

Catalytic oxidation of 2,6-dialkylphenols to the corresponding 2,6-dialkyl-1,4-benzoquinones by molecular oxygen in the presence of P–Mo–V heteropoly acids

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Abstract

A new method for obtaining 2,6-dialkyl-1,4-benzoquinones by oxidation of 2,6-dimethyl and 2,6-ditertbutylphenols by molecular oxygen in a two-phase “water–organic” system and in the presence of P–Mo–V heteropoly acids has been proposed. © 2000 Elsevier Science B.V. All rights reserved.

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1. Introduction

2,6-Dimethyl-1,4-benzoquinone (DMQ) and some substituted alkyl-1,4-quinones are semi-products for synthesis of a number of medicines and physiologically active substances [1,2]. Certain alkyl-1,4-quinones are also important as dienophiles in the Diels–Alder reaction [3,4]. In work [5], such reaction was used to design a new synthesis of the taxane analogue possessing a high antitumor activity. 2,6-Ditertbutyl-1,4-benzoquinone (DTQ) is a semi-product for synthesis of pharmaceutical materials and perfumery [6], and 2,6-ditertbutyl-1,4-hydro-

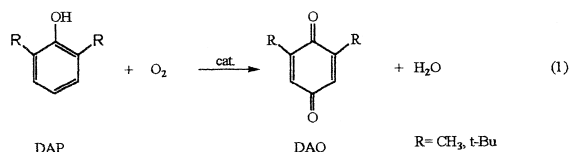
quinone prepared from DTQ is a highly active antioxidant possessing antiageing properties [7].

So, 2,6-dimethylquinone and 2,6-ditertbutylquinone are the key semiproducts for various fine organic synthesis. Unfortunately, these reagents are very expensive. For this reason, an active search for simple and moderately priced synthesis of DMQ and DTQ is in progress.

At present, there is a number of methods to produce dialkylquinone (DAQ) from various substrates. Thus, 2,6-dimethyl-1,4-hydroquinone [8], 3,3',5,5'-tetramethyl-4,4'-diphenylquinone [9], 2,4,6-trimethylphenol [10], and other substances are used as starting reagents for synthesis of DMQ. However, the corresponding dialkylphenols (DAPs) are cheaper and available for DAQ synthesis. The DAQ synthesis via DAP oxidation by molecular oxygen is preferred because the method is environmen-

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tally friendly and the feedstock is less expensive.



Some syntheses of DMQ via oxidation of 2,6-dimethylphenol (DMP) are described in literature. The best catalysts are cobalt complexes [11–14] and soluble complexes of copper and alkyl nitrile [15–17]. Thus, di-(salicylal)-3,3'-diimino-di-*n*-propylamine derivatives of cobalt [11], cobalt amine complexes [12], cobalt(II) phthalocyanine [13], and cobalt-containing zeolites of various composition, were used as catalysts [14]. For Co-containing catalysts, the selectivity towards the desired product is 80%–90%. Unfortunately, the duration of synthesis is 8–10 h because of the low rate of reaction (1). In the presence of the catalysts above, the process goes under mild conditions. However, these catalysts are not stable because of the presence of easily oxidizable ligands.

Cu-containing catalysts are also effective for synthesis of DMQ via the DMP oxidation. Thus, water soluble copper salts CuCl₂, CuCl, CuOAc, and CuNO₃ in combination with benzonitrile or acetonitrile were used in Ref. [15]. The yield of DMQ was 86% at a conversion of 86%. In works [16,17], the salts of one- or two-valence copper (chlorides, bromides, and sulfates) were used as catalysts in reaction (1). The yield of DMQ was 90%. The methods above are subject to some drawbacks. The main drawbacks are that some catalysts cannot be fully recovered and DMP is not completely converted.

There are some effective methods for production of DTQ. Thus, the DTQ yield is 95% in oxidation of 2,6-ditertbutylphenol (DTP) by H₂O₂ in the presence of Zr-containing mesoporous silica gels in the liquid phase [18]. The

yield is > 95% in the DTP oxidation in the presence of V-containing mesoporous molecular sieves at room temperature [19]. In Ref. [20], DTP was oxidized by bromine at room temperature. The yield of DTQ was 96% in a methanol solution. Unfortunately, this noncatalytic method is environmentally unfavorable.

