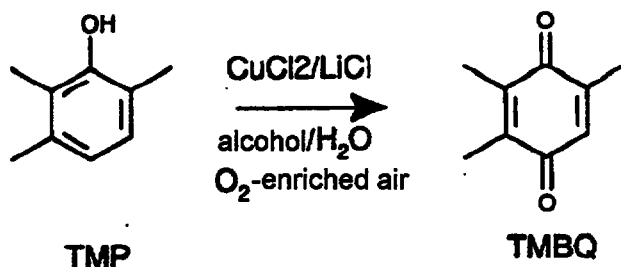


PROCESS FOR PREPARING TRIMETHYLBENZOQUINONE

The present invention relates to a novel process for preparing trimethylhydroquinone (TMHQ) by oxidizing trimethylphenol (TMP). It relates more particularly to a process for oxidizing trimethylphenol by a catalyst system made up of heteropolyacids.

It has long been known in accordance, for example, with the patents of Mitsubishi Gas Chemical Company (EP 127 888 or EP 167 153) to oxidize TMP to TMBQ, the latter molecule being an important intermediate in the synthesis of vitamin E.

According to the abovementioned patents the TMP is oxidized by oxygen-enriched air, the reaction being catalysed by copper salts in a three-phase gas/alcohol/water system. The melted TMP is run in continuously. At the end of the reaction, following decantation, the catalyst in the aqueous phase is recycled and the TMBQ in the alcoholic phase is isolated after various treatments. With this process it is possible to obtain a degree of conversion of the TMP of 100% and a TMBQ yield of 95%.



This process has a number of drawbacks, since

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the catalyst system is partially soluble in the organic phase made up of the TMBQ and the solvent. To regenerate it requires acidic treatment of the organic phase for quantitative recovery of the catalyst. This
5 type of catalysis necessitates the use of special materials in order to avoid the corrosion which is due essentially to the use of chlorinated derivatives from the catalysis.

The drawbacks of this process have been
10 countered by using specific catalysts for this oxidation (heteropolyacid catalysts) and a solvent medium in which the partition coefficients are favourable for the recovery and recycling of the catalyst.

15 By heteropolyacid (HPA) is meant the acid form of a heteropolyanion; the heteropolyanions are oxoanions containing 1 or 2 central atoms, heteroatoms X ($X = B^{3+}, Si^{4+}, Ge^{4+}, P^{5+}, As^{5+}$, etc.), and 4 to
18 peripheral coordinating atoms, polyatom Y ($Y = W,$
20 Mo, V).

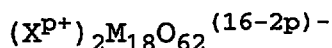
Within the heteropolyacids it is also possible to include the heteropolyanion or one of its salts. In the solid state, the HPAs or their salts are made up of a heteropolyanion, counterions (H^+ ions or
25 metal cation) and molecules of water of crystallization.

A distinction may be made between two main structures of heteropolyanions:

→ KEGGIN's structure for heteropolyanions of
formula: $X^{p+}M_{12}O_{40}^{(8-p)-}$

The structure most often described in the
literature is the KEGGIN structure, for which the metal
5 atom/heteroatom ratio is 12/1. In this structure, the
metal atoms M of group VI (M preferably represents Mo
or W) can be substituted to a greater or lesser extent
by atoms of group V ($M' = V, Co, etc.$). The resultant
HPAs of the type $X^{p+}M_{12-n}M'_nO_{40}^{(8-p+n)-}$ are referred to as
10 mixed and written HPA-n.

→ DAWSON's structure for heteropolyanions of
formula:



In this structure the metal atom/heteroatom
15 ratio is 9/1. This structure is made up of two
fragments $X^{p+}M_9O_{34}^{(14-p)-}$ which are linked.

As far as the various processes of preparing
HPAs are concerned, in general, the heteropolyanions
are synthesized in acidic medium by condensing metal
20 oxides and oxoanions containing the heteroatom X.

