## SOME TECHNOLOGICAL FEATURES OF USING HETEROGENEOUS CATALYSIS IN THE SYNTHESIS OF $\alpha$ -TOCOPHEROL

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Translated from Khimiko-Farmatsevticheskii Zhurnal, Vol. 33, No. 2, pp. 40-42, February, 1999.

Original article submitted October 21, 1996.

The commercial synthesis of  $\alpha$ -tocopherol (III) is based on homogeneous catalytic cyclocondensation of trimethylhydroquinone (I) and isophytol (II) [1] according to the scheme



 $R = (CH_2)_3CHMe(CH_2)_3CHMe(CH_2)_3CHMe_2,$ Cat = BF<sub>3</sub>, AlCl<sub>3</sub>, ZnCl<sub>2</sub>, H<sup>+</sup>, etc.

However, in recent years there has been a clear tendency toward implementation of heterogeneous catalysis in  $\alpha$ -tocopherol synthesis [2]. This trend is favored by the simplicity of separating a solid catalyst from the reaction mass and the absence of washing waters containing used catalyst. The latter circumstance is apparently the main advantage of the heterogeneous catalytic process, which leads to an increase in the  $\alpha$ -tocopherol purity up to 96 – 97%.

Unfortunately, the implementation of heterogeneous catalysis in the commercial synthesis of  $\alpha$ -tocopherol is hindered by the scarce and fragmentary data available on the technological features of these processes. To summarize the published data and the results of our investigations, we may formulate the following main points that should be taken into account for practical realization of heterogeneous catalysis in  $\alpha$ -tocopherol synthesis.

1. The reactions can be catalyzed by various solid materials which bear active surface centers possessing acidity of the Lewis or Brönsted type. These materials include heteropolyacids, aluminosilicates (bentonites, gumbrin, etc.), molecular sieves, cation exchangers in the H<sup>+</sup> form, supported catalysts on inert carriers, etc. From the standpoint of availability, low cost, and technological simplicity, aluminosilicates are the preferred choice, the more so since these systems are regenerated more simply and can be repeatedly used without significant loss of activity [3].

2. The reaction temperature under heterogeneous catalysis conditions is 20 - 30 K higher as compared to the case of homogeneous catalysis, which is explained by the necessity of surmounting the diffusional barrier. A typical level for atocopherol synthesis is 140-150°C, which is quite sufficient for attaining a favorable relationship between the rates of chemisorption of the initial substances, desorption of the products, and the chemical reaction proper. Experiments showed that chemisorption proceeds by the Rideal mechanism, whereby a single reaction component (trimethylhydroquinone) is adsorbed on the active centers of the catalyst and the other component (isophytol) attacks the surface complex, rather than by the Langmuir mechanism, when both participants are adsorbed on the catalyst surface. This is largely determined by the character of the technological process: in the first stage of reaction, trimethylhydroquinone is kept in contact with the catalyst at the solvent boiling point for a rather long time (to provide for the surface complex formation) and then isophytol is gradually added to this system.

3. The heterogeneous process poses stricter and more specific requirements on solvents as compared to the case of homogeneously catalyzed  $\alpha$ -tocopherol synthesis. First, the solvent must possess a higher boiling point while being able (as in the homogeneous case) to form an azeotropic mixture with a high content of water. The second (but most important) condition is that the solvent must be inert with respect to the active surface centers of the catalyst. For example, media such as alcohols, organic acids, esters, ketones, and some other compounds, which can interact with active centers of the catalyst and inhibit (or even completely suppress) its activity, are inapplicable. Aromatic hydrocarbons (toluene, xylene, pseudocumene, etc.) cannot be used because of the probability of being alkylated by isophytol. As a result, there is a very restricted group of solvents meeting the requirements for the heterogeneous process, including high-boiling aliphatic hydrocarbons (octane, nonane, decane) and chlorine-containing organic liquids (tetrachloroethane, tetrachloroethylene, etc.).

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4. The mechanism of heterogeneous catalysis involved in the synthesis of  $\alpha$ -tocopherol is rather complicated, involving sequential stages of external and internal diffusion of the initial compounds, chemisorption followed by the chemical reaction, and, eventually, the internal and external diffusion of final products. Although the diffusion processes play a significant role, the total process rate is controlled by the chemical interaction stage involving a large number of sequential reactions. To understand the essence of the process, it is important to know the characteristics of active surface centers possessing Brönsted and Lewis acidity.

According to the present concepts [4], acid centers of aluminosilicates of both Brönsted and Lewis type form upon isomorphous substitution of trivalent and hexacoordinated aluminum atoms for tetravalent silicon atoms in the  $SiO_2$  lattice. Note that the aluminosilicates initially possess only acidity of the Lewis type represented by aluminum atoms (L-centers), and it is only the secondary interaction with water and other molecules adsorbed on the primary Lewis acid centers that leads to the formation of the Brönsted acids (B-centers):



The free *d*-orbitals of aluminum are capable of binding to nucleophilic substrates (phenols, esters, ketones, etc.). This very interaction serves as a basis for the mechanism involved in  $\alpha$ -tocopherol synthesis:



The Lewis acid centers are characterized by the chemisorption of compound I with the formation of complex Ia, followed by the interaction of this complex with compound II. The intermediate IIa converts into IIb upon detachment of a water molecule. Compound IIb exhibits a Claisen rearrangement and transforms into an intermediate IIc, which is converted by cyclization into the stable chroman nucleus of  $\alpha$ -tocopherol. The final stage involves the desorption of compound III from the active center of the catalyst (note that the Brönsted acid centers also chemisorb compound II, but this leads to a quite different mechanism resulting in isophytol dehydration and the formation of phytadienes and a large number of side products).

