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(54) **Title:** PROCESS FOR THE PREPARATION OF 3,5,5-TRIMETHYL-CYCLOHEX-2-ENE-1,4-DIONE

(57) **Abstract:** The present invention relates to an improved process for the preparation of 3,5,5-trimethylcyclohex-2-ene-1,4-dione by oxidation of 3,5,5-trimethylcyclohex-3-en-1-one in the presence of an oxidizing agent and a catalyst system comprising a transition metal complex catalyst, an auxiliary base, possibly water, and a catalytically active co-additive, characterized in that carboxylic acid amides are employed as the solvent.

Process for the Preparation of 3,5,5-Trimethyl-Cyclohex-2-ene-1,4-Dione

Field of the Invention

This invention relates to an improved process for the preparation of 3,5,5-trimethylcyclohex-2-ene-1,4-dione (ketoisophorone) by oxidation of 3,5,5-trimethyl-cyclohex-3-en-1-one (β-isophorone).

Background of the Invention

Ketoisophorone (KIP) is an important intermediate product in the synthesis of trimethylhydroquinone or trimethylhydroquinone esters, which in turn are an intermediate product in the synthesis of vitamin E. KIP is furthermore an intermediate product for the preparation of various carotenoids, such as, for example, astaxanthine, zeaxanthine and canthaxanthine.

The production of KIP by oxidation of α-isophorone or β-isophorone (β-IP) is known.

According to Hosokawa et al. (Chem. Lett., 1983, 1081-1082), oxidation of α-isophorone to KIP is achieved by tert-butyl hydroperoxide in the presence of 10 mol% palladium acetate and an auxiliary base in yields of a maximum of 55%. In addition to the high amount of catalyst and the low yield which can be achieved, in particular the use of the expensive oxidizing agent tert-butyl hydroperoxide makes the process unattractive for an industrial reaction.

The same applies to the reaction according to WO 96/154094, in which compounds of the sub-group metals of groups Ib, Vb, VIb or VIII, inter alia vanadium(V) oxide and iron(III) chloride, are used as catalysts for the oxidation with tert-butyl hydroperoxide.

Oxidation by means of oxygen or an oxygen-containing gas mixture is considerably more economical here. DE 25 26 851 discloses a corresponding process for the oxidation of α-isophorone under catalysis by e.g. phospho- or silicomolybdic acid, possibly with the addition of copper(II) salts or molybdenum trioxide. However, very long reaction times of 96 hours (h) and high temperatures of 100ºC are necessary to achieve complete conversions. The yield which can be achieved under these conditions is only 45%.

Comparable results with the use of phosphomolybdic acid as the catalyst are described by Freer et al. (Chem. Lett., 1984, 2031-2032) and in EP 0 425 976.

According to JP Sho 61-191645/1986, the selectivity of this process can be increased to up to 96% by employing organic amines or alkali metal salts as additives, in addition to catalytic amounts of phospho- or silicomolybdic acid. However, the maximum conversion which can be achieved in this way is only 59%, which necessitates a working up of the product solution which is expensive and not very desirable from economic aspects.

According to JP Hei 10-182543/1998, similar results are also achieved when a catalyst system comprising salts of the platinum metals and hetero-polyacids or salts thereof is employed. However, the high price of platinum metal salts additionally contributes towards the unprofitability of this process.

According to DE 24 59 148, acetylacetonates of various transition metals, preferably vanadium acetylacetonate, can be employed as catalysts of the oxidation of α-isophorone by molecular oxygen. Here also, however, long reaction times of more than 40 h and high temperatures of 100ºC to 130ºC are necessary, and only unsatisfactory yields of 20% to 40% are obtained.

Overall, no economical process is known for the direct oxidation of α-isophorone to KIP, since the yield of the reaction by the processes described is low. The oxidation of β-IP, which can be obtained from α-isophorone by known processes, can be carried out considerably more efficiently. The most economical variant of this oxidation here also is the procedure using oxygen or an oxygen-containing gas as the oxidizing agent.

Thus, according to DE 24 57 157, the yields in the oxidation reaction catalyzed by transition metal acetylacetonate can be increased to up to 56% by prior isomerization, mediated by sodium acetate, of α-isophorone to β-IP, at the same time somewhat lower temperatures of 25ºC - 75ºC and shorter reaction times of > 26 h being necessary. Nevertheless, these results are still unsatisfactory.

According to DE 25 15 304, a significant improvement was to be achieved by adding pyridine or pyridine derivatives, in addition to the transition metal acetylacetonate, as a result of which the reaction time is shortened to 2 h to 3.5 h and KIP is obtained in yields of 70% to 80%, and in one example even 91%. It proves to be a disadvantage here that large amounts of base (up to 250 mol%, based on the β-IP) and of catalyst (up to 10 per cent by weight (wt.%), based on the β-IP) are required.

According to DE 38 42 547, the above-mentioned amounts of base and catalyst employed can be reduced significantly with comparable KIP yields if specifically copper acetylacetonate is used in the presence of pyridine.

