

Towards the synthesis of (all-*rac*)- α -tocopherol from trimethylhydroquinone and isophytol at reduced pressure

Juraj Gömöry^a, Milan Králik^b, Alexander Kaszonyi^c

^aZentiva a.s., Nitrianska 100, 920 27 Hlohovec,

^bVUCHT j.s.c., Research Institute of Chemical Technology, Nobelova 34, 836 03 Bratislava, Slovak Republic,

^cDepartment of Organic Technology, Slovak University of Technology, Radlinského 9, 812 37 Bratislava, Slovak Republic

alexander.kaszonyi@stuba.sk

Abstract

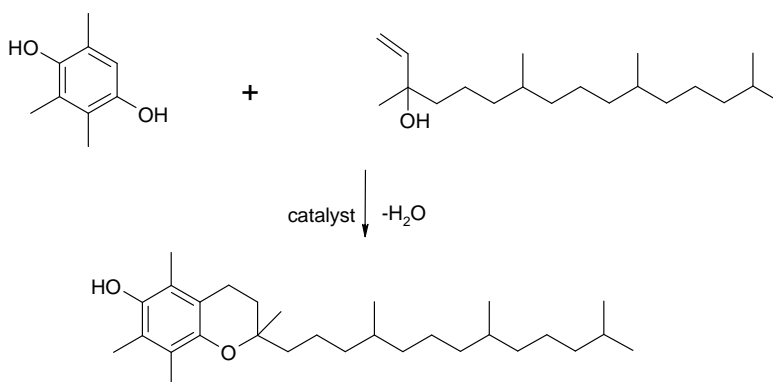
The cyclocondensation of trimethylhydroquinone and isophytol to (all-*rac*)- α -tocopherol was studied at reduced pressure at the presence of water or (all-*rac*)- α -tocopherol as solvent, and ZnCl₂ as catalyst. The obtained results confirm that the yield of (all-*rac*)- α -tocopherol can be increased at reduced pressure due to more efficient removal of reaction water, generated by the condensation reaction of isophytol (IPh) and trimethylhydroquinone (TMHQ). Auxiliary (all-*rac*)- α -tocopherol used as solvent makes a better reaction medium than water and the reached highest yield 89 % is comparable with result obtained at the presence of butyl acetate as solvent.

Keywords: (all-*rac*)- α -tocopherol, trimethylhydroquinone, isophytol, ZnCl₂, catalyst

Introduction

(All-*rac*)- α -tocopherol (synthetic vitamin E) is the most important industrial fat-soluble antioxidant. The majority of its production (74 %) is used in the production of animal fodder (Bonrath, 2007b; Baldenius, 1996). Thus, the production of animal feed represents the most valuable market for vitamin E, one amounting annually to more than 30 000 metric tones (Bonrath, 2007a). Other applications include production of cosmetics (3 %), pharmaceuticals and food. (all-*rac*)- α -Tocopherol as a vitamin is used mainly in the form of acetate (98 %) (Bonrath, 2007b; Baldenius, 1996).

The last step in the industrial synthesis of (all-*rac*)- α -tocopherol involves the reaction of isophytol, phytol, or phytyl halide with trimethylhydroquinone (Bonrath, 2007a; Baldenius, 1996). Traditionally the latter reaction is catalyzed by a combination of a Lewis acid, e.g. Zinc(II) dichloride, and a Brønsted acid, such as hydrochloric acid (Bonrath, 2005, 2007a, 2007b; Baldenius, 1996).



More recent reports (Bonrath, 2007b) mention triflates (tris-trifluoromethanesulfonates) of rare earths, e.g. ($\text{Me}^{\text{III}}(\text{OTf})_3$), such as $\text{Gd}(\text{OTf})_3$ as suitable catalysts for the reaction of trimethylhydroquinone and isophytol monoacetate. The reaction can be carried out in several solvent systems, e.g. two-phase systems based on ethylene or propylene carbonate, and hexane, heptane or octane, respectively. In contrast to zinc dichloride the same conversion and selectivity of (all-*rac*)- α -tocopherol formation can be achieved with significantly lower amount of catalyst.

