## KINETICS OF OXIDATION OF TRIMETHYLHYDROQUINONE IN AROMATIC SOLVENTS

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The major syntheses of tocopherols consists in the condensation of alkyl-substituted hydroquinones with allyl alcohols, such as phytol, isophytol, or their halogen derivatives. The method of condensation of 2,3,5-trimethylhydroquinone (I) with isophytol (II) [1] is also of technical value. It leads to the formation of  $d\mathcal{I}$ -a-tocopherol according to the following scheme:



Various Lewis acids [2], strong mineral and organic acids and their mixtures [3, 4] are used as catalysts in this reaction.

The selection of the solvent is also of a great importance. The method of carrying out the condensation of I and II has been described in both nonpolar (paraffins, petroleum ether, aromatic solvents) and in polar solvents (carbon disulfide, formic acid, acetic acid, and their ester) [5, 6].

The reaction product formed III is unstable towards oxidation. Strong oxidizing agents, such as ozone, potassium permanganate, perbenzoic acid, etc., cause profound changes in the molecule of tocopherol [7]. With milder oxidation, III transforms into o- and p-quinone [toco red (IV) and toco purple (V), respectively], or with opening of the chromane ring into toco yellow (VI) [8].



The process of the oxidation of the nucleus of I itself is also very interesting. We showed that it proceeds at very appreciable rates in aromatic solvents, even at room temperature. The oxidation of I in aprotic solvents proceeds by a radical mechanism with the formation of a resonance stabilized phenoxyl radical (VII) at the first stage [9], and then of quinone (VIII).



2,3,5-Trimethyl-1,4-benzoquinone formed in the reaction is characterized by an intense band in the IR spectrum in the region of 1650 cm<sup>-</sup> (stretching vibrations of the C=O group), absorption maximum in the UV spectrum at 255 nm: PMR spectrum ( $\delta$ , ppm): 1.983 and 1.987 (m, CH<sub>3</sub>-CH=CH-CH<sub>3</sub>), 2.015 (d, j 2.5 Hz, CH<sub>3</sub>-CH=CH-), 6.532 (q, j 2.5 Hz, CH<sub>3</sub>-CH=CH-).

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Fig. 1. Kinetic curves of oxidation of VIII in aromatic solvents: benzene (1), toluene (2); o-xylene (3).

Fig. 2. Dependence of rate of oxidation of VIII on initial concentration of substrate in o-xylene solution.

We studied the principal kinetic characteristics of the oxidation of I at 20°C in various aromatic solvents using GLC as the control method. The kinetic curves of the oxidation of I are shown in Fig. 1.

Figure 1 shows that with increase in the polarity of the aprotic solvent ( $\mu$  changes from 0 to 0.62 debye) the rate of oxidation and also the degree of conversion of I into the corresponding quinone (VIII) increase.

In the study of the kinetics of the oxidation of I in the most polar of the solvents studied, o-xylene, we found that this is a reaction of the 1-st order with respect to I (Fig. 2) with a rate constant K = tan  $\alpha$  = 0.57 h<sup>-1</sup>.

Thus, the kinetic equation of the rate of oxidation of I in the range of the concentrations studied has the form

$$r = 0.57C_{\rm I}.\tag{1}$$

We also studied the temperature dependence of the rate of oxidation of I into quinone VIII in the temperature range from 0 to  $40^{\circ}$ C at a constant partial pressure of oxygen. We could thus determine the value of the observed energy of activation ( $E_{obs}$ ) which was found to be equal to 16.6 kJ/mole. The general expression of the rate of oxidation of I in o-xylene in the range of concentrations and temperatures studied has the following form

$$r = 45e^{-\frac{16\ 600}{RT}}C_{\rm I},\tag{2}$$

where R is the universal gas constant; T is absolute temperature.

It was no doubt interesting to study the influence of various factors inhibiting the oxidation of I, which is one of the side-processes and a most undesirable reaction in the synthesis of  $d\mathcal{I}-\alpha$ -tocopherol.

Figure 3 shows the kinetic curves of consumption of I as the result of the oxidation in o-xylene at 20°C. It is seen that the conversion of I (curve 1 on Fig. 3) is highest in the absence of inhibiting factors. The presence of  $2nCl_2$  in the solution (curves 2-4) decreases the rate of the radical oxidation processes due to the formation of a complex of I with a Lewis acid at the phenolic hydroxyl group, and with increase in the  $2nCl_2$  concentration, the degree of conversion of I into quinone VIII decreases.

Inert gases (curves 5, 6) have a considerable inhibiting influence on the oxidation process. This confirms our previous assumption on the oxidation of the substrate by oxygen dissolved in the solvent studied, for which the values of the Bunsen absorption coefficient  $\alpha$  vary within 0.16-0.17 [10].

Thus, the effect of oxidation of trimethylhydroquinone by atmospheric oxygen dissolved in aromatic hydrocarbons must be borne in mind in both the study of the reaction kinetics of the condensation of I with II, and the technical development of processes for the synthesis of vitamin E.  $C_{l}$  (mole/liter)  $\cdot 10^{-3}$ 



Fig. 3. Kinetic curves of oxidation of trimethylhydroquinone by dissolved oxygen. 1) In o-xylene; 2-4) in o-xylene with Lewis acid (ZnCl<sub>2</sub> concentration  $0.7 \cdot 10^{-3}$ ,  $2.1 \cdot 10^{-3}$ ,  $3.5 \cdot 10^{-3}$  mole/liter, respectively); 5) with preliminary purging with argon; 6) with preliminary bubbling of argon through the reaction mixture.

## EXPERIMENTAL

<u>Oxidation of I.</u> A 5.25 mg portion  $(0.33 \cdot 10^{-4} \text{ mole})$  of I and 5 mg  $(0.2 \cdot 10^{-4} \text{ mole})$  of C<sub>18</sub> chromatographic standard are placed in a hermetically closing reactor, and the volume of the reaction mixture is brought up to 5 ml by the aromatic solvent studied. The mixture is thermostated and thoroughly mixed by a magnetic stirrer. Probes for analysis are withdrawn at given intervals of time.

<u>Gas-Liquid Chromatography</u>. The analysis is carried out on the Hewlett-Packard 7610A apparatus (USA) fitted with a flame-ionization detector in a linear temperature-programming regime, from 140 to 200°C, at a rate of 10°C per min. The  $C_{18}$  hydrocarbon (octadecane) is used as the chromatographic standard. The 180 cm × 2 mm glass column is filled with a solid carrier Chromosorb-W-HP with a grain size of 80-100 mesh (USA), impregnated with a 3% mixed stationary phase containing 75% of SP-400 and 22% of OY-210 (USA). The flow rate of the carrier gas (nitrogen) is 30 ml/min. The volume of the probe introduced is 2 µliter.

Spectroscopy. The IR spectra were obtained on the Perkin-Elmer 141 apparatus (England) in mineral oil.

The UV spectra were run on the Hitachi ESP-3T apparatus (Japan) in methanol.

The PMR spectra were run in deuterochloroform on the Bruker WM 250 apparatus with a working frequency of 250 MHz.

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