In order to synthesize mixed-type
heteropolyanions of KEGGIN structure it is possible to
use certain syntheses which are described in the
literature and which enable mixed-type heteropolyanions
25 to be obtained directly.

a) Case of HPA-ns of type $H_{3+n}PMo_{12-n}V_nO_{40}$
where $1 \leq n \leq 6$:

In the literature, three conventional methods

are described plus a recent original method by electrodialysis.

The earliest method, described by P. COURTIN, F. CHAUVEAU, P. SOUCHAY in a *Compte-rendu de l'Académie des Sciences*, 258, 1964, 1247-1250 makes it possible readily to obtain HPA-ns for which $n \leq 3$. It consists in treating an aqueous solution of sodium molybdate, phosphate and vanadate, after dissolution has been effected by heating at reflux followed by cooling, with concentrated sulphuric acid. The HPA-n formed is extracted from the aqueous solution with ether, after which evaporation of the solvent is enough to give the HPA-n in crystalline form. The yields, however, remain low, a large excess of vanadate must be employed when n increases, and numerous by-products are obtained.

It is also known in accordance, for example, with the patent JP 77138499 to prepare the heteropolyacid of formula $H_5PMo_{10}V_2O_{40}$ from molybdenum oxide (MoO_3) and vanadium oxide (V_2O_5) and phosphoric acid. The three species are dissolved in water by heating at reflux for 20 days. The solution is subsequently concentrated to induce pure crystals of HPA-2.

It is also known, in accordance with ODYAKOV et Al., *Kinetics and Catalysis*, 36, 1995, 733-738 to prepare HPA-ns for which $1 \leq n \leq 6$ from H_3PO_4 , MoO_3 and a solution of decavanadic acid $H_6V_{10}O_{28}$.

The amount of the three species P, Mo and V to be introduced is adjusted depending on the stoichiometry of the HPA-n which it is desired to synthesize. The decavanadic acid solution is obtained by dissolving
5 vanadium oxide V_2O_5 in a cooled aqueous solution containing 4 to 6% of hydrogen peroxide.

To synthesize the HPA-ns where $n = 1-4$ the solution of decavanadic acid is added gradually to a dilute mixture of MoO_3 and H_3PO_4 which has been brought
10 to boiling. Stirring and boiling are continued until dissolution of MoO_3 is complete, after which the mixture is filtered. The filtrate is recovered and is an aqueous solution of HPA-n.

To synthesize HPA-ns where $n > 4$ use is made
15 of solutions of HPA-n' where $1 \leq n' \leq 4$ instead of MoO_3 . The solution of HPA-n' is mixed with H_3PO_4 , the mixture is brought to boiling, and then the slow addition of the decavanadic acid solution is begun. The water is evaporated, the mixture is filtered and the
20 residue is dissolved in a 5% solution of hydrogen peroxide and added to the filtrate again.

In 1995, KHOZHEVNIKOV Catalysis Reviews-
Sciences Engineering, 37, 1995, 311-352 proposed a novel method of synthesis by electrodialysis. The HPA
25 is formed at the anode in aqueous solution while electrolysis of water takes place at the cathode. The two electrodes are separated by a cation exchange membrane. No by-product is formed. The yields approach

100%.

The HPAs are employed in homogeneous catalysis as well as in heterogeneous catalysis. They can be used supported on silica, active carbon or ion
5 exchange resin.

As principal applications of HPAs in acid catalysis mention may be made of condensations, hydrations and dehydrations, esterifications and etherifications, nitrations, reactions on epoxides,
10 acetolyses, carbonylations, isomerizations, oligomerizations, alkylations, dealkylations and transalkylations of phenol.

As far as oxidation is concerned, the most commonly used HPAs are the molybdovanadophosphoric
15 acids, owing to their high oxidation potential and good thermal stability. These HPA-ns catalyse oxidation reactions of both organic and inorganic substances. In this case the oxidant in the reaction may be O_2 or H_2O_2 .

The reduced forms of these HPAs can easily be
20 reoxidized by O_2 .

