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Highly Selective Oxidation of Alkylphenols to *p*-Benzoquinones with Aqueous Hydrogen Peroxide Catalyzed by Divanadium-Substituted Polyoxotungstates

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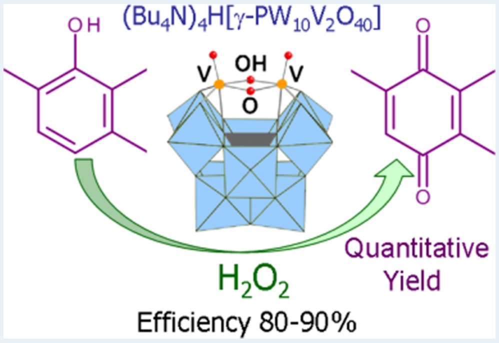
Supporting Information



ABSTRACT: The catalytic performance of divanadium- and dititanium-substituted γ-Keggin polyoxotungstates, $TBA_4H[\gamma\text{-}PW_{10}V_2O_{40}]$ (**I**, TBA = tetra-*n*-butylammonium), $TBA_4H_2[\gamma\text{-}SiW_{10}V_2O_{40}]$ (**II**), and $TBA_8[\{\gamma\text{-}SiW_{10}Ti_2O_{36}(OH)_2\}_2(\mu\text{-}O)_2]$ (**III**) has been assessed in the selective oxidation of industrially important alkylphenols/naphthols with the green oxidant 35% aqueous H_2O_2. Phosphotungstate **I** revealed a superior catalytic performance in terms of activity and selectivity and produced alkylsubstituted *p*-benzo- and naphthoquinones with good to excellent yields. By applying the optimized reaction conditions, 2,3,5-trimethyl-*p*-benzoquinone (TMBQ, vitamin E key intermediate) was obtained in a nearly quantitative yield via oxidation of 2,3,6-trimethylphenol (TMP). The efficiency of H_2O_2 utilization reached 90%. The catalyst retained its structure under turnover conditions and could be recycled and reused. An active peroxo vanadium complex responsible for the oxidation of TMP to TMBQ has been identified using ^{51}V and ^{31}P NMR spectroscopy.

KEYWORDS: *alkylphenols, selective oxidation, hydrogen peroxide, polyoxometalates, benzoquinones*

1. INTRODUCTION

Oxidative transformations of phenolic compounds play a central role in organic synthesis and many biological systems.[1−4] The selective oxidation of substituted phenols offers efficient access to functionalized quinones that serve as building blocks for a wide variety of biologically active compounds.[5−7] Specifically, 2,3,5-trimethyl-1,4-benzoquinone (TMBQ, vitamin E key intermediate) is produced through oxidation of 2,3,5- or 2,3,6-trimethylphenol (TMP),[8−10] whereas 2-methyl-1,4-naphthoquinone (MNQ, menadione, vitamin K_3) can be obtained from 2-methyl-1-naphthalene[11−13] or, alternatively, 2-methyl-1-naphthol (MNL).[14−16] Until recently, stoichiometric oxidations with CrO_3, MnO_2, HNO_3, and other hazardous reagents were the main route for the industrial production of valuable oxygenated compounds, including quinones.[11−13] Clearly, such processes do not meet today's environmental requirements. Therefore, the development of green and sustainable chemical technologies that eliminate the use of hazardous reactants and reduce generation of waste has become a widely accepted strategy.[17,18]

Co(II)-Schiff base complexes have long been known as highly selective catalysts for oxidation of substituted phenols to quinones,[19,20] but they suffer oxidative destruction of the organic ligand, leading to low productivity. Nowadays, TMBQ is produced industrially via oxidation of TMP with molecular oxygen in the presence of copper halides.[8] Large (quasi-stoichiometric) amounts of $CuCl_2$ are required to achieve high (>95%) yields of the target quinone. The main drawbacks of the existing process are the formation of Cl-containing byproducts and the necessity to use special apparatus, resistant to corrosion. TMBQ and other quinones can be obtained using Keggin molybdovanadophosphoric heteropoly acids $H_{3+n}PMo_{12-n}V_nO_{40}$ (HPA-*n*, n = 2−6) as catalysts.[14,21−24] Their advantages are metal oxide-like structure and, therefore, thermodynamic stability to oxidation, solubility in various solvents, and noncorrosiveness, but again, quasi stoichiometric amounts of the catalyst, HPA-*n*, are needed to enable high yields in the desired product. Recently, two groups reported oxidation of substituted phenols with dioxygen over supported gold catalysts.[25,26] In these systems, dimeric C−C coupling products predominated among the oxidation products.

In addition to molecular oxygen, hydrogen peroxide (H_2O_2), is the most green, atom efficient, and relatively inexpensive oxidant that gives water as the sole byproduct.[27−29] A large scientific effort has been directed to the creation of catalyst systems that would activate H_2O_2 to accomplish selective oxygen atom transfer to organic substrates. The microporous titanium silicalite-1 (TS-1) developed by Eni effectively

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catalyzes hydroxylation of phenol to produce hydroquinone and cathechol,[30,31] but it is a poor catalyst for oxidation of bulky phenols because of the pore size limitation. On the contrary, oxidation of substituted phenols and naphthols readily occurs with H_2O_2 over mesoporous titanium silicates;[32−38] however, catalyst stability and oxidant efficiency still remain a problem.[39,40]