The oxidation of β-IP to KIP catalyzed by active charcoal with the addition of triethylamine (DE 26 57 386) or heterocyclic nitrogen bases, such as pyridine (JP Hei 11-49717/1999) in acetone as the solvent is also described. However, the flash point of the solvent acetone of -17ºC is

exceeded by far at the reaction temperatures of 100°C, which is not acceptable for an industrial realization for safety reasons.

An improvement in the oxidation of β-IP to KIP in respect both of the amounts of catalyst employed and of the reaction conditions (low temperature, short reaction time) and the yields which can be achieved at high conversions (high selectivities) resulted from the use of transition metal complexes with polydentate ligands as catalysts of the reaction.

EP-B 0 311 408 employs Mn tetraphenylporphyrin as the catalyst, in addition to triethylamine as a base and water as an additive. Optimum crude yields of 98% are obtained here using a solvent mixture of ethylene glycol dimethyl ether and methylene chloride. The use of a solvent mixture is not appropriate for an industrial realization both from economic and from safety aspects.

In a publication by the same authors which appeared later (Ito et al., Synthesis 1997, 2, 153-155), a selectivity of only a maximum of 93% when ethylene glycol dimethyl ether is employed as the solvent under optimum conditions is reported. The use of ethylene glycol dimethyl ether as the solvent is not desirable for an industrial realization because of the low flash point of -6°C and the associated risk of explosion. Furthermore, the use of porphyrin catalysts, which are very expensive to synthesize and must be prepared in a separate two-stage process in low yields, appears to be a disadvantage. If manganese(III)salen chloride is used as the catalyst, a yield of only 81% is obtained under the conditions described.

According to JP Sho 64-90150/1989 and JP Hei 01-175955/1989, yields of KIP of just above 90% can be achieved using manganese(III)-salen compounds and derivatives under optimum, selected conditions. Ethylene

glycol dimethyl ether is also used here as the solvent, which in turn involves the disadvantages already described.

DE 26 10 254 discloses the oxidation of β-IP to KIP using manganese(II)- or cobalt-salen or related compounds as the catalyst. A selectivity of the reaction catalyzed by manganese-salen of 100% is reported here in one example. Under the conditions described, this corresponds to a space/time yield of 0.09 kilograms of KIP per hour-liter (kg/h*l). Some years after the patent application was laid open, this result is no longer mentioned by the same authors in a scientific publication (M. Constantini et al., J. Mol. Catal., 1980, 7, 89-97). A maximum KIP yield of 85%, which can be achieved with manganese-salen as the oxidation catalyst under optimum conditions, is reported there. According to this publication, it was possible to increase the space/time yield to 0.16 kg KIP/(h*l) under optimum conditions, but this is still unsatisfactory.

An investigation of the influence of the solvent on the space/time yield and the selectivity of the reaction is also presented in this publication. The authors come to the conclusion that if aprotic solvents are employed, as the polarity and basicity increase the rate of reaction indeed increases, but not the selectivity. Various ethers and ketones, in particular ethylene glycol dimethyl ether and acetone, are acknowledged as optimum solvents for the selectivity. However, the use of acetone with a flash point of -17ºC or ethylene glycol dimethyl ether with a flash point of -6ºC as the solvent for an industrial oxidation process in the temperature range described is eliminated by consideration of safety aspects, since the risk of explosion of the reaction mixture can be avoided only by very expensive safety precautions, which in turn means a considerable economic outlay. Moreover, the use of ethers as solvents in the presence of bases and oxygen

results generally in the risk of the formation of highly explosive peroxides, which involves a further safety risk.

US 5,874,632 addresses in detail for the first time the connection between the educt concentration in the reaction mixture and the selectivity which can be achieved. It is found that in the reaction catalyzed by manganese-salen in diethylene glycol dimethyl ether (diglyme) in the presence of triethylamine as the base and water as a reaction accelerator, good selectivities of 91% can be achieved only at low β-IP concentrations of a maximum of 10 wt.%. A dramatic drop in selectivity takes place at a higher concentration. The addition of a catalytically active substance from the class of organic acids with pKa values of between 2 and 7 or the corresponding aldehydes, various enolizable compounds or lithium sulfate, in particular the addition of acetylacetone, is disclosed here as a solution to the problem, ethers and ketones, in particular diglyme, being used as the solvent. Significantly higher educt concentrations can be realized by this measure, without a significant reduction in the selectivity having to be accepted. Space/time yields of up to 0.34 kg KIP/(h*l) can be realized in this way.

For the profitability of a catalytic process, in particular using a homogeneous catalyst, in addition to the space/time yield (product in kg per hour and reaction volume in liters) and the amount of catalyst needed, the choice of additives and solvent is of central importance. When the known processes are reproduced, it is found that by using the preferred solvents and additives described, considerable amounts of by-products are formed in the reaction matrix, which have the effect of a reduction in catalyst output during recycling and therefore a reduction in the selectivity for the desired product KIP if the process is operated in circulation. A considerable consumption both of the solvent and of the additive is

associated with this, and at the same time the need arises to remove the by-products formed by suitable process technology operations with considerable expenditure on apparatus.

