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Aerobic Oxidations of Conjugated Dienes Using a Catalytic Palladium(II)−Quinone−Heteropolyacid System for Electron Transfer from Organic Substrates to Molecular Oxygen

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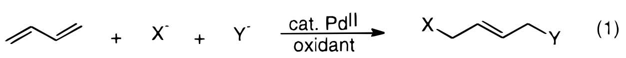
The heteropolyacid $H_5PMo_{10}V_2O_{40}\cdot 34H_2O$ was found to be an efficient oxygen activating agent in palladium-catalyzed reactions. Aerobic 1,4-oxidations of conjugated dienes were carried out by employing a triple catalytic system consisting of palladium−quinone−heteropolyacid. With this system a mild electron transfer from the organic substrate to molecular oxygen occurs. 1,4-Diacyloxylations and 1,4-dialkoxylations were studied using this mild reoxidation system. 1,4-Diacetoxylation of 1,3-cyclohexadiene was studied in some detail. Some advantages of the heteropolyacid over previously employed metal macrocycles are high stability, easy access to an active catalyst, and simpler workup procedures.

Introduction

In the past decade, several selective palladium-catalyzed 1,4-oxidations of conjugated dienes employing both external and internal nucleophiles have been developed in this laboratory (eq 1).[1−9] In these reactions



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p-benzoquinone has been used either as a stoichiometric reoxidant or as a catalytic electron transfer mediator in combination with MnO_2. The stereoselectivity can be efficiently controlled by variation of the ligands on palladium. Products can be selectively formed with either a cis or trans relationship between the two added nucleophiles, which makes the reaction a useful tool in stereoselective synthesis.

From an economical and environmental point of view molecular oxygen is an attractive oxidant, and more recently these reactions have been further developed into aerobic processes. Molecular oxygen can be used as the terminal reoxidant either via reoxidation of hydroquinone by the use of metal macrocycles as the oxygen activating agents[10−16] or directly for the oxidation of zerovalent palladium by the use of palladium clusters in DMSO.[17−20] Among the metal macrocycles investigated so far, iron phthalocyanine, a porphyrin analogue, has been found to be one of the most versatile catalysts due to its stability under the reaction conditions.[10] Co(salophen) encapsulated in zeolites has also been found to be a very good oxygen activating agent in palladium-catalyzed oxidations.[15] However, we were interested in developing aerobic catalytic systems with oxygen activating agents that would be more suitable for large-scale reactions in terms of easy workup procedures and catalyst accessibility. In addition, it would be desirable to have a catalyst that tolerates a wider variety of reaction conditions than the metal macrocycles previously employed.

Heteropolyoxometalates constitute an interesting class of inorganic compounds that are used as catalysts in oxidation reactions.[21−24] Important properties of these

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catalysts are their high stability toward oxidative degradation and their solubility in solvents of different polarities. Heteropolyoxometalates where one of the d^0 addenda atoms has been replaced with a d-electron-containing transition metal are often referred to as "inorganic porphyrin analogues".[24-27] These have been used, for example, in olefin epoxidations and hydroxylations of alkanes in combination with a wide variety of terminal oxidants, such as hydrogen peroxide, iodosylbenzene, and molecular oxygen. In a second class of heteropolyoxometalates more than one type of d^0 metal is present. These mixed-addenda heteropolyoxometalates have been used as oxygen activating agents in oxidations of both inorganic and organic substrates.[24,28-32] For example, zerovalent palladium has been reoxidized to Pd(II) in an aerobic process for Wacker-type oxidations invented by Matveev *et al*,[33] and this has been further developed into an industrial process by Catalytica, Inc.[34] We considered these mixed-addenda heteropolyoxometalates to be an interesting group of catalysts for our purposes.

We recently developed an aerobic system for reoxidation of Pd(0) in allylic acetoxylation of olefins.[35] Herein we describe the further extension of this triple catalytic system (Pd(II)−quinone−heteropolyoxometalate) applied to 1,4-oxidations of conjugated dienes. The mixed-addenda heteropolyoxometalate used in this work is $H_5PMo_{10}V_2O_{40}\cdot 34H_2O$, which hereafter will be referred to as *the heteropolyacid*.

Results and Discussion

A. Preparation of the Heteropolyacid Catalyst. The heteropolyacid $H_5PMo_{10}V_2O_{40}\cdot 34H_2O$ was prepared according to a procedure by Tsigdinos.[36] It is probably formed as a mixture of one or more structural isomers with different organizations of the constituent ions.[24] In comparison to the previously employed iron phthalocyanine catalyst, the heteropolyacid gives batches with better reproducibility with regard to the catalytic activity.[37] In addition, workup procedures are much more simplified since the heteropolyacid is very water soluble.