Several efficient homogeneous catalytic systems have been reported for the selective oxidation of phenols/naphthols with H_2O_2.[41−47] Shimizu et al. developed a method for TMBQ production in 70−85% yields based on the oxidation of TMP with H_2O_2 (60%) in acetic acid catalyzed by Keggin heteropolyacids $H_nXM_{12}O_{40}$ (M = W, Mo, X = P or Si, n = 3 or 4).[41] Methyltrioxorhenium (VII) catalyzed oxidation of alkylphenols using 83 or 35% aqueous H_2O_2 in acetic acid or dimethyl carbonate, respectively, to afford the corresponding *p*-benzoquinones in moderate to good yields.[42,43] Ruthenium and iron compounds were successfully employed as catalysts for oxidation of substituted phenols with H_2O_2.[44−47] Ito et al. reported 89 and 71% yields in TMBQ for TMP oxidation in acetic acid as solvent in the presence of $RuCl_3$ and $FeCl_3$, respectively.[44] Ruthenium(2,2′,6′:2″-terpyridine)(2,6-pyridinedicarboxylate)-catalyzed oxidation of alkylated phenols and naphthols led to benzo- and naphthoquinones with 78−83% yields using 4.4 equiv of H_2O_2 in MeOH solvent.[46] A three-component system consisting of $FeCl_3{\cdot}6H_2O$, pyridine-2,6-dicarboxylic acid (H_2Pydic), and different benzylamines ($FeCl_3/H_2$Pydic/amine = 1/1/2.2) was applied for the oxidation of methylated phenols and naphthols.[47] TMBQ and MNQ were obtained in 79 and 55% yields, respectively, using 7.5 mol % of catalyst and 4 equiv of H_2O_2. The drawbacks of all these methods are insufficiently high yields (selectivity) of the target quinones and rather low efficiency of the hydrogen peroxide utilization; that is, large excesses of the oxidant have to be used. Yet, conventional transition-metal complexes are disposed to destruction owing to thermodynamically favorable oxidation of organic ligands. Therefore, the development of green catalytic routes for the production of TMBQ, MNQ, and other important quinones remains a challenging goal of the fine chemicals industry.

Early transition-metal oxygen anion nanosize clusters or polyoxometalates (POMs) have attracted significant attention as oxidation catalysts because (i) they have completely inorganic, metal oxide-like structure and are not prone to oxidative and thermal degradation in comparison with organometallic complexes (generally POMs are stable to at least 350−450 °C in the presence of molecular oxygen); (ii) their redox and acid−base properties as well as solubility can be controlled by changing the chemical composition or structure; (iii) most POMs possess good hydrolytic stability over a wide pH range;[48−52] and finally, (iv) POMs can be converted to solid materials using different immobilization/heterogenization techniques.[50−52] Solvolytic degradation of some POMs can be caused by high excesses of hydrogen peroxide, but susceptibility to this process is decreased with increasing negative charge of the polyanion.[51]

Recently, Mizuno and co-workers demonstrated that divanadium-substituted γ-Keggin polyoxotungstates $TBA_4H[\gamma\text{-}PW_{10}V_2O_{40}]$ (**I**, TBA = tetra-*n*-butylammonium) and $TBA_4H_2[\gamma\text{-}SiW_{10}V_2O_{40}]$ (**II**) are efficient catalysts for a range of liquid-phase oxidations with aqueous H_2O_2.[53−59] Although **II** selectively catalyzes alkene epoxidation,[53] **I** also enables oxidation of electron-deficient alkenes[57] and organic sulfides;[58] oxidative bromination of alkenes, alkynes, and aromatics;[59] and hydroxylation of alkanes[54,55] and alkylbenzenes.[56] The latter reactions become possible only in the presence of 1 equiv (with respect to **I**) of a mineral acid. A dititanium-substituted tetramer, $TBA_8[\{\gamma\text{-}SiW_{10}Ti_2O_{36}(OH)_2\}_2(\mu\text{-}O)_2]$ (**III**), was reported to be an effective catalyst for alkene epoxidation and thioether sulfoxidation using H_2O_2.[60] In this POM, each half of the γ-Keggin fragment contains a dinuclear titanium center bridged by two hydroxo groups, and the resulting $Ti_2(\mu\text{-}OH)_2$ core connects to the other one of the paired γ-Keggin subunit through Ti−O−Ti linkages.[60]

Recently, titanium di(oligo)nuclear species have been identified as the active centers responsible for the highly selective oxidation of alkylphenols to *p*-benzoquinones.[37] This inspired us to explore catalytic properties of compounds **I**−**III** in the oxidation of TMP and other representative phenolic compounds. To the best of our knowledge, dimetal-substituted γ-Keggin POMs (hereafter, $\gamma\text{-}XW_{10}M_2$) comprising a heterometal di-μ-hydroxo (oxo) dimer placed into the lacuna of the polyoxotungstate $[\gamma\text{-}XW_{10}O_{36}]^{n-}$ (Figure 1) have never been used for the selective oxidation of phenolic compounds.

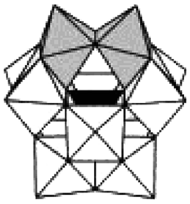


Figure 1. Polyhedral view of polyanions $[\gamma\text{-}XW_{10}M_2O_{40}]^{n-}$ (heterometal di-μ-oxo (hydroxo) dimer is in gray).

2. EXPERIMENTAL SECTION

2.1. Materials. 2,3,6-Trimethylphenol (TMP, 97+%) was obtained from Fluka. 2,6-Di-*tert*-butylphenol (DTBP, 99%), 2,6-dimethylphenol (DMP, 99%), 2-methyl-1-naphthol (MNL), and 2,6-di-*tert*-butyl-1,4-benzoquinone (DTBQ, 98%) were purchased from Aldrich. Acetonitrile (Panreac, HPLC grade) was dried and stored over activated 4 Å molecular sieves. All the other compounds were the best available reagent grade and were used without further purification. The concentration of H_2O_2 (∼35 wt % in water) was determined iodometrically prior to use.