Of the above-mentioned processes, the reaction of β-IP with oxygen in the presence of manganese-salen and metal porphyrin and phthalocyanine catalysts of the composition known in the prior art shows the best selectivities and space/time yields. The process according to US 5,874,632 appears to be the most suitable for industrial realization on the basis of the high space/time yield which can be achieved, the relatively simple catalyst, which is inexpensive to prepare and which already leads to complete conversions with high selectivities when added in small amounts, and on the basis of the relatively high flash point of the preferred solvent diglyme of 53°C. Nevertheless, the process has some disadvantages, which are to be explained in the following.

When this process is operated as a circulation process with distillative working up and removal of the solvent diglyme from the product, it is found that the use of diglyme as the solvents indeed renders possible very good yields and selectivities of > 90%, but decomposition of the solvent, base and additive leads to the formation of carboxylic acids, which are recycled to the reactor again during recycling of the solvent or must be separated off with considerable outlay. Formic acid and acetic acid are to be mentioned in particular here, but also methoxyacetic acid and 2-methoxyethoxyacetic acid. These by-products become concentrated in the circulation solvent and lead to a continuous decrease in the selectivity of the oxidation reaction.

Another considerable disadvantage for an industrial procedure is the instability of the catalyst components premixed in the solvent. Since direct metering of the

catalyst as a solid is usually to be avoided, it is desirable to initially introduce the catalyst into the reaction vessel in the solvent together with the catalyst base and the catalytically active co-additives before the reaction and to bring this solution continuously into contact with β-IP and to feed it to the reaction part. If ethylene glycol ethers, which are optimum for the selectivity, are used, a considerable aging of the catalyst solution as the service life of the premixture increases is found, which manifests itself in a drastic decrease in the selectivity of the reaction in a continuous process.

Another problem which has so far not been solved satisfactorily is the formation of by-products during the oxidation, in particular hydroxyisophorone, which is formed in an amount of between 5%-20% in the preparation by conventional processes, depending on the reaction procedure. Under optimum conditions, a minimum formation of hydroxyisophorone of 5% (based on the β-IP employed) can be obtained if manganese-salen is used as the catalyst in the system NEt_3/water/diglyme. The formation of by-products in this order of magnitude is not desirable from economic aspects.

The use of ethers as the solvent for the oxidation reactions moreover involves the risk of formation of highly explosive peroxides already described. Furthermore, diglyme is a very expensive solvent, which has an adverse effect on the preparation costs of the process, so that the use of diglyme as the solvent for the reaction investigated is not very desirable from economic aspects.

Summarizing, no satisfactory overall concept for the industrial reaction has yet been found which takes into account the following criteria simultaneously:

a) use of a favorable, readily accessible solvent,

b) use of a stable solvent which is inert under the reaction conditions,

c) use of only one uniform solvent to avoid expensive separations of substances during working up,

d) use of solvents which do not tend to form explosive peroxides under the reaction conditions,

e) use of a suitable solvent which stabilizes the reaction matrix (the solution of any additives and catalyst) and thus forms a solution which is stable to storage over a relatively long period of time.

Summary of the Invention

The object of the present invention is thus to discover, on the basis of the prior art, a suitable, stable reaction system, in particular solvent, which avoids the disadvantages described for the processes already known, which are in come cases considerable, while retaining or increasing the good selectivities and reaction yields, specifically in the catalyst system manganese-salen / auxiliary base / optionally water / co-additive.

This invention provides an improved process for the preparation of 3,5,5-trimethylcyclohex-2-ene-1,4-dione (ketoisophorone, KIP) by oxidation of 3,5,5-trimethyl-cyclohex-3-en-1-one (β-isophorone, β-IP) in the presence of an oxidizing agent and a catalyst system comprising a transition metal complex catalyst, an auxiliary base, possibly water, and a catalytically active co-additive chosen from the group consisting of:

1. an organic acid with a pKa of between 2 and 7 or the corresponding aldehyde;

2. an aliphatic alcohol with 1-4 C-atoms or phenol;

3. compounds which can form an enol structure; and

4. lithium sulfate;

characterized in that carboxylic acid amides are employed as the solvent.

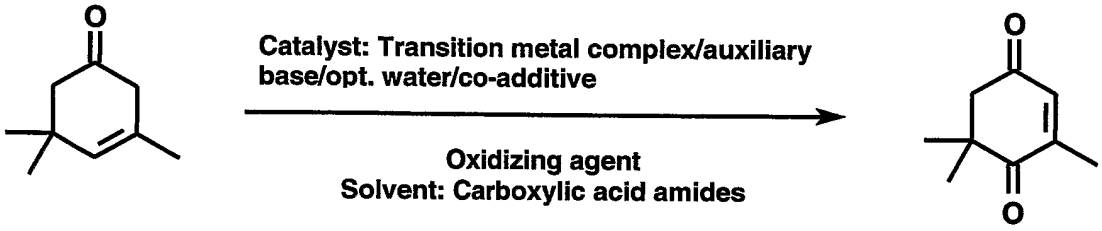
Brief Description of the Figures

Figure 1 depicts diagram showing the KIP yield as a function of the β-IP concentration.