The synthesis of (all-*rac*)- α -tocopherol, starting from trimethylhydroquinone and isophytol, using microencapsulated catalysts (MC), e.g. $\text{MC}-(\text{CF}_3\text{SO}_2)_2\text{NH}$ and resulting in both, good selectivity and good yield (Schager, 2000), has been described. However, MC-catalysts used in the described procedure are quickly deactivated and their activity cannot be restored.

The synthesis of (all-*rac*)- α -tocopherol, catalyzed by nanocomposite catalysts Nafion/ SiO_2 (Nafion content between 5 and 20 %) (Wang, 2004) under a stream of nitrogen also starts from trimethylhydroquinone and isophytol. The nanocomposites were produced by an in-situ hydrolysis of tetraethoxysilane in the presence of a freshly prepared Nafion (fluorinated ion-exchanging resin). The positive aspects of the procedure are high yield and selectivity, but attempts to reuse the above nanocomposite catalysts caused a significant

decrease in its activity. The use of composite Nafion/diatomaceous earth catalyst for the synthesis of pure chemicals including tocopherol has been described by Hinze et al. (2009). Authors compared the dependence of (all-*rac*)- α -tocopherol yields, produced by several composite catalysts, on the Nafion content, whereby the highest tocopherol yield (88 %) was achieved at 40 % of Nafion. Nafion, similarly as earlier mentioned catalysts, is prepared from the perfluorinated organic compound. Generally, the reused catalysts made from Nafion displayed significantly lower activity.

Kemnitz and coworkers in their European patent (2009) described the reaction of isophytol (IPh) and trimethylhydroquinone (TMHQ), catalyzed by a heterogeneous fluoride catalyst of the general formula $\text{MgF}_{2-x}(\text{OH})_x$ or $\text{AlF}_{3-x}(\text{OH})_x$ in a two-phase solvent system (propylene carbonate and heptane). The reaction is carried out at solvent reflux or in a closed system. A quantitative, relative to IPh, yield of tocopherol has been achieved at molar ratio of TMHQ : IPh exceeding 2 : 1, at catalyst content of about 7 % wt. However, the examples in patent did not mention reuse of catalysts. The same authors (Coman, 2008) described also the preparation of a nanocomposite catalyst from aluminium isopropylate by a “sol-gel” fluorination with hydrofluoric acid. The reaction conditions, reactants, as well as the results are similar to ones in the above mentioned patent. Once again, the reuse of catalysts was not mentioned. Xing et al. (2009) described a continuous process of the synthesis of (all-*rac*)- α -tocopherol, catalyzed by the ionic solution of tetrafluoroborate. The propylene carbonate solution of TMHQ and the solution of IPh in supercritical CO_2 were continuously fed into a reactor. During the reaction the product was continually separated from the reaction mixture by extraction with supercritical CO_2 . Decompression of supercritical mixture affords a product devoid of catalyst. The adjusted temperature/pressure regime affects the continuous reaction as well as product separation. (all-*rac*)- α -Tocopherol was prepared with 90.4 % yield at 100 °C, 20 MPa, at IPh/TMHQ/propylene carbonate/ CO_2 molar ratio of 1/1.5/35/3358 at a retention time of 12.6 min.

From the so far published data it appears that catalysts containing fluorine in organic or inorganic form have been intensely studied, albeit their use is hampered by high price and problematic reuse. For the selection of environmentally acceptable and recyclable catalysts as well as reaction medium, multiphase solvent systems were used as alternatives, including supercritical liquids (Wang, 2000; Bonrath, 2005). The use of polar aprotic and above all two-phase solvent system containing e.g. ethylene or propylene carbonate as the polar and heptane

as the non-polar component gave good results even with “traditional” catalysts such as ZnCl_2/HCl . Nevertheless bulk production has led to the discharge of waste water contaminated with zinc and halide ions, an environmental problem that has to be dealt with by e.g. effective recycling of catalysts and solvents.