The principal applications in redox catalysis are the oxidation of alkanes (preparation of maleic anhydride, oxidation of cycloalkanes to alcohols and ketones, oxidative dehydrogenation, oxidation of
25 methane, etc.), alkenes, alcohols (primary, secondary, etc.), aldehydes, and inorganic substances (N_2H_4 , NO , H_2S , etc.).

Various authors have envisaged the

possibility of catalysing the oxidation of TMP to TMBQ by means of a system containing HPAs in a homogeneous H₂O/AcOH system. Various types of HPA have been tested in accordance with different procedures.

5 Thus it is known, in accordance with the publications of KHOLDEEVA et al., which have appeared in Journal of Molecular Catalysis, 75, 1992, 235-244, that a molar ratio of 20 = TMP/HPA (H₇PMo₈V₄O₄₀ KEGGIN structure) enables a TMBQ yield of 86% to be obtained.

10 It is also known, in accordance with the article by SHIMIZU et al., which appeared in Tetrahedron Letters, 30, 1989, 471-474, that the oxidation of TMP to TMBQ can be carried out in the presence of a HPA of formula H₇PMo₁₂O₄₀ and hydrogen
15 peroxide. The yield of TMBQ obtained reaches 78.3%.

 R. NEUMANN in Tetrahedron Letters, 33, 1992, 1795-1798 describes the oxidation of 2,3,5-trimethylphenol to TMBQ, catalysed by H₅PV₂Mo₁₀O₄₀ in hexanol under 1 atmosphere of oxygen at 60°C for 4h for
20 a TMP/HPA ratio of 50. He obtains a selectivity of 73% for a degree of conversion of 75%.

 There exist other studies which have enabled TMP to be oxidized to TMBQ by means of HPAs supported on carbon; mention may be made in this category of the
25 studies by JANSEN and co-workers, which have appeared in Journal of Molecular Catalysis A chemical, 107, 1996, 241-246.

 No article describes the realization of this



oxidation with easy recycling of the catalyst. The present invention has achieved this objective. It relates to a process for preparing trimethylhydroquinone by oxidizing trimethylphenol in the presence of an oxidizing agent selected from oxygen and hydrogen peroxide and of a heteropolyacid, the reaction being characterized in that it is carried out in a two-phase liquid medium.

The trimethylphenol is preferably 2,3,6-trimethylphenol and the trimethylhydroquinone obtained is, in particular, 2,3,5-trimethylhydroquinone.

The heteropolyacid is preferably selected from Keggin-structure heteropolyacids or Dawson-structure heteropolyacids, it being understood that the salts of heteropolyacids can also be used within the context of the present invention.

The reaction medium consists of an aqueous mixture consisting of water and a mono- or dibasic organic carboxylic acid containing 2 to 6 carbon atoms, preferably acetic acid. It is preferred to employ a volume ratio between the organic acid and the water of between 95/5 and 20/80; very particularly it is preferred to use a volume ratio of between 80/20 and 60/40.

The water-immiscible solvent which makes it possible to obtain the two-phase system with the aqueous phase is selected from aliphatic or aromatic hydrocarbons and from their halogenated derivatives,



preferably their chlorinated derivatives. Very particular preference is given to using ortho-dichlorobenzene.

The volume ratio between the solvent and the aqueous system (water and organic acid) is preferably between 30/70 and 90/10 and more preferably still between 30/70 and 50/50.

The molar ratio between the trimethylphenol and the heteropolyacid is preferably between 200/1 and 5/1 and more preferably still is approximately 10/1.

The weight ratio between the HPA and TMP assembly relative to the liquid medium made up of the solvent and the aqueous medium is preferably between 0.1% and 15% and more preferably still is approximately preferably 6%.

As far as the reaction conditions are concerned it is preferred to operate at a temperature greater than 30°C and preferably of between 50 and 70°C. The oxygen pressure is preferably between 0.2 and 1 bar.