Figure 2 depicts diagram showing the KIP yield as a function of the oxygen supplied.

Detailed Description of the Invention

The reaction is illustrated clearly in the following equation:



β-Isophorone Ketoisophorone

Weak organic acids or bidentate complexing compounds have proved to be particularly advantageous co-additives in respect of the reaction kinetics. Particularly preferred co-additives are acetic acid, butyric acid, salicylic acid, oxalic acid, malonic acid, citric acid and further aliphatic or aromatic mono-, di- or tricarboxylic acids. Amino acids, such as e.g. glycine, leucine, methionine or aspartic acid, are also suitable.

It has also been found that aliphatic alcohols, such as methanol, ethanol, butanol, isobutanol and tert-butanol, or phenol serve as the co-additive. Co-additives which can form an enol structure, such as e. g. acetoacetic esters, phenylacetone and, in particular, acetylacetone, are particularly advantageous. Acetylacetone is particularly

preferably employed as the co-additive, since it additionally allows higher reaction selectivities to be achieved than with other suitable co-additives.

The use of acetylacetone has shown that higher concentrations of β-IP, based on the total amount of the mixture, can be employed and therefore higher space/time yields can be achieved without a serious reduction in the selectivity occurring.

A molar ratio of the co-additive to the catalyst of 1:1 to 100:1, preferably 4:1 to 40:1, based on the catalyst, can be employed.

The outstanding properties of carboxylic acid amides as the solvent for the oxidation reaction under consideration have not hitherto been acknowledged and found in any of the publications. Instead, ethers and ketones have preferably been mentioned and employed as the optimum solvent in all the disclosures relevant to the present invention, resulting in the above-mentioned disadvantages.

Suitable carboxylic acid amides in the process according to the invention are dimethylformamide, diethylformamide, dimethylacetamide, diethylacetamide or mixtures thereof. Dimethylformamide is particularly preferred as the carboxylic acid amide. The amount in which the suitable carboxylic acid amides can be used is not critical for carrying out the process according to the invention, but it is preferable to use carboxylic acid amides in amounts of 50 wt.% to 95 wt.%, preferably 65 wt.% to 85 wt.%, based on the total amount of the reaction mixture.

It has been found that the KIP selectivity which can be achieved in the oxidation in carboxylic acid amides unexpectedly reacts very sensitively to a lower supply of oxygen. In a pilot bubble column with very efficient introduction of gas via a fine-pored frit, the enormous

potential of this solvent class began to become visible only from the relatively high metering in of oxygen of 0.5 liters of oxygen per hour and gram of β-IP (a specific value for the pilot apparatus used). A drastic drop in selectivity took place below this value. Such an effect is not to be observed to this extent with the solvents conventionally employed, such as diglyme.

To achieve optimum yields, the oxygen supply in the carboxylic acid amides even had to increased up to at least about 0.8 liter of oxygen per hour and gram of β-IP. Not taking account of or not knowing these circumstances thus unavoidably leads to poor results in the reaction procedure in carboxylic acid amides, from which a supposedly lower suitability of carboxylic acid amides as the solvent for the reaction under consideration compared with the ethers and ketones described as having priority has been incorrectly assumed.

The fact is that not only does carrying out the oxidation in carboxylic acid amides allow KIP to be prepared in high selectivities and yields with a simultaneously reduced formation of by-products, but also in carboxylic acid amides the catalyst system reacts considerably less sensitively to the presence of carboxylic acids unavoidably obtained when the process is operated in circulation than is the case with ethers.

The catalyst system also has a significantly better stability in carboxylic acid amides than in ethers, which allows premixing of the reaction matrix in continuous operation of the process, without a drop in the selectivity of the reaction taking place over a period of time.

Another great advantage of carboxylic acid amides is that the effect of the catalytically active co-additive described on the educt concentration which can be realized without a serious loss in selectivity is significantly more

pronounced than, for example, in diglyme, which results in economic advantages in respect of the space/time yield of the reaction. Thus, even at a β-IP concentration of 40 wt.%, a selectivity of more than 85% is still observed, a value which can be achieved in diglyme only at educt concentrations up to a maximum of 20 wt.%.

At the same time, due to the weakly basic properties of the carboxylic acid amide solvent, the amount of auxiliary based employed can be reduced down to 10 mol%, based on the β-IP employed, without serious losses in the selectivity of the reaction which can be achieved occurring.

Furthermore, the use of carboxylic acid amides as the solvent, in particular inexpensive dimethylformamide, offers an enormous economic advantage over the use of the very expensive ethylene glycol ethers, such as diglyme and ethylene glycol dimethyl ether, which have hitherto been described as the preferred solvents for achieving high selectivities.