All mentioned facts as well as experience from industrial production of (all-rac)- α -tocopherol inspired us to study the synthesis of this substance more intensively. The laboratory procedure described in this article uses reduced pressure and zinc dichloride, classic homogeneous catalyst in the production of (all-rac)- α -tocopherol from trimethylhydroquinone and isophytol.

Experimental

Chemicals used:

Isophytol (Hoffman La Roche), min. 95 %, trimethylhydroquinone (Hoffman La Roche) min. 98.5 %, water (Zentiva a.s.) conductivity 2 μS , zinc dichloride (mikroCHEM) min. 99 %, buthyl acetate (Zentiva a.s.) min. 99 %, sodium hydroxide (mikroCHEM) min. 98 %, hydrochloric acid (mikroCHEM) 35 %.

Method of analysis:

(All-rac)- α -tocopherol – was determined by the Hewlett-Packard gas chromatograph with autoinjection, column – HP-5 (Ultra 2), 50 m x 0.32 mm, (5%-phenyl)-methylpolysiloxane, column temperature 245 °C, temperature delay 2 minutes, temperature gradient 10 °C/min up to 300 °C, injector temperature 260 °C, FID detector, temperature of FID 300 °C, carrier gas helium, flow rate 1,4 mL/min, injection – 0.2 μL , sample concentration – 0.02 g/10 mL hexane, tocopherol was identified using external standard, duration of analysis 30 min. *Concentration of zinc dichloride in aqueous solution* was determined by argentometry and complexometry.

Preparation of (All-rac)- α -tocopherol:

Description of apparatus:

The synthesis was carried out in a rotating round-bottomed glass flask attached to the laboratory rotary evaporator Heidolph VV2000 equipped with a speed control.

The vacuum in reactor was generated by the laboratory aspirator Simax, or by the rotary vacuum pump KVAC/21, the pressure was measured by the Wika vacuumeter, the vapor temperature was measured according to the Czechoslovak norm CSN 258130 by a mercury thermometer TKS; both temperature and pressure sensor were located at the site of reflux ratio control of the evaporator. The reaction temperature was maintained by an electrically heated mineral oil bath; the measured temperature thus corresponded to the bath temperature regulated by a Vertex thermometer.

Procedure

The 1 liter round/bottomed glass flask was charged with water and zinc dichloride. After its dissolution, isophytol and trimethylhydroquinone were added. In selected experiments the reaction medium was composed solely of (all-rac)- α -tocopherol, i.e. it was used as the solvent. $ZnCl_2$ was either dissolved in water or dispersed in (all-rac)- α -tocopherol. Tocopherol is too lipophilic for $ZnCl_2$ to be soluble in it. Water was evaporated prior to the addition or during addition of isophytol.

The charged flask was then attached to the rotary evaporator and its revolutions was set approx. to 90/min at running aspirator or rotary oil pump. The flask was put into the bath, set to reach the reaction temperature, and the reaction time counting started from the moment, the pressure has been stabilized and reaction temperature reached. In experiments with (all-rac)- α -tocopherol as a reaction medium the aspirator was turned on only after the reaction temperature has been reached. After reaching the planned reaction time, aspirator and heating were turned off, the flask was separated from the evaporator and the phase separation was facilitated by addition of butyl acetate. The content of flask was thoroughly shaken and poured into a 1 liter separatory funnel. The flask was flashed with another 50 mL portion of butyl acetate and the combined acetate solutions were transferred into the separatory funnel.