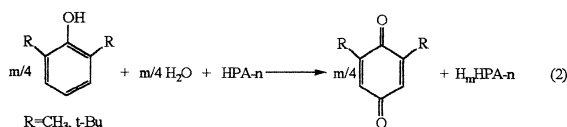
Because these methods are not profitable and environmentally not safe, the catalysts above can be used for laboratory synthesis only.

The aim of the present work is to find out a catalytic system suitable for commercial oxidation of DAP into DAQ. In choosing a suitable catalyst for reaction (1), we were guided by such properties as high activity and selectivity, good technological parameters, and environment safety.

Mo–V–phosphoric heteropoly acids of the Keggin structure, H_{3+n}PMo_{12–n}V_nO₄₀ (HPA-*n*, *n* = 1–6), are effective catalysts for oxidation of the substituted phenols of benzene and naphthalene families to the corresponding 1,4-quinones by molecular oxygen [21,22] in two-phase “water–organic solvent (OS)” systems of a rather high selectivity (75%–90%). The advantage of two-phase systems in catalytic organic synthesis is recognized at present [23]. In contrast to one-phase systems [18], two-phase catalytic systems, where HPA-*n* catalyst is in the water phase, and a substrate and the product are in the organic phase, have the following advantages: separation of the reaction products from the catalyst is simple, and the catalyst selectivity increases because of decreasing instantaneous concentration of the substrate interacting with HPA-*n*.

In our work, HPA-*n* catalyzes oxidations of DMP and DTP to the corresponding 1,4-benzoquinones. Oxidations of DMP to DMQ and DTP to DTQ in the presence of these catalysts proceed via reaction (1) under moderate conditions. Dioxygen presented in reaction (2) results in a wide amplification of side reactions. That is why the overall reaction (1) consists of two steps — (2) and (3) — which are performed separately. Step 2 is performed in a two-phase

system in inert atmosphere, and the reduced H_m HPA- n is oxidized by dioxygen (stage 3) when the reaction products are separated from the catalyst. More precisely, HPA- n acts as a reversible oxidizer during the nonstationary two-stage oxidation of DAP into DAQ by O_2 .



The selectivity towards the desired quinones is 77%–85%, and the rate of their production is rather high.

2. Experimental

Heteropoly acids $H_{3+n}PMo_{12-n}V_nO_{40}$ (HPA- n , $n = 1$ –6) and their acidic salts used as catalysts were prepared from H_3PO_4 , MoO_3 , and V_2O_5 by the procedure described elsewhere [24].

Reaction (2) was performed in a 100-ml reactor in CO_2 atmosphere using two-phase OS system. DMP or DTP and the reaction products (DMQ or DTQ) were dissolved in the organic phase (10 ml), and the catalyst (HPA- n) was dissolved in water (50 ml). The reaction was performed under intensive mixing of phases by a magnetic stirrer at 313–353 K. After reaction closed, the phases were separated, and the traces of quinone were extracted by chloroform from the water phase. The catalyst was regenerated in flowing oxygen at 100°C for 35–40 min via reaction (3). During the catalyst regeneration, a small amount of HNO_3 (69%), 0.15–0.2 ml, was added repeatedly (after four to five cycles) to the boiling solution of HPA- n to provide complete combustion of high molecular organic compounds (resins). The regenerated catalysts were used for 25–30 cycles and preserved their activity and selectivity. The completeness of the

catalyst regeneration was controlled by measuring of the oxidative potential of the HPA- n solution.

The products of reaction (2) were identified in a mixed organic solution (OS + $CHCl_3$) by the gas–liquid chromatography using a Tsvet-500 chromatograph with a flame-ionization detector and temperature programming from 100 to 250°C, duroquinone being the internal standard. A capillary column 40 m in length with an SE-30 phase was used.

The chromatographic analysis was done using a multi-channel chromatographic processor, a “MultiChrom” providing high accuracy ($\pm 1.8\%$) [25].

The selectivity of reaction (2) was calculated from a ratio between the estimated quantity of quinone and the theoretically expected one.

In all runs, the phenol conversion was 100%. The reaction duration was determined experimentally by sampling. If the substrate solution was added dropwise to the HPA- n solution, the reaction proceeded for 1 h.