According to a preferred embodiment of the invention, after reaction the reaction medium is decanted in order to separate the solvent containing the TMBQ from the aqueous phase containing the HPA. The organic phase is subsequently dewatered, the solvent is distilled and then recycled to a new oxidation stage, and the TMBQ is distilled. The aqueous phase is optionally treated with ortho-dichlorobenzene in order

to remove the dissolved TMBQ and then optionally concentrated before being recycled to the oxidation stage.

By virtue of this process, no saline aqueous treatment is required and no mineral salts are produced, all of the solvents used are recycled, and the TMBQ prepared is of high purity. Owing to the nature of the reactants employed, the choice of compatible materials is simplified, since the problem of corrosion described above with the chlorinated catalysts disappears.

The present invention will be described more completely with the aid of the following examples.

EXAMPLES

15 I) PREPARATION OF HETEROPOLYACIDS

Preparation of $H_7PMo_8V_4O_{40}$ according to the procedure described by ODYAKOV et Al, Kinetics and Catalysis, 36, 1995, 733-738.

II) Oxidation of TMP to TMBQ

20 Some experiments were carried out BATCHwise, with all of the reactants being introduced at the beginning of the reaction; other experiments were carried out SEMIBATCHwise, with gradual introduction of the quantity of TMP to be oxidized.

25 a) Assembly

The reactions were carried out in a 250 ml four-necked round-bottomed flask equipped with a

condenser, a frit and a mechanical stirrer. The reaction medium was heated using a thermostatic bath. The oxygen pressure of 1 atmosphere above the reaction medium was obtained by circulating pure oxygen within
5 the reactor. A flow meter allowed the rate of circulation flow of the oxygen to be regulated.

In the case of a semi-batch experiment the TMP dissolved in the organic solvent was introduced dropwise into the reaction medium with the aid of a
10 syringe and a syringe pump. Since the speed of the syringe pump was adjustable, it was possible to set the rate of addition.

b) Procedure

All of the experiments were conducted in a
15 bath thermostated at 50°C with an oxygen flow rate of 12 l/h.

Case of the experiments carried out batchwise:

3 g of TMP were charged to the reactor in
20 melted form, i.e. after having been heated to 70°C in an oven. 15 ml of aqueous HPA solution (H7PMo8V4O40) with a concentration of 0.15 mol/l were added, followed by 55 ml of acetic acid and then 50 ml of ortho-dichlorobenzene.

25 Stirring and oxygen circulation were commenced. The reaction medium was placed in the water bath at 50°C.

After reaction for 2 hours, the reaction

mixture was emptied into a decanting funnel and the reactor was rinsed with 30 ml of ortho-dichlorobenzene. The aqueous phase recovered was washed twice with 30 ml of ortho-dichlorobenzene in order to extract the TMBQ
5 dissolved in the catalyst at the bottom. All the phases were recovered and weighed and their relative volume was measured.

Case of the experiments carried out semi-batchwise:

10 The procedure described above was followed, with the following modifications:

The 3 g of TMP were dissolved in the organic solvent (50 ml) and the solution was fed in over 1 hour and 30 minutes with the aid of a syringe and a syringe
15 pump; at the end of addition, a finishing time of 30 minutes was allowed, with stirring and under oxygen pressure.

The treatments to recover the TMBQ and the catalyst at the bottom are identical to the BATCHwise
20 process.

c) Results

The two phases, aqueous and organic, are analysed by HPLC:

The degree of conversion of the TMP is
25 DC=100% and the yield of TMBQ, i.e. the amount of TMBQ obtained over the TMP introduced, is RY=84%. The major impurity is hexamethyldiphenol (HMDP), which is well known as a by-product of the reaction, in addition to

heavy products which are not assayed. The BATCH and SEMICONTINUOUS results are substantially the same.

One of the most interesting results is that the catalyst remained quantitatively in aqueous phase and that it was recycled as it was without additional treatment.