Double extraction with water (2x100 mL) removed $ZnCl_2$ from the butyl acetate solution of reaction mixture. Emulsion, accidentally generated during the first extraction, was filtered through paper filter, using Buchner funnel and vacuum, which decomposed the emulsion and facilitated phase separation, so that in further extractions it is no longer needed. The reaction mixture was then extracted by 50 mL of 8 % NaOH to remove the unreacted trimethylhydroquinone and the rest of $ZnCl_2$. Traces of alkali were removed by double extraction with diluted hydrochloric acid (2x50 mL), prepared by mixing of 0.5 mL of 33 % HCl and 100 mL of water. The product – raw (all-rac)- α -tocopherol - was obtained from the

butyl acetate solution after removal of solvent under reduced pressure (6 kPa) until constant weight at temperatures up to 120 °C, using the same rotary evaporator. The product was subsequently sampled to evaluate the tocopherol content.

Results and Discussion

Data showed in the Table 1 demonstrate the dependence of the yield of (all-*rac*)- α -tocopherol formation on the temperature of oil bath at given reaction time (50 min) and under the given reaction conditions. It can be seen that the highest (all-*rac*)- α -tocopherol yield (66.9 %) was achieved at the highest temperature used (120 °C). The higher yield was caused by the higher selectivity, which follows from the negligible changes in the weight of the raw tocopherol. Since in this series of experiments zinc dichloride was dissolved in water, higher reaction temperatures cause higher water evaporation, facilitates dissolution of catalyst and enhances homogeneity of the reaction mixture. All these factors accelerate the formation of (all-*rac*)- α -tocopherol.

Table 1. Dependence of (all-*rac*)- α -tocopherol yield on the oil bath temperature, *reaction conditions:* Charge: 46.6 g (0.3 mole) of TMHQ, 5.7 g (0.04 mole) of ZnCl₂, 92 g (0.3 mole) of isophytol, 50 mL of H₂O, reaction time 50 min., pressure 6 kPa

Experiment No.	Temperature [°C]	Raw TPh [g]	TPh content ^a [%]	TPh yield [%]
1.	100	116.4	61.2	55.1
2.	115	117.6	66.7	60.7
3.	120	112	77.2	66.9

^a Content of (all-*rac*)- α -tocopherol (TPh) in the raw TPh

Data in Table 2 document the dependence of the yield of (all-*rac*)- α -tocopherol formation on the reaction time at constant temperature of the oil bath (120°C). It appears that by increasing reaction time from 35 to 75 minutes there is only approx. 10 % increase in the weight of raw tocopherol. However, the TPh content in the product and thus TPh yield reaches maximum at reaction time of 50-60 minutes. At the reaction time 75 minutes significant destruction of tocopherol was observed, leading to its lower final yield. Because of this decomposition the use of higher reaction temperatures was avoided in the subsequent experiments. Interestingly, the maximum of (all-*rac*)- α -tocopherol yield, reached in the

standard batch after about 60 minutes of reaction time, could be reached already after 25 minutes of reaction time at half batch. The reason for such acceleration may be the faster homogenization of the reaction mixture on the rotating wall of the reactor containing only 50 % of starting materials and thus its thinner layer, which facilitates diffusion of zinc dichloride (catalyst) into it and evaporation of water from the reaction mixture. This can be corroborated by the data in Table 3, showing that higher revolutions of the evaporator flask (reactor), creating a thinner layer of the reaction mixture, also led to a slight increase in the (all-*rac*)- α -tocopherol yield. Faster rotation of the reaction flask improves stirring, creates a thinner layer of reaction mixture and improves contact of TMHQ and IPH.

Table 2. Dependence of (all-*rac*)- α -tocopherol yield on the reaction time, *reaction conditions:* Charge: 46.6 g (0.3 mole) of TMHQ, 5.7 g (0.04 mole) of ZnCl₂, 92 g (0.3 mole) of isophytol, 50 mL of H₂O, reaction temperature 120 °C, pressure 6 kPa, temperature of vapors 26 -29 °C, revolutions 90/min

Experiment No.	Reaction time [min.]	Raw TPh [g]	TPh content [%]	TPh yield [%]
1.	35	109	69.5	58.6
2.	45	119	71.7	66.0
3.	50	112	77.2	66.9
4.	60	117.3	77.5	70.4
5.	75	122.4	60.7	57.5
6. ^a	25	55.3	77.6	66.4

