## Phase-transfer oxidation of 2-methyl-1-naphthol into 2-methyl-1,4-naphthoquinone in the presence of vanadomolybdophosphoric heteropolyacids

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2-Methyl-1-naphthol is oxidized into 2-methyl-1,4-naphthoquinone (menadione) by air in the presence of vanadomolybdophosphoric heteropolyacids and their salts. The reaction proceeds in a biphasic system, and the yield of menadione is up to 85 %. The influence of the composition of the heteropolyacids on the rate and the selectivity of the reaction was studied, and the reaction mechanism was proposed.

**Key words:** 2-methyl-1-naphthol; 2-methyl-1,4-naphthoquinone; phase-transfer catalysis; oxidation; heteropolyacids.

Vitamins of the K group are of great importance for medicine and livestock. They regulate blood functions, normalize mineral metabolism and prevent cancer.<sup>1</sup> Menadione or vitamin  $K_3$  is the key compound in the synthesis of all vitamins of this group. For instance, vicasol is a water-soluble bisulfite derivative produced from menadione.

Until recently 2-methylnaphthalene, which is noncatalytically oxidized into menadione by a bichromate sulfuric acid,<sup>2</sup> has been the main source of the K group vitamins.

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Usually, the yield of menadione in reaction (1) is not high, 30-50 %, and an industrial process based on it does not meet environmental requirements due to the volume of waste.

The catalytic oxidation of 2-methyl-1-naphthol (1) into menadione (2) with vanadium-containing heteropolyacids (HPA) and their acid salts<sup>3</sup> described in this paper may form the basis for a novel synthesis of the K group vitamins. It is expedient to carry out oxidation in

two steps. At the first step, substrate 1 transforms into menadione 2 by the action of HPA in the absence of oxygen, and  $V^{V}$  atoms of HPA are reduced to  $V^{IV}$ .



In the absence of oxygen, further oxidation does not occur. At the second step, the reduced form of  $(H_mHPA)$  is oxidized by oxygen.

$$H_m HPA + m/4 O_2 \xrightarrow{100 \circ C} HPA + m/2 H_2O$$
 (3)

The oxidized form of HPA may be repeatedly involved in reaction (2).

### Experimental

In the present work, V—Mo—P heteropolyacids of the general formula  $H_{3+n}PMo_{12-n}V_nO_{40}$  (n = 1 to 4) obtained as described earlier<sup>4</sup> and their acid salts were used as catalysts.

In the systems studied, substrate 1 and a catalyst (HPA) were dissolved in two immiscible liquids (1, in an organic solvent and HPA in water). Reaction (2) occurs at the interface and intense stirring is required. Oxidation of 1 involved HPA and water was carried out under non-steady-state conditions, however, the structure of the HPA molecules was preserved.<sup>3</sup> After completing reaction (2), the phases were separated (product 2 remained in the organic layer). The aqueous phase was washed with an organic solvent and the organic phase was washed with water to prevent losses of menadione 2 and the catalyst. The organic solvent was distilled off and returned to reaction (2). Compound 2 was steam distilled or recrystallized. The aqueous phase that contained the solution of reduced HPA was concentrated to the initial volume and then regenerated by reaction (3).

The reaction products (except for nonvolatile resins) were analyzed with a Tsvet-500 chromatograph with temperature programming, a katharometer as the detector, and He as the carrier gas (40 mL min<sup>-1</sup>). A column (1 m×3 mm), filled with 5 % SE-30 on Inertone NW-D-4 CS (0.16–0.20 mm) was used.

To determine its concentration compound 2 was reduced to menadiol by Zn in acetic acid in the presence of iodine and the menadiol was titrated with  $I_2$  in an acetate buffer. This method permits one to reduce the analysis time, and is therefore preferable to the conventional one.<sup>5</sup>

Taking into account that the products of the condensation of 2 could not be detected by chromatography, the conclusions on the selectivity of the catalyst were drawn from quantitative experiments. After completing reaction (2), the phases were thoroughly separated, and the product was isolated from the resins by steam distillation. Menadione 2 was extracted from the distillate with chloroform, the extract was concentrated to dryness at 30-40 °C, and the pure product obtained was weighed. The remaining resin was extracted with chloroform. Then the solvent was evaporated and the resin was weighed. The yield of menadione 2 was determined as the ratio of the product obtained to the theoretical amount. Small losses of the reaction products occured due to the formation of watersoluble resins and phthalic acid, which remained in the solution of the catalyst and burned during regeneration of the catalyst according to reaction (3).