2.2. Catalyst Preparation and Characterization. Heteropolyacid $H_5PMo_{10}V_2O_{40}$ was prepared according to the literature.[61] The cesium salt of the divanadium-substituted phosphotungstate $Cs_5[\gamma\text{-}PV_2W_{10}O_{40}]$ was synthesized as described previously.[62] TBA salts **I**, **II**, and **III** were prepared according to the published protocols.[53,54,60] Compound **I** was purified following the procedure described by Mizuno and co-workers[57] with some modifications. Crude **I** (1.0 g, ∼90% purity) was dissolved in MeCN (100 mL), and then the solvent was removed by evaporation, followed by addition of acetone (10 mL). The immediately precipitated yellow admixture of β-isomer (−541 and −555 ppm in ^{51}V NMR;[62] −13.26 ppm in ^{31}P NMR) was removed by filtration. After a few days of storage of the acetone solution at 5 °C, pure (>99.5%, confirmed by ^{51}V and ^{31}P NMR) yellowish orange crystals of **I** were obtained.

The protonated form of **III** (H-**III**) was prepared by interaction of an aqueous solution of the potassium salt of **III**[60] with a cation-exchange resin in H^+ form, followed by addition of TBABr. Typically, $TiOSO_4$ (1.0 g, 6.25 mmol) was dissolved in 100 mL of water, and then the pH of the solution was adjusted to 1.3 with 70% HNO_3 followed by addition of $K_8[SiW_{10}O_{36}]\cdot 12H_2O$ (7.5 g, 2.52 mmol) to the resulting suspension. After stirring for 15 min, a clear solution of K-**III** was obtained, and the cation-exchange resin (H^+ form; 10 mL) was added. The resulting mixture was stirred for 15 min, and then the resin was removed by filtration. TBABr (2.5 g in 15 mL H_2O) was added in a single step. The resulting white precipitate was separated by centrifugation, washed with an excess of H_2O, and dried overnight at 35 °C and then at 100 °C for 1 h.

The number of TBA cations was determined by ignition of POMs at 600 °C. Potentiometric titration with TBAOH was used to determine the number of acid protons in the POMs. In general, the two methods gave a good cation charge balance. All POMs were characterized by FT-IR and NMR (^{51}V and ^{183}W) spectroscopic techniques. The corresponding spectra are given in the Supporting Information (Figures S1−S3).

2.3. Catalytic Oxidation Tests and Product Analysis.

Catalytic oxidations of alkylphenols with H_2O_2 in the presence of POMs were carried out in temperature-controlled glass vessels at 25−80 °C under vigorous stirring (500 rpm). Concentrations of the reactants were in the range of [POM] = 0.0015−0.012, [phenol] = 0.1−0.4, and $[H_2O_2]$ = 0.2−1.4 M. Typically, the reactions were initiated by the addition of H_2O_2 to a mixture containing phenolic substrate and POM catalyst in 1 mL of MeCN. Samples were taken during the reaction course by a syringe and analyzed by GC and GC/MS. The oxidation products were identified by GC/MS and ^1H NMR. The substrate conversions and product yields were quantified by GC using biphenyl as the internal standard. Each experiment was reproduced at least three times. The experimental error in the determination of the substrate conversions and product yields normally did not exceed 2%.

2,3,5-Trimethyl-1,4-benzoquinone (TMBQ). GC/MS (EI): m/z (relative int.): 150 (100) $[M]^+$, 122 (47) $[M - CO]^+$, 107 (64) $[M - CO, - CH_3]^+$, 79 (48) $[M - 2CO, - CH_3]^+$. ^1H NMR (400.13 MHz, $CDCl_3$): δ = 6.59 (s, 1 H), 2.05−2.10 ppm (m, 9H).

2,2′,3,3′,5,5′-Hexamethyl-4,4′-bisphenol (BP). GC/MS (EI) m/z (relative int.): 270 (100) $[M]^+$, 255 (57) $[M - CH_3]^+$, 240 (61) $[M - 2CH_3]^+$, 225 (15) $[M - 3CH_3]^+$, 210 (3) $[M - 4CH_3]^+$, 195 (7) $[M - 5CH_3]^+$. ^1H NMR (400.13 MHz, $CDCl_3$): δ = 6.72 (s, 2 H), 4.57 (s, 2 H), 2.22 (s, 12 H), 1.94 ppm (s, 6H).

2,3,6-Trimethyl-2,3-epoxy-1,4-benzoquinone (EQ). GC-MS (EI) m/z (relative int.): 166 (7) $[M]^+$, 151 (100) $[M - CH_3]^+$, 138 (17) $[M - CO]^+$, 124 (33) $[M - CCH_3, - CH_3]^+$, 109 (13), $[M - CCH_3, - 2CH_3]^+$). The choice in favor of this isomer was made based on the chemical shift (6.7 ppm) of the signal of the quinoid proton in the ^1H NMR spectrum.

2,5,6-Trimethyl-2,3-epoxy-1,4-benzoquinone (EQ). GC/MS (EI) m/z (relative int.): 166 (3) $[M]^+$, 151 (73) $[M - CH_3]^+$, 138 (79) $[M - CO]^+$, 124 (100) $[M - CCH_3, -CH_3]^+$, 109 (20) $[M - CCH_3, - 2CH_3]^+$, 95 (38) $[M - CCH_3, - CH_3, - CHO]^+$.

