td>
<td>93.2% (i.e. selectivity:93.2%)</td>
</tr>
<tr>
<td>Yield of TMBC-DA</td>
<td>4.3% (i.e. selectivity:4.3%)</td>
</tr>
</tbody>
</table>

[0042] The reaction solution was hydrolyzed with 100 ml of water and heated for 3 hours under reflux to complete the hydrolysis reaction. Then the mixture was concentrated on a rotary evaporator and crystallized with the addition of water. Colourless crystals were obtained at 20°C and these contained < 1% TMBC according to GC.

<table>
<thead>
<tr>
<th>Conversion of TMHQ-DA</th>
<th>99.2%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yield of TMHQ</td>
<td>13.5 g; 88.5% of theoretical with respect to DH-KIP GC concentration</td>
</tr>
<tr>
<td>GC concentration</td>
<td>99.3%</td>
</tr>
</tbody>
</table>

Claims

1. A process for preparing trimethylhydroquinone diesters of the general formula (2)
in which R represents an optionally substituted by halogen aliphatic, alicyclic or aromatic hydrocarbon group, or 2,3,5-trimethylhydroquinone of the general formula (3) by reacting 2,2,6-trimethyl-cyclohexane-1,4-dione of the general formula (1) with an acylating agent, wherein the reaction is performed under oxidative conditions with a sulfonating agent and in the presence of a proton acid with a pKₐ value of 3 or less and/or a Lewis acid at a temperature between -50°C and 200°C, wherein the ratio between acylating agent and 2,2,6-trimethyl-cyclohexane-1,4-dione is at least 1.

2. A process according to Claim 1, wherein sulfuric acid or oleum is used as the sulfonating agent.

3. A process according to Claim 1, wherein the acylating agent is chosen from the group of carboxylic anhydrides of the general formula (4)

wherein R and R' are identical or different substituents and represent an optionally substituted by halogen aliphatic, alicyclic or aromatic group with 1-10 carbon atoms.

4. A process according to Claim 1, wherein acetylanhydride is used as the acylating agent.
5. A process according to Claim 1, wherein carboxylic acid halides, enolesters or ketenes are used as acylating agents.

6. A process according to Claim 1, wherein the reaction is also carried out in the presence of proton acids from the group nitric acid, perchloric acid, nitrous acid, hydrochloric acid, hydrobromic acid, hydrofluoric acid, methanesulfonic acid, ethanesulfonic acid, halosulfonic acids, perhaloalkanesulfonic acids, benzenesulfonic acid, para-toluenesulfonic acid, phosphoric acid, phenylphosphonic acid, nitrotetraphthalic acid, picric acid, trifluoroacetic acid, chloroacetic acid, mixtures of boric acid derivatives and chelating carboxylic acids, mixtures of boric acid and oxalic acid, oleum, sulfuric acid or HB(HSO₄)₄-H₂SO₄.

7. A process according to Claim 1, wherein proton acids are used which have a Hammett constant of < - 11.9 (superacidic acids).

8. A process according to Claim 1, wherein a solid acidic or superacidic catalyst is used as the Lewis acid and the reaction is performed in the presence of the heterogeneous solid catalyst.

9. A process according to Claim 8, wherein the acidic catalyst is used in an amount of 0.01 - 1000 mol.%, with respect to 2,2,6-trimethylcyclohexane-1,4-dione.

10. A process according to Claim 1, wherein mixtures of Lewis acids and Brønsted acids are used.

11. A process according to one or more of the preceding Claims, wherein the trimethylhydroquinone diacetate being produced is saponified without isolation, optionally after distilling off unreacted acetaldehyde, by adding water and/or dilute acid and the trimethyl hydroquinone being produced is separated.

12. A process according to one or more of the preceding Claims, wherein the trimethylhydroquinone diacetate being produced is isolated from the reaction mixture and is then optionally saponified using dilute acid in the presence of a phase promoter and the trimethylhydroquinone being produced is separated.