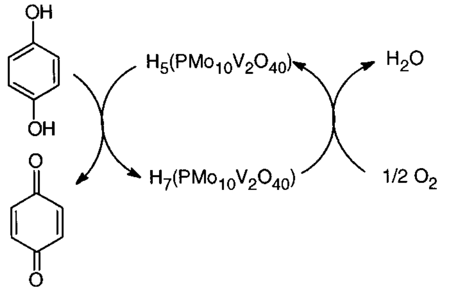


Figure 1. Aerobic oxidation of hydroquinone catalyzed by a heteropolyacid.

Table 1. Added Ligands in the 1,4-Oxidation of 1,3-Cyclohexadiene Using a Heteropolyacid in Combination with Molecular Oxygen as the Terminal Oxidant[a]

entry no.	ligand L	yield (%)	trans:cis
1[b]	none	30	65:35
2	maleic anhydride	57	84:16
3[c]	*p*-benzoquinone	63	87:13
4	cyclohexylSOQ (**3**)	56	88:12
5[d]	PhSOQ (**4**)	73	88:12
6[e]	*p*-benzoquinone + DMSO	60	86:14

[a] Reaction conditions: 5 mol % of $Pd(OAc)_2$, 2 mol % of $H_5PMo_{10}V_2O_{40}\cdot 34H_2O$, 8 mol % of maleic anhydride (entry 2) or 5 mol % of a quinone (entries 3−5), 0.45−0.66 M LiOAc, 2:1 pentane−HOAc, 1 atm of O_2, 24 h at room temperature. [b] 10 mol % of $Pd(OAc)_2$ was used. [c] 0.8 mol % of $H_5PMo_{10}V_2O_{40}\cdot 34H_2O$ was used; 5 mol % of hydroquinone was added but was oxidized quickly to *p*-benzoquinone under the reaction conditions. [d] The reaction time can be decreased to 5 h and 30 min without a loss in yield and stereoselectivity. [e] 0.8 mol % of $H_5PMo_{10}V_2O_{40}\cdot 34H_2O$, 5 mol % of hydroquinone, and 8 mol % of DMSO were used.

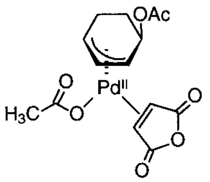
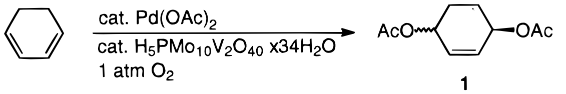


Figure 2. Maleic anhydride as a ligand in the intermediate π-allyl complex.

The catalytic activity of the heteropolyacid was investigated by oxidation of 1 mmol of hydroquinone by molecular oxygen (1 atm) using 2 mol % of the heteropolyacid catalyst (Figure 1).[37-39] The progress of the reaction was monitored by measurements of the amount of oxygen consumed, and in most cases the reaction was found to be complete within less than 1 h.

B. Palladium-Catalyzed Oxidations. 1. 1,4-Diacetoxylation. Oxidation of 1,3-cyclohexadiene employing $Pd(OAc)_2$ and the heteropolyacid as catalysts under an oxygen atmosphere was found to proceed slowly, with low yield (30%) of the desired 1,4-diacetoxy-2-cyclohexene (**1**; eq 2) (Table 1, entry 1).



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The slow reaction under these conditions could be due to an inefficient electron transfer either from Pd(0) to

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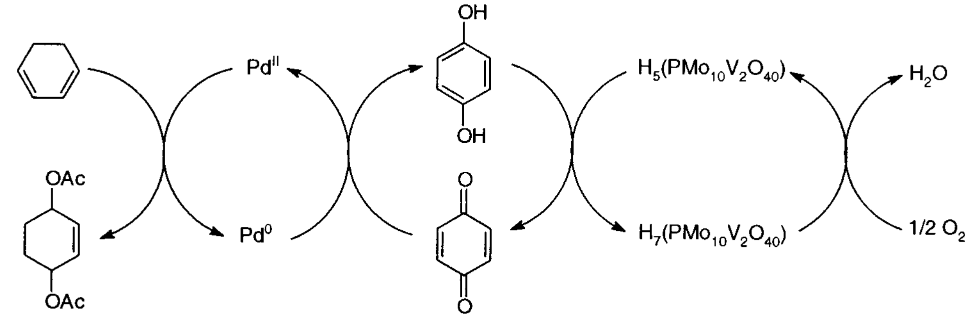
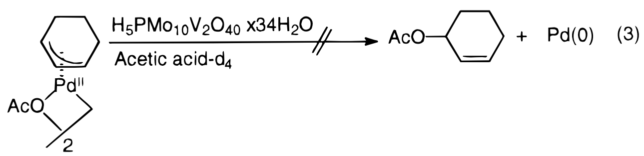


Figure 3. Triple catalytic system.