To carry out the reaction, β-IP is continuously or discontinuously brought into contact with the reaction matrix, which comprises the catalyst and the auxiliary base, as well as a catalytically active co-additive and optionally water and which is dissolved or suspended in a carboxylic acid amide as the solvent, and reacted with oxygen or an oxygen-containing gas mixture under normal pressure or increased pressure.

Catalysts which are used are the transition metal-containing complex catalysts mentioned in the prior art, such as manganese-salen, manganese-tetraphenylporphyrin and manganese-phthalocyanine, manganese-salen being preferred. The catalyst is conventionally added in amounts of 0.001 to 3 wt.%, based on the β-IP, preferably in amounts of 0.05 to 1 wt.%.

The organic and inorganic bases known according to the prior art can be used as the auxiliary base, such as e.g. alkylamines, di- and trialkylamines, aromatic and aliphatic heterocyclic bases, sodium or potassium hydroxide solution or alcoholates, or a quaternary ammonium hydroxide, preferably trialkylamines, in particular triethylamine. These bases can be employed in conventional amounts, such as e.g. 5 to 60 mol%, based on the β-IP, amounts of 10 to 35 mol% being particularly preferred.

Carboxylic acid amides, such as e.g. dimethylformamide (DMF), diethylformamide (DEFA) and the corresponding acetamides, such as dimethylacetamide or diethylacetamide, are employed as the solvent in the process according to the invention. In a particularly preferred embodiment, the reaction is carried out in dimethylformamide. The content of carboxylic acid amide in the reaction mixture is conventionally 50 wt.% to 95 wt.%, and amounts of 65 wt.% to 85 wt.% are preferably employed.

The water content in the total reaction mixture can vary between 0 and 30 wt.%. Without the addition of water, very high selectivities are achieved, but with uneconomical reaction times. Water is therefore preferably employed as a reaction accelerator, in particular between 0.05 wt.% and 30 wt.%, preferably between 0.5 and 20 wt.%, particularly preferably between 0.5 wt.% and 5 wt.%, based on the total weight of the reaction mixture.

Oxidizing agents which can be employed in this invention are oxygen or oxygen-containing gas mixtures, such as e.g. air or oxygen diluted by addition of an inert gas, such as, for example, nitrogen.

The reaction can be carried out under normal pressure or increased pressure. For example, the reaction can be carried out under between 1 and 12 bar, depending on the volume content of oxygen in the oxidizing agent employed.

The reaction temperature can be between -30ºC and 80ºC, preferably between 10ºC and 45ºC.

The process according to the invention is simple to carry out and gives the reaction product in a good yield and high purity. The reaction product can be isolated from the product mixture by the usual processes, in particular by vacuum distillation.

The yields were determined on an HP 5890 or an HP 6890 gas chromatograph using a J&W DB-5 capillary column of 30 m length, 0.32 mm internal diameter and 1 µm film thickness. Diethylacetamide was used as the internal standard. KIP, which was purified by distillation, was used as the reference substance.

The HPLC measurements were carried out on a system comprising a Biotronik BT 3035 UV detector, a Jasco 880 PU pump and a Spectra Physics Chrom Jet integrator. The column used was an RP 18, 5 µ, 250 x 4 mm internal diameter. The KIP reference substance described above was used as the external standard.

The following examples are intended to illustrate the invention in more detail.

Examples 1 to 12

58.0 g of the solvent stated in table 1, 1.2 g water, 0.16 g acetylacetone, 2.53 g triethylamine and the amount of manganese-salen which can be seen from Table 1 are initially introduced into a glass beaker and stirred for either 15 min (variant A) or 16 h (variant B). 15.4 g β-IP are then added and the reaction mixture is stirred briefly and transferred to a bubble column. It is gassed with oxygen (12 l/h) for 2.5 hours at 35ºC under normal pressure and the yield of KIP is then determined by gas chromatography with an internal standard. The results are listed in Table 1.

Comparative Examples A to F

58.0 g diglyme, 1.2 g water, 0.16 g acetylacetone, 2.53 g triethylamine and the amount of manganese-salen which can be seen from Table 1 are initially introduced into a glass beaker and stirred for either 15 min (variant A) or 16 h (variant B). 15.4 g β-IP are then added and the reaction mixture is stirred briefly and transferred to a bubble column. It is gassed with oxygen (12 l/h) for 2.5 hours at 35°C under normal pressure and the KIP yield is then determined by gas chromatography with an internal standard. The results are listed in Table 1.