2-Hydroxy-3,5,6-trimethyl-1,4-benzoquinone (OH-TMBQ). GC/MS (EI): m/z (relative int.): 166 (100) $[M]^+$, 137 (21) $[M - COH]^+$, 121 (23) $[M - 3CH_3]^+$, 109 (19) $[M - CCH_3, - 2CH_3]^+$, 95 (30) $[M - CCH_3, - CH_3, - COH]^+$.

2,6-Di-tert-butyl-1,4-benzoquinone (DTBQ). ^1H NMR (CD_3CN, 400.13 MHz): δ = 6.48 (s, 2 H), 1.26 ppm (s, 18H).

2,6-Dimethyl-1,4-benzoquinone (DMBQ). GC/MS (EI) m/z (relative int.): 136 (80) $[M]^+$), 108 (70) $[M - CO]^+$, 96 (25) $[M - CCO \text{ or } M - HCCCH_3]^+$, 79 (44) $[M - 2CO, H]^+$, 68 (100), $[M - HCC(CH_3)CO]^+$. ^1H NMR ($CDCl_3$, 400.13 MHz): 6.54 (s, 2 H), 2.04 ppm (s, 6H).

2-Methyl-1,4-naphthoquonone (MNQ). ^1H NMR ($CDCl_3$, 400.13 MHz): δ = 8.0−8.15 (m, 2 H), 7.65−7.80 (m, 2 H), 6.84 (m, 1 H), 2.19 ppm (s, 3H).

2.4. Instrumentation.

GC analyses were performed using a gas chromatograph Tsvet-500 equipped with a flame ionization detector and a quartz capillary column (30 m × 0.25 mm) filled with BPX5. GC/MS analyses were carried out using an Agilent 7000B system with the triple-quadrupole mass-selective detector Agilent 7000 and GC Agilent 7890B (quartz capillary column 30 m × 0.25 mm/HP-5 ms). ^1H, ^{31}P, ^{51}V, and ^{183}W NMR spectra were recorded on a Brüker Avance-400 spectrometer at 400.13, 161.67, 105.24, and 16.67 MHz, respectively. Chemical shifts, δ, are given relative to tetramethylsilane, 85% H_3PO_4, $VOCl_3$, and Na_2WO_4, respectively. For convenience, secondary external standards were used: 0.2 M $H_4PVMo_{11}O_{40}$ for ^{51}V (−530 ppm) and ^{31}P (−3.70 ppm), and 0.4 M $H_4[SiW_{12}O_{40}]$ for ^{183}W NMR (−103.6 ppm). Infrared spectra were recorded for 0.5−1.0 wt % samples in KBr pellets on a Varian 660 FT-IR spectrometer.

3. RESULTS AND DISCUSSION

3.1. Effect of POM Composition on TMP Oxidation with H_2O_2.

First, we evaluated the effects of the POM composition, that is, the nature of the central atom (P versus Si), heterometal (V versus Ti), and cations (H versus TBA) on the oxidation of alkylphenols with aqueous H_2O_2 using TMP as model substrate. The catalytic tests were carried out under standard reaction conditions (substrate/oxidant/catalyst =1:3.5:0.03, 80 °C, MeCN as solvent) that had been previously established as optimal for TMP oxidation to TMBQ over mesoporous titanium-silicates.[34−38] The main results are presented in Table 1.

In the absence of any catalyst, only 2% of TMP conversion was found after 40 min at 80 °C (Table 1, entry 1). All POMs studied revealed high catalytic activity in TMP oxidation, and 92−100% substrate conversions were attained within 30 min. However, the selectivity of the TMBQ formation in the

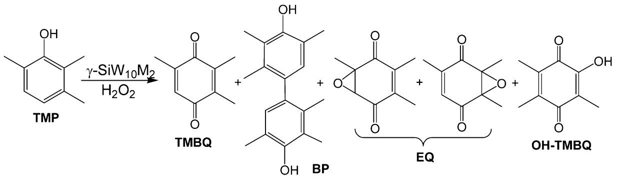
Table 1. Effects of Pom Composition on Tmp Oxidation with H_2O_2.[a]

entry	catalyst	time (min)	TMP conv (%)	TMBQ selectivity[b] (%)
1	no catalyst	40	2	
2	**III**	30	97	38
3	H-**III**[c]	20	98	58
4	**II**	15	92	78
5	**I**	5	>99	>99
6	**I** + 1 equiv of TBAOH	7	93	97
7	**I** + 1 equiv of $HClO_4$	3	>99	>99
8	$H_3PW_{12}O_{40}$	30	62	22
9	$H_5PMo_{10}V_2O_{40}$	30	>99	51

[a] Reaction conditions: TMP, 0.1 mmol; POM, 0.003 mmol; H_2O_2 (35% in water), 0.35 mmol; MeCN, 1 mL; 80 °C. [b] GC yield on the substrate consumed. [c] $TBA_{6.6}H_{1.4}[(\gamma\text{-}SiW_{10}Ti_2O_{38}H_2)_2O_2]$.

presence of **III** was rather poor (Table 1, entry 2). Dimeric 2,2′,3,3′,5,5′-hexamethyl-4,4′-biphenol (BP) along with TMBQ overoxidation products, that is, two isomeric epoxy derivatives (EQ) and 2-hydroxy-3,5,6-trimethyl-1,4-benzoquinone (OH-TMBQ), were identified as the main reaction byproducts (Scheme 1).