^a Half charge used

Table 3. Effect of reaction conditions on the tocopherol yield, *reaction conditions:* Charge: 46.6 g (0.3 mole) of TMHQ, 5.7 g (0,04 mole) of ZnCl₂, 92 g (0.3 mole) of isophytol, 50 mL of H₂O, temperature of vapors 26-29 °C

Experiment No.	time [min.]	Pressure [kPa]	Temperature [°C]	Revolutions [min ⁻¹]	Raw TPh [g]	TPh content [%]	TPh yield [%]
1.	60	6	120	120	118.6	78.5	72.1
2.	60	6	120	90	117.3	77.5	70.4
3.	90	0.4	85	90	116.8	52.3	47.3
4.	60	0.4	120	90	116.0	71.0	63.7

High vacuum in the reaction flask (0.4 kPa) led to very fast evaporation of water, consequently to lower content of TPh in the reaction product as well as to lower (all-*rac*)- α -tocopherol yield (see Table 3). Higher vacuum in evaporator during reaction had an additional negative effect, namely sublimation of trimethylhydroquinone from the reaction mixture into the flask neck and even into the vacuum pump itself. The extent of sublimation was directly proportional to the quality of vacuum. In this way it contributes to lowering of the (all-*rac*)- α -tocopherol yield. This effect is intensified as higher vacuum allows higher water vapor mobility. However, the increasing amount of water from 35 to 65 mL did not lower the yield of (all-*rac*)- α -tocopherol significantly. Change in the yield of TPh, shown in the Table 4, falls within the range of reproducibility of experiments.

Table 4. Effect of water amount on the (all-*rac*)- α -tocopherol yield, *reaction conditions:* Charge: 46.6 g (0.3 mole) of TMHQ, 5.7 g (0.04 mole) of ZnCl₂, 92 g (0.3 mole) of isophytol, temperature of vapors 26-29 °C, reaction time 60 min., pressure in the apparatus 5.5 kPa, revolutions 90/min

Experiment No.	Water amount [mL]	Raw TPh [g]	TPh content [%]	TPh yield [%]
1.	0	Not observed	traces	-
2.	35	116.3	77.8	70.0
3.	50	116.6	77.1	69.6
4.	65	112.1	78.9	68.5

Data in the Tables 1 to 4 should be supplemented by the finding that blank experiment (without catalyst) failed to produce tocopherol, i.e. a suitable catalyst is a basic condition for carrying out this reaction. An insignificant amount of (all-*rac*)- α -tocopherol was formed in the experiments with ZnCl₂ catalyst, but without solvent, which is responsible for contact of reactants with the catalyst. The sole liquid component of the starting reaction mixture – isophytol – does not fulfill the role of solvent as it does not dissolve ZnCl₂. Thus, the shorter the time available for making the mixture homogeneous, the lower (all-*rac*)- α -tocopherol yields can be expected. Water in the reaction mixture does not act as a solvent, since it dissolves only ZnCl₂. However, water acts as a dispersant of catalyst, as a moisturizing agent, enhancing the contact of the catalyst, isophytol and trimethylhydroquinone. Better contact

thus allows an easier penetration of IPh and TMHQ into the ZnCl_2 coordination sphere, where the actual reaction takes place (Gömöry, 2011). The complex of ZnCl_2 , IPh and TMHQ is dissolved more easily in the reaction mixture as ZnCl_2 alone. After the IPh and TMHQ have been converted to (all-*rac*)- α -tocopherol, ZnCl_2 can release TPh and capture a new, more tightly bound molecule of IPh and TMHQ, thus allowing ZnCl_2 to act as a catalyst (Gömöry, 2011). Visually the complex formation and homogenization of reaction mixture manifests itself in color change from yellowish reactant layer on the reaction flask to a brown-reddish reaction mixture.