13. A process according to Claim 12, wherein acetic acid, n-butanol or n-butyl acetate or mixtures of these are used as phase promoters.

Patentansprüche

1. Verfahren zur Herstellung von Trimethylhydrochinonodiester der allgemeinen Formel (2)

![Diagram](image)

wobei R eine optional durch Halogen substituierte aliphatische, alicyclische oder aromatische Kohlenwasserstoffgruppe repräsentiert, oder 2,3,5-Trimethylhydrochinon der allgemeinen Formel (3)
durch Reagieren von 2,2,6-Trimethylcyclohexan-1,4-dion der allgemeinen Formel (1)

mit einem Acylierungsmittel,

wobei die Reaktion unter oxidativen Bedingungen mit einem Sulfonierungsmittel und in Gegenwart einer Protonensäure mit einem $pK_a$-Wert von 3 oder weniger und/oder einer Lewissäure bei einer Temperatur zwischen -50°C und 200°C stattfindet, wobei das Verhältnis zwischen Acylierungsmittel und 2,2,6-Trimethylcyclohexan-1,4-dion mindestens 1 beträgt.

2. Verfahren nach Anspruch 1, bei dem als Sulfonierungsmittel Schwefelsäure oder Oleum verwendet wird.

3. Verfahren nach Anspruch 1, bei dem das Acylierungsmittel ausgewählt wird aus der Gruppe der Carbonsäureanhydride der allgemeinen Formel (4)

wobei $R$ und $R'$ gleiche oder unterschiedliche Substituenten repräsentieren und eine optional durch Halogen substituierte aliphatische, alicyclische oder aromatische Gruppe mit 1-10 Kohlenstoffatomen repräsentieren.

4. Verfahren nach Anspruch 1, bei dem als Acylierungsmittel Essigsäureanhydrid verwendet wird.

5. Verfahren nach Anspruch 1, bei dem Carbonsäurehalogenide, Enolester oder Ketene als Acylierungsmittel eingesetzt werden.

6. Verfahren nach Anspruch 1, bei dem die Reaktion außerdem in Gegenwart von Protonensäuren aus der Gruppe Salpetersäure, Perchloressigsaure, salpetrige Säure, Chlorwasserstoffsäure, Bromwasserstoffsäure, Fluorwasserstoffsäure, Methansulfonsäure, Ethersulfonsäure, Halogensulfonsäuren, Perhalogenalkansulfonsäuren, Benzolsulfonsäure, para-Toluolsulfonsäure, Phosphorsäure, Phenylphosphonsäure, Nitrotolualdehyd, Pikrinsäure, Trifluorstoffsäure, Chlorostoffsäure, Mischungen aus Borsäurederivaten und chelatisierenden Carbonsäuren, Mischungen aus Borsäure und Oxalsäure, Oleum, Schwefelsäure oder HB(HSO4)4·H2SO4 verwendet werden.

7. Verfahren nach Anspruch 1, bei dem Protonensäuren eingesetzt werden, die eine Hammettconstante $< -11.9$ aufweisen (supersaure Säuren).

8. Verfahren nach Anspruch 1, bei dem als Lewissäure ein fester saurer oder supersaurer Katalysator eingesetzt wird und die Reaktion in Gegenwart des heterogenen festen Katalysators durchgeführt wird.
9. Verfahren nach Anspruch 8, bei dem der saure Katalysator in einer Menge von 0,01 bis 1000 Mol-% bezogen auf 2,2,6-Trimethylcyclohexan-1,4-dion eingesetzt wird.