Scheme 1. TMP Oxidation with Aqueous H_2O_2 Catalyzed by III and II



A partial replacement of TBA cations for H^+ in the cationic sphere of **III** (H-**III**, extra protons are most likely located at the Ti−O−Ti bridges linking two γ-Keggin subunits) has led to the increase of TMBQ selectivity from 38 to 58% (Table 1, entry 3). Lowering the oxidant to substrate molar ratio resulted in the reduction of both TMP conversion and TMBQ selectivity.

In the presence of **II**, which has the same central atom as **III** but the heterometal is V(V) instead of Ti(IV), the selectivity toward TMBQ had already reached 78% at 92% TMP conversion after 15 min (Table 1, entry 4). The main byproducts were the same as those depicted in Scheme 1.

For both **II** and **III**, the carbon mass balance in TMP oxidation depended on the reaction conditions. At 80 °C and with a 1.75-fold excess of H_2O_2 (conditions of Table 1), it was not complete because of the formation of some unidentified overoxidation products. Meanwhile, at 40 °C with a stoichiometric amount of the oxidant, when the substrate conversion was not complete, the mass balance was close to 96−98% (Figure 2).

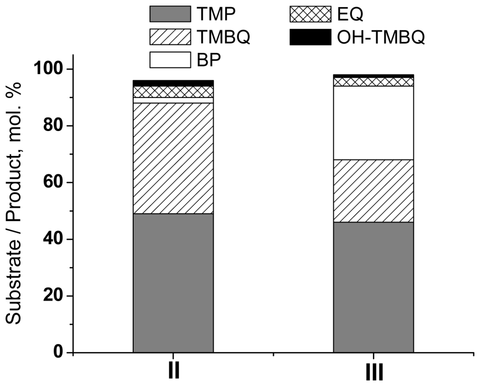


Figure 2. Product distribution in TMP oxidation with 2 equiv of H_2O_2 at 40 °C catalyzed by compounds **II** and **III**.

It is noteworthy that replacement of Si for P in γ-$SiW_{10}V_2$ led to a significant increase in both the reaction rate and quinone selectivity. With **I**, TMP was quantitatively converted to TMBQ in 5 min (Table 1, entry 5). We also investigated the impact of protons in the cationic sphere of $TBA_4H[\gamma\text{-}PW_{10}V_2O_{40}]$ on the catalytic performance. The addition of 1 equiv of TBAOH with respect to **I** resulted in some reduction of both TMP conversion and TMBQ selectivity (Table 1, entry 6). However, this effect was not so dramatic as the effect caused by deprotonation of **II** in the alkene epoxidation,[53] and TMBQ could be obtained in 90% yield after 7 min. In contrast to the oxidation of alkanes,[54] alkylbenzenes,[56] and electron-deficient alkenes,[57] the oxidation of alkylphenols does not require one additional equivalent of acid ($HClO_4$) with respect to **I**. Although the acid produces a rate-accelerating effect, without it, TMBQ is obtained in approximatly quantitative yield after 5 min (Table 1, compare entries 7 and 5). Therefore, we may conclude that the impact of protons is less pronounced in the case of the selective oxidation of alkylphenols catalyzed by **I** than in the oxidation of less reactive hydrocarbon substrates.

Heteropoly acid $H_3PW_{12}O_{40}$, which according to ^{31}P NMR was stable under the conditions used, revealed a substantially lower activity and poor TMBQ selectivity (Table 1, entry 8) relative to **I** and **II**, which proves that vanadium atoms play a central role in the title reaction. A possible product of its solvolytic destruction, $[PW_4O_{24}]^{3-}$, was active but not selective: after 3 h at 40 °C, it converted 90% of TMP, but the TMBQ yield was only 10%. On the other hand, conventional $H_3PMo_{10}V_2O_{40}$, which possesses two vanadium atoms statistically distributed over 12 positions of the α-Keggin structure, also showed much lower selectivity toward TMBQ than the di-V-substituted γ-Keggin POMs (Table 1, entry 9), indicating that, namely, the presence of the dimeric vanadium core in the latter is crucial for the selective formation of the quinone.

3.2. Optimization of Reaction Conditions in TMP Oxidation Using I. Optimization of the reaction conditions was carried out for TMP oxidation with H_2O_2 using **I** as the most prospective homogeneous catalyst. First, we evaluated the effect of solvent nature on the catalytic performance. The reaction was carried out under standard conditions of Table 1 in MeCN, *tert*-BuOH, and 1:1 (v/v) mixtures of MeCN with *tert*-BuOH and MeOH (Figure 3). In *tert*-BuOH, the solubility of **I** was not complete, and a significant deterioration of all the reaction parameters took place. In the other cases, **I** was fully soluble. In MeCN/*tert*-BuOH (1:1), the reaction was even faster than in pure MeCN, and the maximal TMP conversion (97%) was already achieved after 3 min, TMBQ being the only product. On the contrary, the reaction rate decreased, and the selectivity to TMBQ reduced to 55% in MeCN/MeOH (1:1). Therefore, we performed further optimization of the reaction conditions using MeCN as solvent.

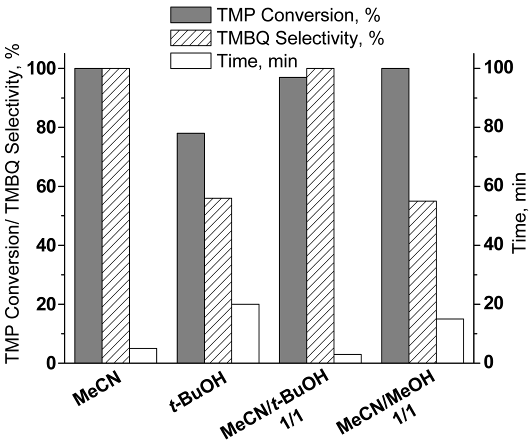


Figure 3. Effect of solvent nature on TMP oxidation with H_2O_2 catalyzed by **I**. Reaction conditions as in Table 1.