Table 1

Example/ Comp. Example	Solvent	Variant	Amount of catalyst [wt.% based on β-IP]	Yield of KIP [%]
1	DMF	A	0.2	91.4
2	DMF	B	0.2	89.7
3	DEFA	A	0.2	90.5
4	DEFA	B	0.2	89.6
A	diglyme	A	0.2	90.3
B	diglyme	B	0.2	85.3
5	DMF	A	0.3	92.2
6	DMF	B	0.3	91.9
7	DEFA	A	0.3	92.0
8	DEFA	B	0.3	90.3
C	diglyme	A	0.3	90.1
D	diglyme	B	0.3	87.0
9	DMF	A	0.4	92.8
10	DMF	B	0.4	92.0
11	DEFA	A	0.4	92.1
12	DEFA	B	0.4	92.5
E	diglyme	A	0.4	90.5
F	diglyme	B	0.4	88.8

Examples 13 to 15

72.5 g DMF, 1.56 g water, 0.21 g acetylacetone, 3.18 g triethylamine, the amounts of acid stated in Table 2 and 75 mg manganese-salen are initially introduced into a glass beaker and stirred for 15 min. 19.25 g β-IP are then added and the reaction mixture is stirred briefly and transferred to a bubble column. It is gassed with oxygen (16 l/h) for 2.5 hours at 35°C under normal pressure and the yield of KIP is then determined by gas chromatography with an internal standard. The results are listed in Table 2.

Comparative Examples G to I

72.5 g diglyme, 1.56 g water, 0.21 g acetylacetone, 3.18 g triethylamine, the amounts of acid stated in Table 2 and 75 mg manganese-salen are initially introduced into a glass beaker and stirred for 15 min. 19.25 g β-IP are then added and the reaction mixture is stirred briefly and transferred to a bubble column. It is gassed with oxygen (16 l/h) for 2.5 hours at 35°C under normal pressure and the yield of KIP is then determined by gas chromatography with an internal standard. The results are listed in Table 2.

Table 2

Example/ Comp. Example	Solvent	Acid added [mg/kg solvent]	Yield of KIP [%]
13	DMF	formic acid: 2059	91.7
14	DMF	acetic acid: 2011	88.5
15	DMF	formic acid: 1031 acetic acid: 1007	92.3
G	diglyme	formic acid: 1999	84.6
H	diglyme	acetic acid: 1742	86.5
I	diglyme	formic acid: 1044 acetic acid: 1028	86.0

It has again been confirmed that higher yields can be achieved with the process according to the invention.

Examples 16 to 22

About 100 g of a solution of β-IP, triethylamine, water, acetylacetone and manganese-salen in the concentrations which can be read off from Table 3 in DMF are gassed with oxygen (16 l/h) in a laboratory bubble column for 2.5 hours at 35°C under normal pressure and the yield of KIP is then determined by gas chromatography with an internal standard. The results are listed in Table 3.

Table 3

Example	β-IP [mol/l]	Triethylamine [mol/l]	Water [mol/l]	Acetylacetone [mol/l]	Manganese-salen [mol/l]	Yield of KIP [%]
16	0.54	0.30	0.80	115	3.81	92.6
17	1.08	0.30	0.81	113	3.79	91.7
18	1.59	0.30	0.81	167	5.57	89.4
19	2.11	0.29	0.79	222	7.38	87.7
20	2.62	0.29	0.78	273	9.14	85.7
21	3.85	0.29	0.78	375	12.55	70.0
22	5.61	0.28	0.75	571	19.10	64.7

The yields of KIP in examples 16 to 22 were compared with the yields of KIP according to table 3 of US Patent 5,874,632. The result is shown in Figure 1.

In Figure 1, it can be clearly seen that the yields of KIP of this invention are significantly improved, i.e. increased, at the same β-IP concentrations, compared with the prior art.

Examples 23 to 26

58.0 g dimethylformamide, 1.2 g water, 0.16 g acetylacetone, 2.53 g triethylamine and 45 mg manganese-salen are initially introduced into a glass beaker and stirred for 15 min. 15.4 g β-IP are then added and the reaction mixture is stirred briefly and transferred to a bubble column. It is gassed with oxygen in the metered amount which can be seen from Table 4 for 2.5 hours at 35ºC under normal pressure and the yield of KIP is then determined by HPLC with an external standard. The results are listed in Table 4.

Comparative Examples J to M

58.0 g diglyme, 1.2 g water, 0.16 g acetylacetone, 2.53 g triethylamine and 45 mg manganese-salen are initially introduced into a glass beaker and stirred for 15 min. 15.4 g β-IP are then added and the reaction mixture is stirred briefly and transferred to a bubble column. It is gassed with oxygen in the metered amount which can be seen from Table 4 for 2.5 hours at 35ºC under normal pressure and the yield of KIP is then determined by HPLC with an external standard. The results are listed in Table 4.

Table 4

Example/ Comp. Example	Solvent	Oxygen metered in		Yield of KIP
		[l/h]	[l/h*g β-IP]	[%]
23	DMF	6	0.40	75.8
24	DMF	8	0.53	87.4
25	DMF	10	0.66	89.2
26	DMF	12	0.80	90.2
J	diglyme	6	0.40	86.8
K	diglyme	8	0.53	87.9
L	diglyme	10	0.66	89.0
M	diglyme	12	0.80	88.9

Examples 23 to 26 illustrate the enormous influence the oxygen supply has on the ketoisophorone selectivity in the solvent DMF which can be achieved. Comparative Examples J to M demonstrate that such an effect is to be observed to only a small extent in the solvent diglyme, which is particularly preferred according to the prior art. Not knowing this sensitivity of the selectivity of the reaction in DMF to a deficient supply of oxygen thus unavoidably leads to poor results (Examples 23 to 24), from which a supposedly lower suitability of carboxylic acid amides as the solvent for the reaction under consideration compared with the ethers and ketones described as having priority in the prior art results.