In another series of experiments (all-*rac*)- α -tocopherol was used as a solvent for preparation of (all-*rac*)- α -tocopherol at reduced pressure. This (all-*rac*)- α -tocopherol increased the amount of raw (all-*rac*)- α -tocopherol by 75 % in average, thus automatically led to higher TPh content in the raw product. Since the yields of TPh were related to IPh, the differences in TPh yields achieved with and without (all-*rac*)- α -tocopherol as solvent inform more directly about the effect of solvent change than the content and amount of TPh. Even when TPh was used as the solvent both, the highest TPh yields (82.9 %) and the highest TPh content in raw product were reached at a temperature of 120 °C (Table 5). Additionally, these yields were significantly higher than those, achieved by the use of water under otherwise identical conditions. Generation of water in the reaction manifested itself only by misting the evaporator cooler. It could not be isolated as condensed water and hence its amount could be used neither for assessing conversion of reaction products, nor for assessing the end of condensation reaction.

Table 5. Dependence of (all-*rac*)- α -tocopherol yield on the oil bath temperature – (all-*rac*)- α -tocopherol as solvent,
reaction conditions: Charge: 46.6 g (0.3 mole) of TMHQ, 5.7 g (0.04 mole) of ZnCl_2 , 92 g (0.3 mole) of isophytol, 86 g of tocopherol, reaction time 120 min., reactor pressure 6 kPa, temperature of vapors 24-27 °C, revolutions 90/min

Experiment No.	Temperature [°C]	Raw TPh [g]	TPh content [%]	TPh yield [%]
1. ^a	80	200.7	69.7	45.8
2.	80	201.3	69.7	46.0
3.	100	201.0	86.9	72.6
4.	120	194.4	96.7	82.9

^a Pressure in the apparatus 0.1 kPa

In contrast to experiments with water as solvent, TPh as solvent allowed to reach maximum of yield and maximum of TPh content in raw product after 120 minutes of reaction. A significant TPh decomposition was observed only after 210 minutes (Table 6). In the time window between 30 and 90 minute of reaction time the TPh content in the raw product remained roughly around 86 weight percent.

Table 6. Dependence of (all-*rac*)- α -tocopherol yield on the reaction time, *reaction conditions:* Charge: 46.6 g (0.3 mole) of TMHQ, 5.7 g (0.04 mole) of ZnCl₂, 92 g (0.3 mole) of isophytol, 86 g of tocopherol, reaction temperature 120 °C, reactor pressure 6 kPa, temperature of vapors 24-27 °C, revolutions 90/min

Experiment No.	Reaction time [min.]	Raw TPh [g]	TPh content [%]	TPh yield [%]
1.	30	203.6	86.5	73.7
2.	50	196.7	90.9	75.8
3.	60	208.5	87.0	77.8
4.	90	211.5	86.8	79.5
5.	120	194.4	96.7	82.9
6.	210	211 ^a	86.9	79.3

^a Decomposition onset

When the experiment was carried out at atmospheric pressure, there was no reaction observed during the first hour (Table 7). Thus when TPh was added to reaction mixture as a solvent, removal of water formed by the reaction is an important factor. Another important factor represents the thickness of the reaction layer. In order to achieve sufficiently thin layer, the largest possible reaction flask was used at rotation speeds high enough to prevent thickening of liquid layer by back flowing. In these experiments, pressure no longer affects the time of homogenization, as in the case of experiments with water as solvent. However, it directly affects the rate of water removal. Thus higher vacuum leads to increased yield and increased content of TPh in the raw product.

Table 7. Effect of reaction conditions on the tocopherol yield,
reaction conditions: Charge: 46.6 g (0.3 mole) of TMHQ, 5.7 g (0.04 mole) of ZnCl₂, 92 g (0.3 mole) of isophytol, 86 g of tocopherol, reaction temperature 120 °C, temperature of vapors 26-28.5 °C, reaction time 60 min., revolutions 90/min

Experiment No.	Pressure [kPa]	Raw TPh [g]	TPh content [%]	TPh yield [%]
1. ^a	atmospheric	-	-	-
2.	0.01	202.0	91	79.7
3.	6	208.5	87	77.8

^a No reaction water released, product was not isolated

When tocopherol was used as the reaction medium, trimethylhydroquinone no longer sublimed, since TPh managed to homogenize it in the reaction mixture and TMHQ remained dissolved in it.