Table 2 shows the influence of temperature and concentrations of the reactants on the achievable TMP conversion and TMBQ selectivity. A 2-fold increase in the substrate-to-catalyst molar ratio led to a minor decrease in both the conversion and selectivity, and the target product was obtained in 97% yield (Table 2, entry 2).

Table 2. Effects of Reaction Conditions on TMP Oxidation by H_2O_2 in the Presence of I[a]

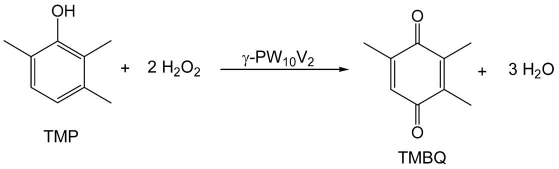
entry	I (mM)	TMP (M)	H_2O_2 (M)	T (°C)	time (min)	TMP conversion (%)	TMBQ selectivity[b] (%)
1	3	0.1	0.35	80	5	>99	>99
2	1.5	0.1	0.35	80	7	98	99
3	6	0.2	0.7	80	4	>99	>99
4	12	0.4	1.4	80	2	>99	78
5	3	0.1	0.35	40	30	99	>99
6	3	0.1	0.35	25	240	98	>99
7	3	0.1	0.25	80	10	90	>99
8	3	0.1	0.2	80	10	80	>99
9	3	0.1	0.3	40	30	99	>99
10	3	0.1	0.25	40	35	96	>99
11	3	0.1	0.2	40	40	90	>99
12[c]	3	0.1	0.2	40	40	90	65

[a] Solvent: MeCN, 1 mL. [b] GC yield on the substrate consumed. [c] β-$PW_{10}V_2$ was used instead of γ-$PW_{10}V_2$.

We also attempted to enlarge proportionally concentrations of all reactants to assess whether higher TMBQ volume yields are possible. Entry 3 in Table 2 shows that a 2-fold increase in all concentrations does not impair the product selectivity and substrate conversion that remain close to 100%; that is, the volume yield of TMBQ can be increased, at least, twice. However, a subsequent 2-fold increase in the reactants load results in the reduction of selectivity (entry 4, Table 2). Importantly, the reaction temperature can be lowered without a notable decline of the product yield (Table 2, entries 5 and 6). Even at room temperature, TMBQ is produced with 98% yield in a reasonable reaction time (4 h).

Finally, we concentrated on optimization of the oxidant-to-substrate molar ratio to get a better efficiency of the hydrogen peroxide utilization. According to the reaction stoichiometry, TMP oxidation to TMBQ requires 2 equiv of H_2O_2 (Scheme 2). On the other hand, an excess of H_2O_2 is often needed to compensate unproductive decomposition of peroxide that may occur parallel to the target oxidation reaction.[32−38]

Scheme 2. Stoichiometry of TMP Oxidation to TMBQ with H_2O_2



Indeed, comparison of entries 1, 7, and 8 (as well as entries 5 and 9−11) in Table 2 shows that the decrease in H_2O_2 concentration resulted in the reduction of TMP conversion. With the stoichiometric amount of the oxidant (2 equiv of H_2O_2), the maximal TMP conversion attained 80 and 90%, at 80 and 40 °C, respectively. Therefore, hydrogen peroxide utilization efficiency and TMBQ yield can be improved by lowering the reaction temperature to 40 °C (Figure 4). Further decrease in the temperature produced a minor improvement of both parameters but significantly increased the reaction time.

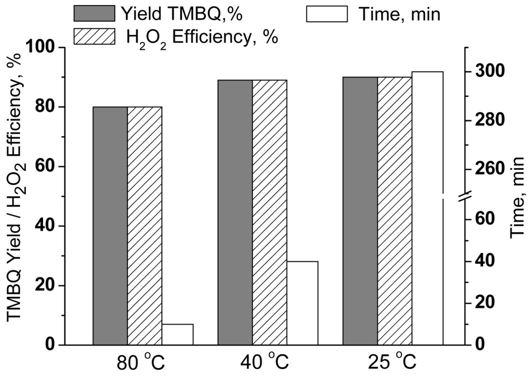


Figure 4. Effect of temperature on TMP oxidation with a stoichiometric amount of H_2O_2 in the presence of **I**. Other reaction conditions as in Table 2, entry 11.

Importantly, isomeric β-$PW_{10}V_2$ separated during purification of crude **I** (see the Experimental Section) gave TMBQ with only 65% selectivity at 90% TMP conversion under the optimal reaction conditions (Table 2, entry 12), thus indicating that the β-isomer is significantly less selective than the γ-isomer in the title reaction.

3.3. Reaction Scope. With optimal conditions in hand, we carried out oxidation of other representative alkylphenols as well as 2-methyl-1-naphthol (MNL) to estimate the reaction scope (Table 3).

Table 3. Oxidation of Various Alkylphenols and 2-Methyl-1-naphthol with H_2O_2 Catalyzed by I[a]

substrate	product	H_2O_2 (M)	T (°C)	time (min)	substrate conv (%)	product select.[b] (%)
2,3,5-TMP	TMBQ	0.2	40	60	60	62
		0.35	80	10	95	66
DMP	DMBQ	0.2	40	40	90	98
DTBP	DTBQ	0.2	40	40	98	90
MNL	MNQ	0.2	40	15	>99	73
		0.35	40	15	>99	80
		0.35	80	10	>99	82

[a] Substrate, 0.1 mmol; I, 0.003 mmol; MeCN, 1 mL. [b] GC yield on the substrate consumed.