On the other hand, if a sufficiently high supply of oxygen (Examples 25 to 26) is ensured, the unexpectedly high potential, described in the present invention, of

carboxylic acid amides as the solvent for the oxidation under consideration becomes clear. See Figure 2.

Examples 27 to 30

72.5 g dimethylformamide, 1.5 g water, 0.22 g acetylacetone, the amount of triethylamine which can be seen from Table 5 and 75 mg manganese-salen are initially introduced into a glass beaker and stirred for 15 min. 19.3 g β-IP are then added and the reaction mixture is stirred briefly and transferred to a bubble column. It is gassed with oxygen (16 l/h) for 3 hours at 35ºC under normal pressure and the yield of KIP is then determined by gas chromatography with an internal standard. The results are listed in Table 5.

Comparative Example N

In this Comparative Example, diglyme was used as the solvent instead of DMF with the same relative composition of the solution as in Examples 27 to 30. The yield of KIP was determined by HPLC with an external standard. The results are listed in Table 5.

Table 5

Example/ Comp. Example	Solvent	Triethylamine concentration		Yield of KIP
		[mol% with respect to β-IP]	[wt.% with respect to β-IP]	[%]
27	DMF	5	3.6	84.5
28	DMF	10	7.3	90.1
29	DMF	15	10.9	91.1
30	DMF	20	14.6	91.2
N	diglyme	11.4	8.3	86.8

It has been proved again that better yields are achieved with the process according to the invention, i.e. using dimethylformamide as the solvent instead of diglyme. See Example 28 versus Comparative Example N.

What is claimed is:

1. Process for the preparation of 3,5,5-trimethylcyclohex-2-ene-1,4-dione by oxidation of 3,5,5-trimethyl-cyclohex-3-en-1-one in the presence of an oxidizing agent and a catalyst system comprising a transition metal complex catalyst, an auxiliary base, possibly water, and a catalytically active co-additive chosen from the group consisting of:

    1. an organic acid with a pKa of between 2 and 7, or the corresponding aldehyde;

    2. an aliphatic alcohol with C_1-C_4 atoms [sic] or phenol;

    3. compounds which can form an enol structure; and

    4. lithium sulfate;

    wherein carboxylic acid amides are employed as the solvent.

2. Process according to claim 1, wherein the carboxylic acid amides are dimethylformamide, diethylformamide, dimethylacetamide, diethylacetamide or mixtures thereof.

3. Process according to claim 1 or 2, wherein the carboxylic acid amide is dimethylformamide.

4. Process according to claim 1, 2 or 3, wherein manganese-salen is used as the catalyst.

5. Process according to claim 4, wherein catalyst is added in amounts of 0.001 to 3 wt.%, based on the β-IP.

6. Process according to claim 1, 2 or 3, wherein triethylamine is used as the auxiliary base.

7. Process according to claim 1, 2 or 3, wherein acetylacetone is added as the co-additive.

8. Process according to claim 7, wherein the acetylacetone is added in a molar ratio of 1:1 to 100:1, based on the catalyst.

9. Process according to claim 1, 2 or 3, wherein water is added in an amount of 0.05 wt.% to 30 wt.%, based on the total reaction mixture.

10. Process according to claim 1, wherein dimethylformamide is employed as the solvent, and a mixture of manganese-salen, triethylamine, water and acetylacetone is employed as the catalyst system.

11. Process according to claim 1, wherein the oxidizing agent is oxygen or an oxygen-containing gas mixture.

12. Process according to claim 11, wherein the oxidizing agent is oxygen.

13. Process according to claim 11, wherein the oxidizing agent is air or oxygen diluted with nitrogen.

14. Process according to claim 1, wherein the oxidative reaction is carried out under normal pressure or increased pressure.