3. Results and discussion

It was studied how the OS nature, composition of the HPA- n molecule, reaction temperature, AcOH concentration, and molar ratio between HPA- n and substrate affect the selectivity of reaction (2). As found, the selectivity of oxidation of DAP to DAQ depends on the nature of the OS used as a component in the two-phase catalytic system. Tables 1 and 2 show the effect of the OS on the selectivity towards DMQ and DTQ, respectively. Solvents of different nature were used in the runs. Diphenylquinones and resins of various compositions are the side products of the DAP oxidation.

In the DMP oxidation, the highest selectivity of 85% is achieved if trichloroethylene is used as an OS (Table 1). For the DTP oxidation proceeding in the presence of toluene, the selectivity is 75% (Table 2). Going from nonpolar or

Table 1

Effect of the nature of organic solvent on the catalyst selectivity in oxidation of DMP to DMQ

Conditions: $T = 333$ K; CO_2 atmosphere; $[\text{Co}_{0.5}\text{H}_6\text{PMo}_8\text{V}_4\text{O}_{40-4}] = 0.3$ M; $[\text{AcOH}] = 15$ vol.%; $[\text{Co}_{0.5}\text{HPA-4}]/[\text{DMP}] = 7.5$; Reaction time, 1 h.

Cycle ^a	Organic solvent	Selectivity (%)
1	Trichloroethylene	85.3
2	Chloroform	55.6
3	1-Octanol	57.7
4	<i>n</i> -Amyl acetate	62.5
5	2-Octanone	59.8
6	Capryl acid	72.0
7	<i>m</i> -Xylene	46.6
8	Toluene	49.3
9	Benzyl alcohol	41.9
10	3-Phenylpropanol	48.7
11	Undecanoic acid	37.6

^aAll experiments were performed on the same catalyst sample regenerated via reaction (3) in each cycle.

weakly polar solvents to polar solvents as alcohols, the selectivity decreases especially in the DTP oxidation. The solvent nature affects both the catalyst selectivity and activity (see, for example, time of reaction in Table 2). By choosing the optimal OS, one can control both activity and selectivity of the “HPA-*n* + OS” system. Such relation between selectivity and

Table 2

Effect of the nature of organic solvent on the activity and selectivity of the catalyst serving oxidation of DTP to DTQ

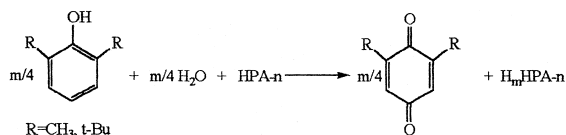
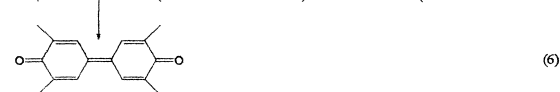
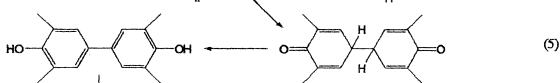
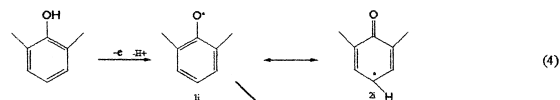
Conditions: $T = 353$ K; CO_2 atmosphere; $[\text{H}_9\text{PMo}_6\text{V}_6\text{O}_{40}] = 0.3$ M; $[\text{AcOH}] = 30$ vol.%; $[\text{HPA-6}]/[\text{DTP}] = 7.5$.

Cycle ^a	Organic solvent	Time of reaction (h)	Selectivity (%)
1	Carbon tetrachloride	> 5	69.0
2	Trichloroethylene	> 4	71.4
3	Toluene	3.5	77.0
4	Mesitylene	4	70.2
5	<i>m</i> -Xylene	3	71.9
6	<i>p</i> -Xylene	2.5	72.2
7	1-Octanol	< 1	20.8
8	Benzyl alcohol	< 1	22.7
9	Capryl acid	< 1	69.9

^aAll experiments were performed on the same catalyst sample regenerated via reaction (3) in each cycle.

activity indicates that molecules of particular solvents can selectively solvate “redundant” reaction centers of the substrate molecule. This action inhibits some side processes involving free radicals formed at the intermediate stages of reaction (2).

Oxidation of DMP and DTP and the other phenols proceeds via the radical mechanism [26]. At the first step, phenoxy radical **1i**, exhibiting high reactivity, forms. That is why the oxidation of DAP is accompanied by side reactions as dimerization (5), (6) and further polymerization.