At 40 °C with 2 equiv of the oxidant, isomeric 2,3,5-TMP was oxidized to TMBQ with a moderate yield (37%) that could be increased up to 63% by increasing the reaction temperature and H_2O_2 concentration. On the other hand, 2,6-dimethyl- and 2,6-di-*tert*-butylphenols gave corresponding *p*-benzoquinones with ∼90% yields using only stoichiometric amounts of the oxidant. Oxidation of MNL produced MNQ in 73−82% yields, depending on the reaction conditions. Hence, the **I**/H_2O_2 catalytic system can be applied to oxidation of various kinds of phenolic compounds.

3.4. Catalyst Reuse and Recycling. To verify the possibility of the catalyst reuse and recycling, we performed two types of experiments. First, after the oxidation of TMP in the presence of **I** for 40 min under the reaction conditions of entry 11, Table 1, additional portions of the reactants (0.1

mmol of TMP and 0.2 mmol of 35% aqueous H_2O_2) were added into the reaction solution. As one can judge from Figure 5, the oxidation reaction again proceeded with the same conversion, selectivity to TMBQ, and reaction time as those observed for the first run (90% conversion and $\geq$99% selectivity). In the third use, there was only a slight deterioration of the catalytic performance, indicating that the catalyst system is intrinsically reusable. Although water accumulated in the system as a byproduct, no precipitation of the catalyst occurred.

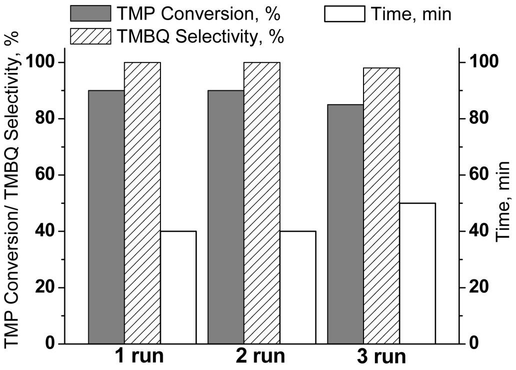


Figure 5. Reuse of catalyst **I**. Reaction conditions as in Table 2 (entry 11).

Importantly, ^{51}V and ^{31}P NMR spectra of **I** run before and after the catalytic reaction were very close (Figure 6), pointing out that the catalyst structure is fairly stable under the turnover conditions. After the second use, minor peaks of the β isomer (−541 and −555 ppm in ^{51}V NMR and −13.3 ppm in ^{31}P NMR) appeared, which is consistent with some deterioration of the catalytic performance (Figure 5).

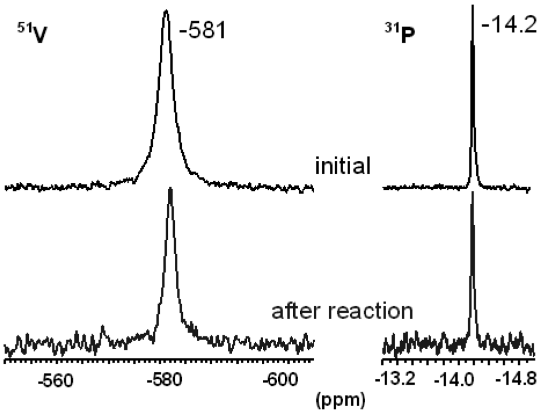


Figure 6. ^{51}V and ^{31}P NMR spectra of **I**: initial and after catalytic reaction. Reaction conditions as in Table 2 (entry 11).

In another experiment, **I** was separated from the reaction mixture by precipitation with diethyl ether, dried in air, and then reused in the oxidation of TMP under the conditions of entry 1, Table 2. Again, the reaction proceeded at the same rate and produced TMBQ with nearly the same conversion and selectivity (Figure 7). The FT-IR spectrum of **I** recovered from the reaction mixture revealed all the main vibrations present in the spectrum of the initial POM (Figure 8), which corroborated that the recycled catalyst maintained its structure.

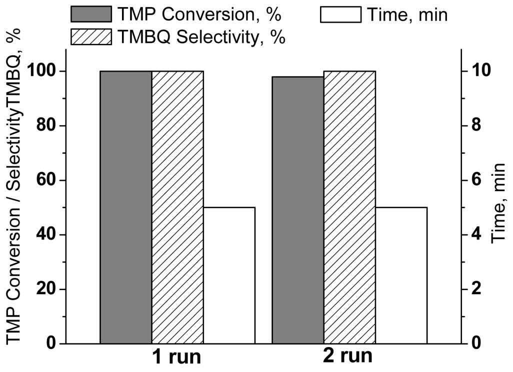


Figure 7. Recycling of **I**. Reaction conditions as in Table 2 (entry 1).

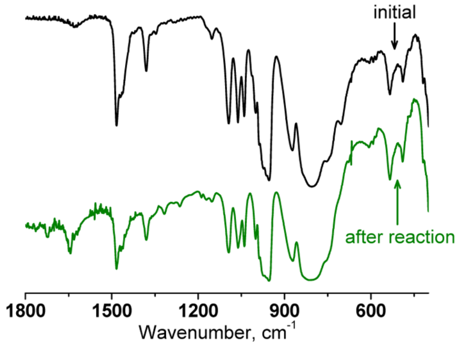


Figure 8. FT-IR spectra of **I**: initial sample and after the catalytic reaction. Reaction conditions as in Table 2 (entry 1).