To compare the rates of reaction (2) with different HPA the half-time of substrate conversion  $(\tau_{1/2})$  was determined by chromatographic analysis of aliquots of the organic phase withdrawn after 1, 2, 3, 4, 5, 10, 15, 20, and 25 min.

#### **Results and Discussion**

Non-steady-state phase-transfer catalysis allows one to rather easily solve the problem of the separation of the catalyst from the reaction products by normal phase separation. Thus, purified menadione 2 contained at least 98 % of the principle compound without even traces of the catalyst, which makes it possible to use it in the synthesis of both vicasol and the vitamin  $K_1$ , the most valuable vitamin of the K group.

Oxidation of 1 into menadione 2 according to reaction (2) is accompanied by side processes of oxidative polymerization.



The product 3 formed can be further polymerized to give a bright-red resin, which is a mixture of diatomic phenols (3, 4), the corresponding quinones, and semiquinones.

The ratio of the rates of reactions (2) and (4a) determines the selectivity of the catalyst with respect to products 2 and 3 and depends on the composition of the HPA molecule, the procedure used, and the conditions of the process.

The optimum temperature of the reaction was found to be 25-50 °C.

Several methods may be used to decrease the yield of resins. One of them is the variation of the concentration of substrate 1 during reaction. With this aim, a solution of 1 in an organic solvent was gradually added to a solution of the catalyst as 1 was consumed in the reaction. In addition the selectivity of the catalyst increases as the molar ratio of the catalyst to the substrate (HPA : S) increases. The optimum ratio is in the range 3 < HPA : S < 4. A further increase in the ratio results in a small increase in the yield of menadione 2, while the volume of the reaction mixture increases considerably.



Fig. 1. The dependence of the oxidation potential of HPA (*E*) relative to SHE (*I*) and half-time  $(\tau_{1/2})$  of conversion of 2-methyl-1-naphthol (2) on the number of vanadium atoms (*n*) in the HPA molecule. [HPA] = 0.1 *M*, HPA : S = 4, T = 25 °C.

The stepwise process that occures when reaction (2) is carried out in the absence of  $O_2$  in a  $CO_2$  atmosphere, also favors the increase in the selectivity.

Both the activity and the selectivity of the catalyst depend on the composition of HPA. The effect of the internal coordination sphere of HPA was studied with a set of HPA with different numbers of V<sup>V</sup> atoms:  $H_4PMo_{11}VO_{40}$  (HPA-1),  $H_5PMo_{10}V_2O_{40}$  (HPA-2),  $H_6PMo_9V_3O_{40}$  (HPA-3), and  $H_7PMo_8V_4O_{40}$  (HPA-4). The effect of the composition of the external coordination sphere of HPA was studied with acid salts of HPA-3 with cations of different metals:  $Na_{1.8}H_{4.2}PMo_9V_3O_{40}$  ( $Na_{1.8}HPA$ -3),  $Co_{0.9}H_{4.2}PMo_9V_3O_{40}$  ( $Co_{0.9}HPA$ -3),  $Mg_{0.9}HPA$ -3,  $Cu_{0.9}HPA$ -3,  $Mn_{0.9}HPA$ -3,  $Zn_{0.9}HPA$ -3,  $Fe^{III}_{0.6}HPA$ -3.

The enhanced rate of reaction (2) when the number of vanadium atoms in HPA increases correlates with the increase in oxidation potentials<sup>5</sup> in the series of these acids (Fig. 1). The higher the oxidation potential (*E*) of HPA the shorter the half-time of substrate conversion and the higher the reaction rate. The value of  $\tau_{1/2}$  of HPA-1 is not presented in Fig. 1 due to the low capacity (the number of electrons which can be accepted by the HPA molecule under the specified conditions) of the HPA-1-based catalyst, *i.e.*, HPA-1 could not oxidize the amount of substrate required for determination of  $\tau_{1/2}$ (the oxidation potential of HPA-1 decreases rapidly when the reduction number  $m < 1\bar{e}$ ). Moreover, the reduced HPA-1 is not oxidized by atmospheric oxygen.<sup>3</sup>

Together with the reaction rate, the dependences of both the yield of menadione 2 and the ratio  $W_m/W_r$ (where  $W_m$  and  $W_r$  are the weights of menadione and the resin, respectively) on the composition of HPA were studied (Table 1). In the series of free acids, both the highest selectivity and the greatest yield of menadione 2