To increase the yield of the desired product in reaction (2), it is necessary to find out parameters ensuring the higher rate of the main reaction and lower rates of side reactions. Optimization of the composition of the two-phase

catalytic system and conditions of reaction (2) helps to solve this problem.

In the presence of molecular oxygen, the catalyst selectivity decreases by 30%–40%, because dioxygen interacts with intermediates 1i and 2i formed via reaction (4), and, thus, initiates some side radical processes. That was the reason why reaction (1) was performed nonstationary via steps (2) and (3), which permitted us to avoid participation between dioxygen and HPA-*n* molecules in oxidation of phenols.

Using DMP oxidation as an example, it was shown how the number (*n*) of vanadium atoms in an HPA-*n* molecule ($1 \leq n \leq 6$) affected the selectivity. As *n* increases (Fig. 1), the selectivity towards HPA-*n* rises essentially. For reaction (2), the highest activity was exhibited by HPA-*n* where *n* = 6.¹ Moreover, HPA-*n* with high *n* are more active, because the time of complete DAP conversion reduces in their presence. This may be attributed to the increase in vanadium concentration in the HPA-*n* solution, accompanied by the increase in the oxidation potential of an HPA-*n* molecule [27]. According to the stoichiometry of reaction (2), a substrate molecule loses four electrons in the oxidation of DAPs to DAQs. However, the oxidation potential of H_{*m*}HPA-*n* molecules decreases fast with increasing *m* (the number of electrons accepted by an HPA-*n* molecule). Therefore, the initial HPA-*n* molecule must possess such high oxidation potential that DMP and DTP will be oxidized via reaction (2) and donate not less than four electrons. If the oxidation potential of HPA-*n* is not sufficient, and a molar ratio [HPA-*n*]/[DAP] is low, DAP does not completely convert into quinone, and resin production will prevail.

Because DMP is more active, it completely converts via reaction (2) quicker than DTP. Thus, DMP and DTP completely convert for

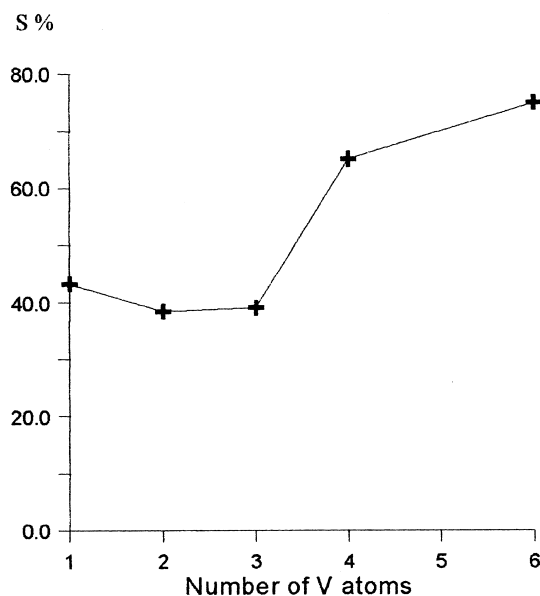


Fig. 1. Catalyst selectivity vs. the number of HPA-*n*. Conditions: [HPA-*n*] = 0.3 M; *T* = 333 K; CO₂ atmosphere; [AcOH] = 20 vol.%; OS trichloroethylene; [HPA-*n*]/[DMP] = 7.5.

10–15 min, and 2 h, respectively, when HPA-6 and CHCl₃ (as OS) are used, [HPA-6]/[DAP] = 7.5 and *T* = 80°C under otherwise equal conditions. A lower activity of DTP is determined by steric disturbances around the hydroxyl surrounded by tertbutyl groups at positions 2 and 6.

Introduction of cations into HPA-*n* molecule decreases its acidity and accelerates oxidation of the reduced HPA-*n* state via reaction (3). For this reason, we studied acidic salts of HPA-*n*, too. If cation M^{z+} substitutes for one proton in an HPA-*n* molecule, the selectivity decreases as was in the interaction between DMP and acidic salts of H₇PMo₈V₄O₄₀. According to Table 3, the selectivity of HPA-4 salts containing Co²⁺, Mg²⁺, Al³⁺, Mn²⁺, Na⁺ cations is significantly lower than that of HPA-4 itself. Only Mg_{0.5}H₆PMo₈V₄O₄₀ and Co_{0.5}H₆PMo₈V₄O₄₀ provide the selectivity comparable to that of HPA-4 (73%–76%). On addition of cations to HPA-*n*, the selectivity of DAP oxidation decreases because of the decreasing oxidative potential of HPA-*n* [27].