Table 8 presents the data concerning the preparation of (all-*rac*)- α -tocopherol at the presence of different amounts of (all-*rac*)- α -tocopherol used as the solvent. The data demonstrate the fact that dilution of reaction mixture by (all-*rac*)- α -tocopherol significantly affects the reaction yield. The highest (all-*rac*)- α -tocopherol yield (89 %) was obtained at the highest (all-*rac*)- α -tocopherol amount (172.5 g) used as solvent. The yield of (all-*rac*)- α -tocopherol related to IPH was calculated only from the formed amount of TPh.

Table 8. Effect of the (all-*rac*)- α -tocopherol amount as a solvent on the (all-*rac*)- α -tocopherol yield,
reaction conditions: Charge: 46.6 g (0.3 mole) of TMHQ, 5.7 g (0.04 mole) of ZnCl₂, 92 g (0.3 mole) of isophytol, reaction time 60 min., reaction temperature 120 °C, reactor pressure 5.5 kPa, temperature of vapors 24-27 °C, revolutions 90/min

Experiment No.	TPh as solvent [g]	Raw TPh [g]	TPh content [%]	TPh yield [%]
1.	57.5	174.3	84.9	72.7
2.	86.0	208.5	87.0	77.8
3.	172.5	283.2	97.8	88.9

Conclusions

The obtained results confirm that the yield of (all-*rac*)- α -tocopherol can be increased at reduced pressure due to more efficient removal of reaction water, generated by the

condensation reaction of IPh and TMHQ. Auxiliary (all-rac)- α -tocopherol used as solvent makes a better reaction medium than water and the highest yield of 89 % was reached, which is comparable with result obtained at the presence of butyl acetate as solvent (Gömöry, 2011). Of course, using the product as a solvent increases the volume of the reaction mixture and the productivity of the used reactor can be decreased. To find proper technological conditions a chemical-economic optimization is necessary.

Acknowledgement

Financial support from the Slovak Grant Agency VEGA 1/0768/08 is gratefully acknowledged.

References

- Baldenius KU, Bussche-Hünnefeld L, Hilgemann E, Hoppe P, Stürmer R, (1996) Ullmann's Encyclopedia of Industrial Chemistry, Vol. A27, 478–488, VCH, Weinheim
- Bonrath W, Netscher T, (2005) Applied Catalysis A: General 280: 55-73
- Bonrath W, Eggersdorfer M, Netscher T., (2007a) Catalysis Today 121: 45-57
- Bonrath W, Dittel C, Giraudi L, Netscher T., Pabst T., (2007b) Catalysis Today 121: 65-70
- Coman SM, Wuttke S, Vimont A, Daturi M, Kemnitz E., (2008) Advanced Synthesis Catalysis 350: 2517–2524
- Cotton FA, Wilkinson G, Gaus PL, (1995) Basic Inorganic Chemistry, John Wiley and Sons: New York, 3rd Edition
- Gömöry J, Králik M, Kaszonyi A., (2011) Chem. Papers (in press, accepted January 2011)
- Wang H, Xu B, (2004) Applied Catalysis A: General 275: 247-255
- Hinze R, Laufer MC, Hölderich WF, Bonrath W, Netscher T, (2009) Catalysis Today 140: 105-111
- Kemnitz E, Coman SM, Rüdiger S, Wuttke S, (2009) Method for the synthesis of d,l- α -tocopherol and means therefore, EP 2050743 A1
- Schager F, Bonrath W, (2000) Applied Catalysis A: General 202: 117-120
- Wang S, Bonrath W, Pauling H, Kienzle F, (2000) Journal of Supercritical Fluids 17: 135-143
- Xing H, Wang T, Dai Y, (2009) Journal of Supercritical Fluids 49: 52–58