Table 1. The dependence of the yield of menadione 2 and the ratio  $W_m/W_r$  on the composition of HPA

HPA	The yield of menadione (%)	$W_{\rm m}/W_{\rm r}$
HPA-1	81.4	6.9
HPA-2	88.9	7.9
HPA-3	85.2	6.1
HPA-4	82.3	4.7
Fe <sup>III</sup> 0.6HPA-3	75.0	5.1
Mg <sub>0.9</sub> HPA-3	70.7	3.8

were observed for HPA-2. This attests that the changes in the reaction rate and the selectivity in the series HPA-2, HPA-3, HPA-4 are opposite. Thus, HPA with moderate oxidation potentials are the best catalysts. In their presence the rate of side reaction (4a) is the lowest.

The reaction rate and the selectivity of the catalyst also depend on the nature of the outer cations of acid salts of HPA. This effect was studied with salts of HPA-3 with singly, doubly, and triply-charged cations; the degree of  $H^+$  ion substitution in acids was the same (1.8) in every case, which provided close pH values (*ca.* 1.2) for the solutions of the respective salts of HPA-3.

At identical concentrations of HPA, the rates of the reaction with free HPA are somewhat higher than with acid salts since the oxidation potential of HPA increases as the acidity of the solution increases.<sup>6</sup> Generally, the rate of reaction (2) did not depend much on the nature of the cation, except for  $Fe^{III}_{0.6}HPA-3$  ( $Fe^{III}_{0.6}H_{4.2}PMo_9V_3O_{40}$ ), which manifested a more intense reaction. Probably this is associated with the oxidation properties of the  $Fe^{3+}$  cation itself, which can be reduced to  $Fe^{2+}$ . The oxidation properties of  $Fe^{3+}$  in the external coordination sphere of HPA increase the capacity of the catalyst and make it possible to decrease its amount.

The selectivity of catalysts based on salts of HPA-3 is lower than that of the original heteropolyacid (see Table 1). The  $\text{Fe}^{\text{III}}_{0.6}$ HPA-3 salt differs from the other HPA-3 salts not only in the higher rate of reaction (2), but also in the higher selectivity. According to the results obtained, the efficiency of the catalyst depends not only on the oxidation potential of the HPA, but also on the specific effect of the outer cation on the transfer of an electron from the oxidized substrate to the HPA.

The mechanism of reaction (2) in this system has not been investigated in detail, however, the fact that both the dimers and the resins are readily formed points to a free radical process. The majority of the HPA participate in the process as one-electron oxidants, resulting in the intermediate formation of radical cations in the oxidized substrates.<sup>3,7</sup> For example, the formation of the radical cation of durol during its oxidation by heteropolyacid  $H_6Co^{III}W_{12}O_{40}$  was determined by ESR.<sup>7</sup> One can assume that oxidation of 1 by a heteropolyacid involves a series of consecutive one-electron processes accompanied by the elemination of a proton. An active complex of the HPA with molecule 1, which is oriented by its polar hydroxyl group towards the aqueous phase, is formed at the interface. The transfer of an electron to the HPA results in the formation of a radical cation, which probably undergoes further transformation according to Scheme 1.

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At high concentrations, species 5 can undergo dimerization to give 3 (reaction (4a)). However, when the concentration of HPA considerably exceeds that of 5, further oxidation occurs (Scheme 2).

The formation of menadione 2 requires the transfer of four electrons from the substrate to the HPA molecule and the transfer of the protons formed to the aqueous phase.

Thus, vanadium-containing HPA and their salts are effective phase-transfer catalysts in the oxidation of 2-methyl-1-naphthol into 2-methyl-1,4-naphthoquinone. In this process HPA acts as a reversible oxidant, oxidizing the substrate with the help of the water oxygen. The reduced forms of HPA are oxidized by molecular oxygen to regenerate the original HPA. The use of a biphasic system with the catalyst in the aqueous phase and both the substrate and the reaction products in the organic phase facilitates the separation of the catalyst from the reaction products.

The selectivity and the rate of the oxidation reaction (1) depend both on the number of vanadium atoms in the internal coordination sphere of the HPA molecule and on the nature of the outer cations (when acid salts of HPA are used). The specific effect of the outer cations is probably related to the formation of complexes with the substrate. The higher the oxidation rate the lower the selectivity of the catalyst.



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Scheme 2