¹ Some amount of sediment was found when the HPA-6 sample was used. This may indicate that HPA-6 is not stable enough in hydrolysis.

Table 3

Effect of the nature of the external cation M^{z+} introduced in HPA-4 on the catalyst selectivity in oxidation of DMP to DMQ. Conditions: $[HPA-n] = 0.3$ M; CO_2 atmosphere; $[AcOH] = 15$ vol.%; OS, trichloroethylene; $T = 333$ K; Reaction time, 1 h; $[HPA-n]/[DMP] = 7.5$.

HPA- <i>n</i>	Selectivity (%)
$H_7PMo_8V_4O_{40}$	76.2
$Mg_{0.5}H_6PMo_8V_4O_{40}$	76.1
$Co_{0.5}H_6PMo_8V_4O_{40}$	73.0
$Al_{0.3}H_6PMo_8V_4O_{40}$	57.3
$NaH_6PMo_8V_4O_{40}$	60.8
$Mn_{0.5}H_6PMo_8V_4O_{40}$	58.5

The catalyst selectivity rises fast as the instantaneous concentration of phenol decreases in reaction (2), which corresponds to the increase in the $[HPA-n]/[DMP]$ molar ratio. In the DMP oxidation (Fig. 2), the selectivity increases

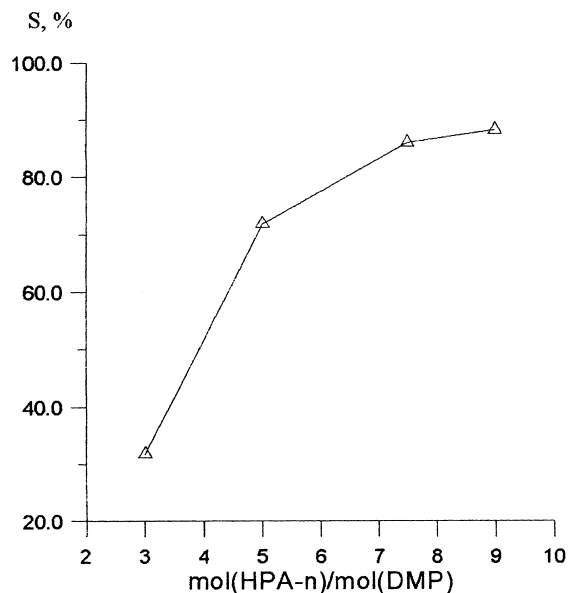


Fig. 2. Catalyst selectivity vs. the $[HPA-n]/[DMP]$ molar ratio. Conditions: $[Co_{0.5}H_6PMo_8V_4O_{40}] = 0.3$ M; $T = 333$ K; CO_2 atmosphere; $[AcOH] = 15$ vol.%; OS trichloroethylene; $[Co_{0.5}HPA-4]/[DMP] = 7.5$. Experiments were performed on the same catalyst sample.

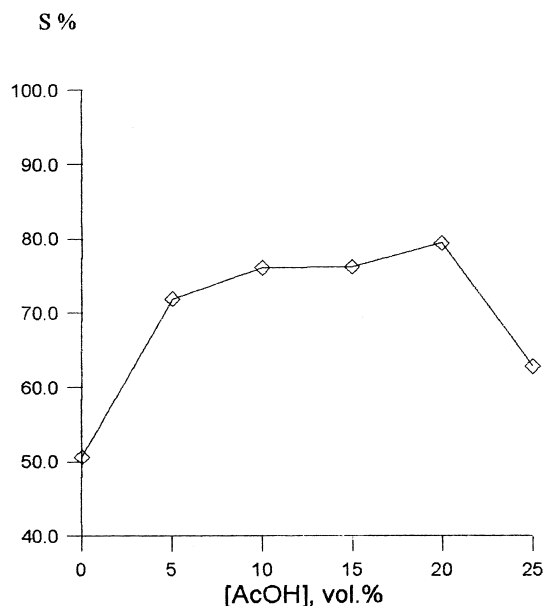


Fig. 3. Catalyst selectivity vs. the AcOH concentration in reaction (2). Conditions: $[H_7PMo_8V_4O_{40}] = 0.3$ M; $T = 333$ K; CO_2 atmosphere; $[HPA-4]/[DMP] = 7.5$; OS trichloroethylene. Experiments were performed on the same catalyst sample.