3.5. Active Peroxo Vanadium Species. Attempts to identify an active peroxo vanadium complex responsible for the oxidation of TMP to TMBQ were performed under quasi-stoichiometric conditions using multinuclear NMR spectroscopy. In agreement with the data reported by Mizuno et al.,[54] the ^{51}V NMR spectrum of pure **I** in CH_3CN revealed a single line at −581 ppm and the ^{31}P NMR spectrum exhibited a peak at −14.2 ppm (Figure 9). The signals were broadened, most likely because of a slow proton exchange on the NMR time scale in the MeCN solution of **I** that contains one H^+ as countercation. After treatment of **I** with 1−2 equiv of 35% H_2O_2, a new signal (δ −557 ppm) appeared in the ^{51}V NMR spectrum (Figure 9) that had previously been assigned to a vanadium μ-hydroxo-μ-hydroperoxo complex V−(OH)(OOH)−V (**IV**).[54] Simultaneously, a new signal emerged in the ^{31}P NMR spectrum at −14.8 ppm (Figure 9). Importantly, no signals that could be attributed to lower-nuclearity peroxotungstates, such as $[PW_2O_{14}]^{3-}$ or $[PW_4O_{24}]^{3-}$, were observed. After subsequent addition of a 10-fold excess of TMP, both ^{51}V and ^{31}P NMR signals promptly disappeared (Figure 9), which allowed us to assign them to the same active peroxo vanadium species. GC analysis confirmed the formation of TMBQ in the reaction mixture; no BP was found. It is noteworthy that the rate of the peroxo complex decomposition in the absence of the phenolic substrate was significantly slower (2 h versus 20 min in the presence of TMP; see Figure S4 in Supporting Information).

In the range of concentrations studied, TMP does not bind to **I**, as evidenced by the absence of new signals in both ^{51}V and ^{31}P NMR spectra upon addition of TMP to a MeCN solution of **I**. All these facts collectively indicate that hydroperoxo complex **IV** formed from **I** and H_2O_2 is the active species responsible for the selective oxidation of TMP to TMBQ.

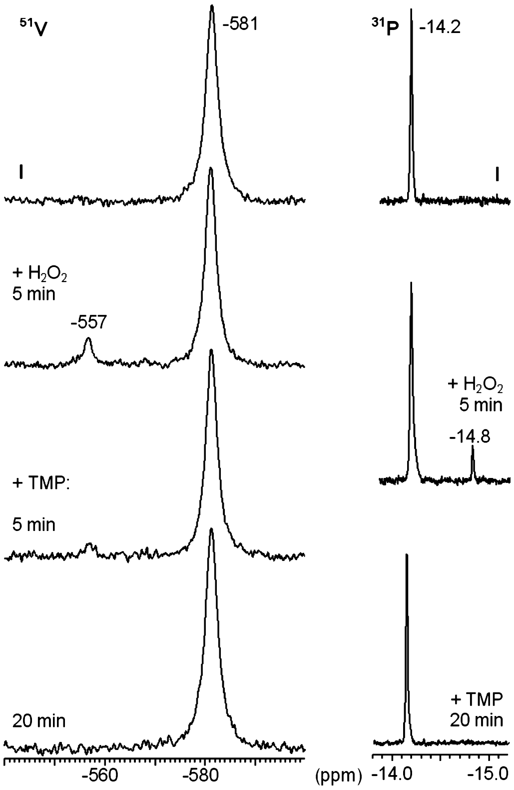


Figure 9. ^{51}V and ^{31}P NMR monitoring of the interaction of **I** with H_2O_2 and then with TMP in MeCN solution. Reaction conditions: **I**, 0.02 mmol; 35% H_2O_2, 0.04 mmol; TMP, 0.2 mmol; MeCN, 2.7 mL; 25 °C.

Further kinetic and mechanistic studies would shed light on the intimate mechanism of the oxidative transformation.

4. CONCLUSION

In summary, an original and versatile procedure for the synthesis of substituted *p*-benzo- and naphthoquinones has been developed using 35% aqueous hydrogen peroxide as green oxidant and the divanadium-substituted *γ*-Keggin polyoxotungstate $TBA_4H[\gamma\text{-}PW_{10}V_2O_{40}]$ (**I**) as homogeneous catalyst. This procedure does not require either rigorously controlled reaction conditions or special handling (e.g., protection from air and water), which makes it safe, inexpensive, and sustainable. Various alkylated phenols/naphthols can be effectively oxidized to corresponding *p*-benzo/naphthoquinones with good to excellent yields, depending on the specific substrate. Under optimal reaction conditions, industrially important 2,3,6-trimethylphenol gives 2,3,5-trimethyl-*p*-benzoquinone (vitamin E key intermediate) with nearly quantitative yields. The efficiency of hydrogen peroxide utilization is in the range of 80−90%, which is unprecedentedly high for the title reaction. Using a ^{51}V and ^{31}P NMR spectroscopic technique, we managed to identify an active peroxo vanadium complex responsible for the selective formation of quinones. The homogeneous catalyst kept its structure under turnover conditions and could be recycled and reused. Attempts to prepare a stable to leaching solid catalyst based on **I** and to realize liquid-phase heterogeneous oxidation of alkylphenols using such a catalyst are in progress in our group.

■ ASSOCIATED CONTENT

Supporting Information

Characterization details (FT-IR, ^{183}W, ^{31}P, and ^{51}V NMR spectra of POMs). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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