**Reivendications**

1. Procédé pour préparer des diesters de triméthylhydroquinone de formule générale (2)

\[
\begin{align*}
\text{O} & \\
\text{O} & \\
\text{R} & \quad \text{(2)}
\end{align*}
\]

dans laquelle R représente un groupe hydrocarboné aliphatique, alicyclique ou aromatique, éventuellement substitué par halogène,
ou une 2,3,5-triméthylhydroquinone de formule générale (3)

\[
\begin{align*}
\text{OH} & \\
\text{OH} & \\
\text{(3)}
\end{align*}
\]
en faisant réagir de la 2,2,6-triméthyl-cyclohexane-1,4-dione de formule générale (1)
avec un agent d'acylation,
dans lequel la réaction est réalisée dans des conditions d'oxydation avec un agent de sulfonation et en présence d'un acide protonique présentant une valeur pKa de 3 ou moins et/ou d'un acide de Lewis à une température entre -50°C et 200°C, le rapport entre l'agent d'acylation et la 2,2,6-triméthyl-cyclohexane-1,4-dione étant d'au moins 1.

2. Procédé selon la revendication 1, dans lequel on utilise de l'acide sulfurique ou de l'oléum en tant qu'agent de sulfonation.

3. Procédé selon la revendication 1, dans lequel l'agent d'acylation est choisi dans le groupe des anhydrides carboxyliques de formule générale (4)

\[
\begin{array}{c}
\text{O} \\
\text{R} \\
\text{O} \\
\text{R'} \\
\end{array}
\]

\( (4) \)

dans laquelle R et R' sont des substituants identiques ou différents et représentent un groupe aliphatique, alicyclique ou aromatique comprenant 1 à 10 atomes de carbone, éventuellement substitué par halogène.

4. Procédé selon la revendication 1, dans lequel on utilise de l'anhydride de l'acide acétique en tant qu'agent d'acylation.

5. Procédé selon la revendication 1, dans lequel on utilise des halogénures d'acide carboxylique, des énolesters ou des cétènes en tant qu'agents d'acylation.

6. Procédé selon la revendication 1, dans lequel la réaction est également effectuée en présence d'acide protonique du groupe constitué par l'acide nitrique, l'acide perchlorique, l'acide chlorhydrique, l'acide bromhydrique, l'acide fluorhydrique, l'acide méthanesulfonique, l'acide éthanesulfonique, les acides halogénosulfoniques, les acides perhalogénoalcanesulfoniques, l'acide benzénesulfonique, l'acide para-toluènesulfonique, l'acide phosphorique, l'acide phénylphosphonique, l'acide nitrotéréphtalique, l'acide picrique, l'acide trifluoroacétique, l'acide chloroacétique, les mélanges de dérivés de l'acide borique et d'acides carboxyliques chélatants, les mélanges de l'acide borique et de l'acide oxalique, l'oléum, l'acide sulfurique ou HB (HSO₄)₄ \cdot H₂SO₄.

7. Procédé selon la revendication 1, dans lequel on utilise des acides protoniques qui présentent une constante de Hammett de ≤ 11.9 (acides superacides).

8. Procédé selon la revendication 1, dans lequel on utilise un catalyseur acide ou superacide solide en tant qu'acide de Lewis et la réaction est réalisée en présence du catalyseur solide hétérogène.

9. Procédé selon la revendication 8, dans lequel le catalyseur acide est utilisé en une quantité de 0.01 à 1000% en mole, par rapport à la 2,2,6-triméthylcyclohexane-1,4-dione.

10. Procédé selon la revendication 1, dans lequel on utilise des mélanges d'acides de Lewis et d'acides de Brönsted.

11. Procédé selon l'une ou plusieurs des revendications précédentes, dans lequel le diacétate de triméthylhydroquinone produit est saponifié sans isolement, éventuellement après élimination par distillation de l'anhydride de l'acide acétique qui n'a pas réagi, par addition d'eau et/ou d'acide dilué et la triméthylhydroquinone produite est séparée.

12. Procédé selon l'une ou plusieurs des revendications précédentes, dans lequel le diacétate de triméthylhydroquinone produit est isolé à partir du mélange réactionnel puis est éventuellement saponifié en utilisant un acide dilué en présence d'un promoteur de phases et la triméthylhydroquinone produite est séparée.

13. Procédé selon la revendication 12, dans lequel on utilise de l'acide acétique, du n-butanol ou de l'acétate de n-butyle ou des mélanges de ceux-ci en tant que promoteurs de phases.