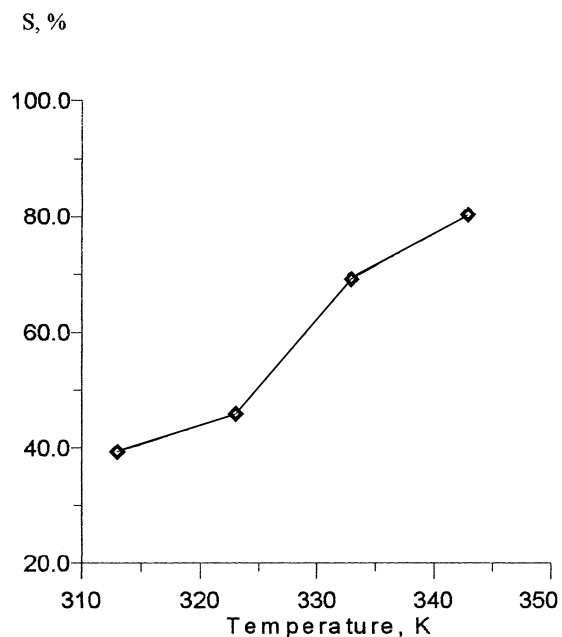


Fig. 4. Catalyst selectivity vs. the temperature of reaction (2). Conditions: $[H_7PMo_8V_4O_{40}] = 0.3$ M; $T = 333$ K; CO_2 atmosphere; $[AcOH] = 20$ vol.%; OS trichloroethylene; $[HPA-4]/[DMP] = 7.5$. Experiments were performed on the same catalyst sample.

from 32% to 88% when the [HPA-*n*]/[DMP] molar ratio increases from 3 to 9.

The optimal molar ratio [HPA-*n*]/[DAP] ranges from 5 to 7, and the selectivities towards DMQ and DTQ are 75%–85% and 70%–77%, respectively.

Using the dependence between selectivity and the [HPA-*n*]/[DAP] ratio, the procedure for gradual introduction of DAP into reaction (2) (through a dropping funnel) was chosen. This procedure permits a 15%–20% increase in the selectivity compared to the single introduction of substrate.

The rate and selectivity in reaction (2) are strongly dependent on the concentration of AcOH. The optimal concentration of AcOH in the catalyst is different for oxidations of DMP and DTP. For DMP, the optimal concentration of AcOH is about 10–20 vol.% (Fig. 3). As [AcOH] increases from 0 to 10 vol.%, the selectivity increases from 50 to 70 vol.%. At [AcOH] ranging from 10 to 20 vol.%, the selectivity is maximal, and then it decreases.

For DTP, concentration of AcOH (10–40 vol.%) slightly affects the selectivity, but the rate of reaction (2) increases significantly. Thus, at [AcOH] = 15 vol.%, the DTP conversion attains only 60% for 4.5 h, and at [AcOH] = 40 vol.%, DTP completely converts in less than 1 h. The nature of the strong solvating effect of AcOH will be studied later.

Fig. 4 presents the curve of the catalyst selectivity vs. temperature in DMP oxidation by HPA-4 via reaction (2). The highest selectivity is observed at 343 K. At 313–343 K, selectivity increases gradually from 40% to 80%. Because the reactivity of DTP is lower than that of DMP, reaction (2) was carried out at elevated temperatures (353 K).

In summary, DMP and DTPs were oxidized to the corresponding quinones in the presence of catalytic systems (HPA-*n* + OS) providing the selectivity ranging from 77% to 85%. In the presence of P–Mo–V heteropoly acids, the oxidation of DAP to DAQ is environmentally friendly, and catalysts of the specified compo-

sition exhibit high stability: the activity and selectivity hold constant at least during 25–30 cycles. It is very promising to increase the selectivity and activity of the (HPA-*n* + OS) catalytic systems by varying the solvent nature and HPA-*n* composition.

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