III) STUDY OF THE RECYCLABILITY OF THE CATALYST SYSTEM

Recyclability experiments

We studied the recyclability of the catalyst system in the most highly performing two-phase system, i.e. in the medium ortho-dichlorobenzene/acetic acid/water = 50 ml/56 ml/14 ml. We worked BATCHwise.

a) Assembly

The assembly used for the recycling experiments is identical to that used for the BATCH experiments in heterogeneous medium.

b) Procedure

The aqueous phase containing the catalyst obtained at the end of the first catalytic cycle described in the preceding paragraph was evaporated on a Rotavapor until a blackish oil was obtained. This was then made up to 56 ml with acetic acid, after which 14 ml of water were added.

The TMP (3 g) was charged to the reactor in melted form, i.e after having been heated to 70°C in an oven. The above catalytic solution was added, followed by 50 ml of otho-dichlorobenzene.

The procedure followed thereafter was the same as in the first catalytic cycle.

c) Results

We carried out three cycles starting from the same catalyst system. Each oxidation took place under the same operating conditions.

HPA used: $\text{H}_7\text{PMo}_8\text{V}_4\text{O}_{40}$

T = 50°C

P = 1 atm of oxygen

Number of moles of TMP/number of moles of HPA = 10

Composition of the organic solvent/acetic acid/water medium: 50 ml/56 ml/14 ml

Duration = 2 h

	DC %	Selectivity %	RY TMBQ %	RY HMDP %
1st catalytic cycle	100	84	84	0.2
2nd catalytic cycle	100	86	86	1
3rd catalytic cycle	100	85	85	2

The activity of the catalyst system did not decrease between each cycle.

CLAIMS

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1 - Process for preparing 2,3,5-trimethylhydroquinone by oxidizing 2,3,6-trimethylphenol in the presence of an oxidizing agent
5 selected from oxygen and hydrogen peroxide and of a heteropolyacid, the reaction being characterized in that it is carried out in two-phase liquid medium.

2 - Process according to Claim 1, characterized in that the heteropolyacid is selected
10 from Keggin-structure heteropolyacids or Dawson-structure heteropolyacids.

3 - Process according to Claim 1 characterized in that the reaction medium consists of an aqueous mixture consisting of water and a mono- or
15 dibasic organic carboxylic acid of type C2 to C6 and of a water-immiscible organic solvent.

4 - Process according to Claim 3 characterized in that the volume ratio between the acetic acid and the water is between 95/5 and 20/80 and
20 preferably between 80/20 and 60/40.

5 - Process according to Claim 3 characterized in that the water-immiscible solvent is selected from aliphatic or aromatic hydrocarbons and from their halogenated derivatives.

25 6 - Process according to Claim 5 characterized in that the water-immiscible solvent is ortho-dichlorobenzene.

7 - Process according to Claim 3



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characterized in that the volume ratio between the solvent and the aqueous system is between 30/70 and 90/10 and preferably between 30/70 and 50/50).

8 - Process according to Claim 1

5 characterized in that the molar ratio between the trimethylphenol and the heteropolyacid is between 200/1 and 5/1 and is preferably approximately 10/1.

9 - Process according to Claim 1

10 characterized in that the weight ratio between the HPA and TMP assembly relative to the liquid medium made up of the solvent and the aqueous medium is between 0.1% and 15% and is preferably approximately 6%.

10 - Process according to Claim 1

15 characterized in that the reaction temperature is greater than 30°C and is preferably between 50 and 70°C.

11 - Process according to Claim 1

characterized in of that the oxygen pressure is between 0.2 and 1 bar.

20 12 - Process according to Claim 1

characterized in that after reaction the reaction medium is decanted to separate the solvent containing the TMBQ from the aqueous phase containing the HPA, the organic phase is subsequently dewatered, the solvent is 25 distilled and then recycled for a new oxidation stage and the TMBQ is distilled, the aqueous phase is optionally treated with ortho-dichlorobenzene to remove the dissolved TMBQ and then is concentrated and



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recycled to the oxidation stage.