Figure 1

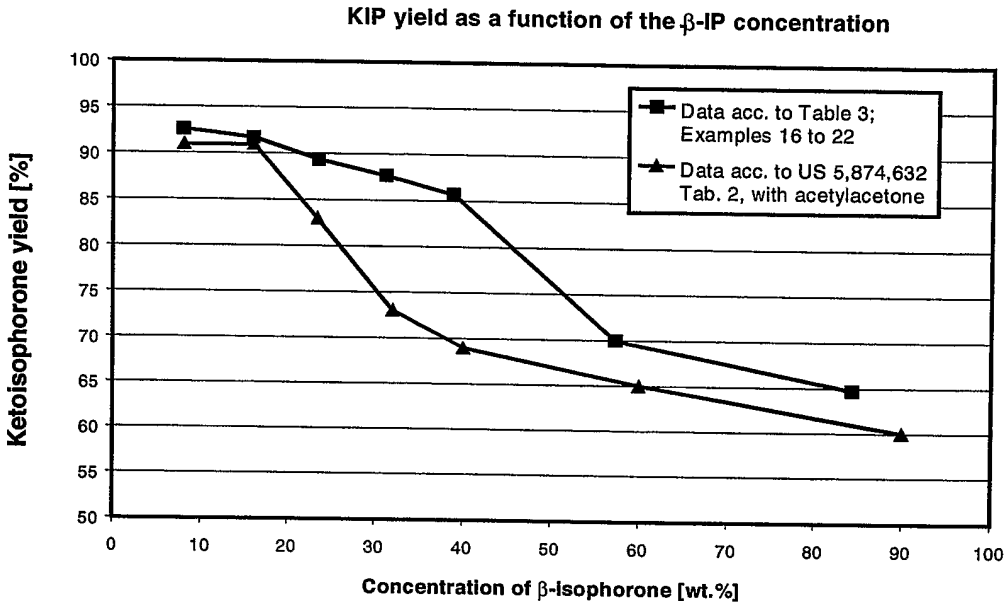
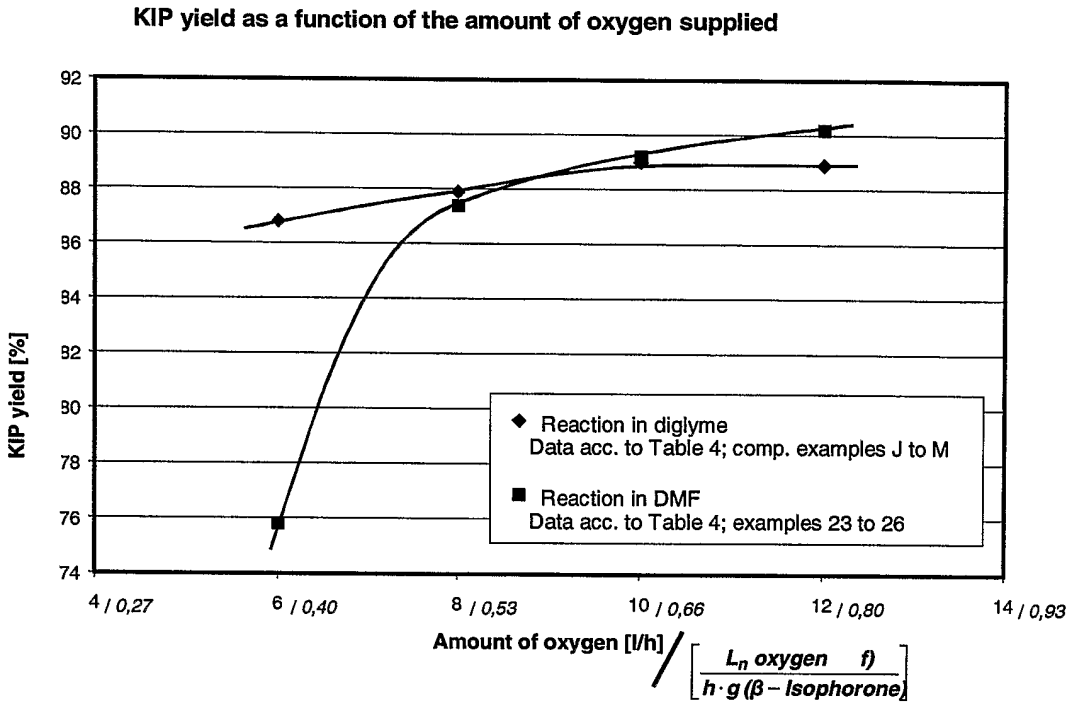

KIP yield as a function of the β-IP concentration
Ketoisophorone yield [%]
100
95
90
85
80
75
70
65
60
55
50
0
10
20
30
40
50
60
70
80
90
100
Concentration of β-isophorone [wt.%]
Data acc. to Table 3; Examples 16 to 22
Data acc. to US 5,874,632 Tab. 2, with acetylacetone

Figure 2


KIP yield as a function of the amount of oxygen supplied
KIP yield [%]
92
90
88
86
84
82
80
78
76
74
Reaction in diglyme
Data acc. to Table 4; comp. examples J to M
Reaction in DMF
Data acc. to Table 4; examples 23 to 26
4 / 0,27
6 / 0,40
8 / 0,53
10 / 0,66
12 / 0,80
14 / 0,93
Amount of oxygen [l/h] / [Ln oxygen f) / h·g (β – Isophorone]

INTERNATIONAL SEARCH REPORT

In tional Application No
PCT/EP 02/00621

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07C49/603 C07C45/34

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 874 632 A (HAHN ET AL) 23 February 1999 (1999-02-23) cited in the application claims	1
A	EP 1 063 217 A (BASF AG) 27 December 2000 (2000-12-27) claims	1-4,6
E	DE 100 62 260 A (DEGUSSA) 20 June 2002 (2002-06-20) claims	1-14

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

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"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

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Date of the actual completion of the international search	Date of mailing of the international search report
17 September 2002	25/09/2002

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INTERNATIONAL SEARCH REPORT

Information on patent family members

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PCT/EP 02/00621

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