The mechanism outlined above is confirmed by the data of TLC and gas chromatography (GC), by the spectroscopic characteristics of compounds IIb and IIc, and by the liberation of water in the phase corresponding to the stage of formation of compound IIb. It is interesting to note that the structures of compounds IIb and IIc proved to be identical to the structures of intermediates appearing during  $\alpha$ -tocopherol synthesis catalyzed homogeneously by Lewis acids [5]. This fact is indicative of the common mechanism of both processes and is indirect evidence of the principally unified character of chemical phenomena involved in homogeneous and heterogeneous catalysis [6].

5. An important feature of heterogeneous catalysis which must be taken into account in the synthesis of  $\alpha$ -tocopherol is the necessity of using a considerable amount of the catalyst. Stable and reproducible results are usually obtained provided the catalyst / trimethylquinone ratio is not less than two. Apparently, this circumstance complicates both the process of synthesis and the subsequent separation of the catalyst from the reaction mass for regeneration. The reason is that, despite the rather large free surface of the catalyst (~250 m<sup>2</sup>/g for bentonite aluminosilicates), the catalytically active centers occupy only a small part of this area (not exceeding 1-2%). According to the data of Tanabe [4], the average value of total acidity for the natural aluminosilicates is 0.1-0.5 mmole / g. This circumstance markedly increases the role of pretreatment aimed at increasing the catalyst activity. However, the best technological solution in the future will probably be related to the use of heterogeneous catalysts immobilized on inert carriers. This technology will not require extracting the catalyst from the reactor, thus combining the advantages of both homogeneous and heterogeneous processes.

## EXPERIMENTAL PART

Initial substances and reagents. The experiments were performed with 2,3,5-trimethyl-1,4-hydroquinone (I) and isophytol (II) (of 98 and 95.1% purity, respectively) purchased from BASF (Germany) and natural and synthetic aluminosilicates (gumbrin, AShNTs-3, Tseokar, AS-37, KV-8, askana, and others) from manufacturers in Russia. 100

Analytical procedures. The GC measurements were performed on a Hewlett-Packard Model 7610A chromatograph (USA) equipped with a plasma-ionization detector (glass column, 3 mm  $\times$  1.8 m; immobile phase, 5% SE-30 on the chromatron NA-W; column temperature, 250°C; evaporator temperature, 300°C; internal standard, octadecane). The TLC procedure was carried out on Silufol UV-254 plates eluted in a petroleum ether – diethyl ether (3 : 1) system and developed by exposure to iodine vapor. The IR spectra were measured on a Perkin-Elmer Model 275 spectrophotometer (USA) using samples prepared as thin films or KBr disks. The UV spectra were recorded on a Hitachi EPS-31 spectrophotometer (Japan) using samples dissolved in ethanol or dioxane.

Synthesis of a-tocopherol. A mixture of 7.7 g (0.06 mole) trimethylhydroquinone and 15.2 g powdered catalyst (gumbrin) in 50 ml of nonane was heated with stirring to the boiling point (140-150°C) and treated at this temperature for 0.5 - 1.0 h to remove the residual water adsorbed on the catalyst surface. To this mixture was gradually added dropwise (over a time period of 1 h) 15.5 g (0.06 mole) of isophytol, while continuously distilling off water formed during the reaction. Upon the complete introduction of isophytol, the reaction mixture was boiled for 10-20 min and cooled to 80°C, after which the catalyst was rapidly filtered off and washed with nonane  $(2 \times 10 \text{ ml})$ . The filtrates were combined and evaporated in vacuum of a water-jet pump. The residue was distilled in vacuum to obtain 17.6 g (88%) of the target compound (98% purity by the GC data); m.p., 203 - 205°C (0.3 Torr).

Isolation of intermediate compounds. Compounds IIb and IIc were isolated under the conditions of low-temperature condensation of I and II (90 – 100°C) favoring accumulation of these intermediates. The ratio of reagents and the character of reaction were analogous to those used in the general condensation method, except for the nonane being replaced by heptane (boiling at a lower temperature). The course of the process was monitored by TLC. At the time moment corresponding to maximum accumulation of intermediate compounds, the reaction mass was cooled to  $70-80^{\circ}$ C and the catalyst was rapidly filtered off and washed with heated solvent. The heptane solutions were combined and passed through a layer of aluminum oxide (degree of activity, II; thickness, 4-6 cm) in a funnel with a porous filter (No. 4). The filtrate, containing neither  $\alpha$ -tocopherol ( $R_f = 0.62$ ) not trimethylhydroquinone ( $R_f = 0.15$ ), was evaporated and the residue applied onto a column ( $3.5 \times 100$  cm) filled with 200 g of silica gel (L100 / 160, Czech Republic) and eluted with hexane. Finally, the solvent was distilled off and the intermediates were analyzed. The data of elemental analyses agree with the results of analytical calculations according to the empirical formulas.

Compound IIb:  $C_{29}H_{50}O_2$ ; UV spectrum in isooctane ( $\lambda_{max}$ , nm): 225 (log  $\varepsilon$  = 2.8), 300 (1.5); IR spectrum ( $\lambda_{max}$ , cm<sup>-1</sup>): 1010, 1070, 1200 (C–O–C).

Compound IIc:  $C_{29}H_{50}O_2$ ; UV spectrum in isooctane ( $\lambda_{max}$ , nm): 240 (log  $\varepsilon = 2.5$ ), 280 (1.4); IR spectrum ( $\lambda_{max}$ , cm<sup>-1</sup>): 1120 (OH), 1250, 1320 (C–O–H).

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