the oxidized form of the heteropolyacid or from the reduced form of the heteropolyacid to molecular oxygen. The rate-limiting step could also be the nucleophilic attack on the palladium π-allyl complex, which is an intermediate in the reaction. It has previously been demonstrated that this attack is facilitated by coordination of a potential electron-acceptor ligand, such as p-benzoquinone or maleic anhydride, to palladium.[2,40] Although heteropolyacids are known to act as ligands for Pd(II),[21] no activation toward nucleophilic attack was observed when the heteropolyacid was added to complex **2** (eq 3). Fast product formation from π-allyl complexes has been observed under similar reaction conditions upon addition of activating ligands.[2,41]



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To investigate if the low reaction rate and yield were results of a slow attack by the second nucleophile on the intermediate palladium π-allyl complex, maleic anhydride was added to the reaction mixture.[2] This would act as a ligand to palladium in a similar way as would a quinone (Figure 2), but without oxidizing Pd(0). We indeed observed an improved aerobic oxidation, and the desired product **1** was now isolated in 57% yield. Moreover, the reaction was faster and also more selective toward formation of the trans product (trans:cis = 84:16; Table 1, entry 2). This supports the idea that the low reaction rate in the absence of an activating ligand is due to an inefficient attack by the second nucleophile.

The aerobic system was further improved when maleic anhydride was replaced by p-benzoquinone, and now **1** was obtained in 63% yield (Table 1, entry 3). The quinone plays the dual role of being an electron transfer mediator (Figure 3) and a ligand that activates the palladium π-allyl complex toward nucleophilic attack (step iv in Figure 4). The resulting electron transfer from Pd(0) to molecular oxygen (Figure 3) is in this case similar to that of the allylic acetoxylation of olefins previously described.[35]

The improvement of yield and reaction rate (Table 1, Figure 5) when maleic anhydride is replaced by p-benzoquinone probably reflects a more efficient electron transfer from Pd(0) to the oxidized form of the heteropolyacid.

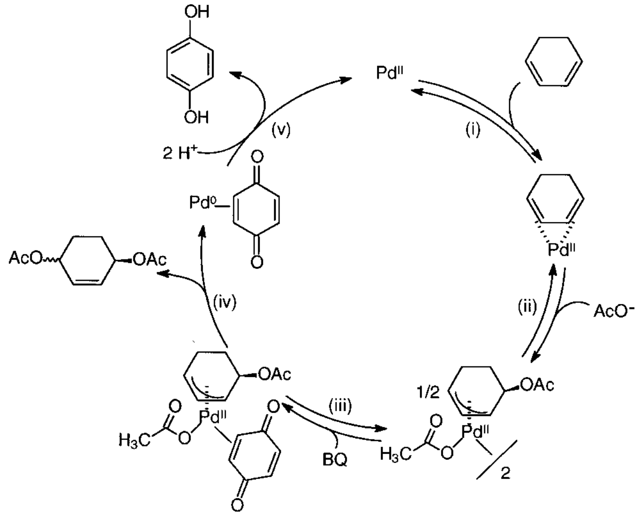

Figure 4. Catalytic cycle.

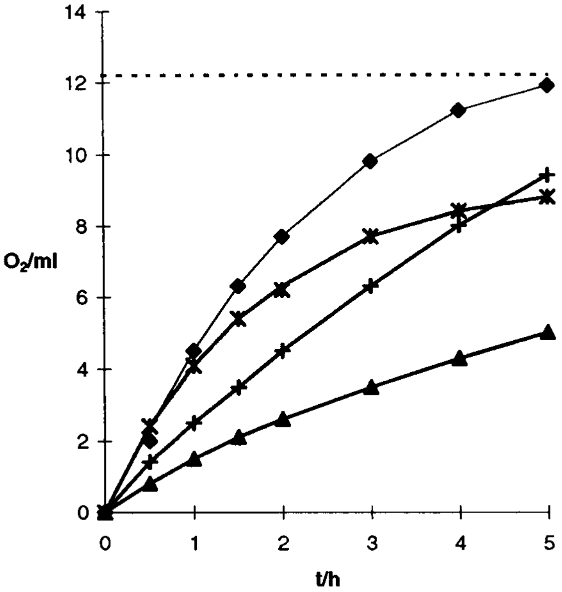

Figure 5. Oxygen uptake for aerobic 1,4-diacetoxylation of 1 mmol of 1,3-cyclohexadiene employing $H_5PMo_{10}V_2O_{40}\cdot 34H_2O$ as oxygen activating agent and different ligands L to palladium (mean values of n experiments): (▲) L = maleic anhydride ($n = 3$); (+) L = p-benzoquinone ($n = 2$); (*) L = 2-(cyclohexylsulfinyl)-1,4-benzoquinone (**3**) ($n = 4$); (◆) L = 2-(phenylsulfinyl)-1,4-benzoquinone (**4**) ($n = 6$). A theoretical uptake corresponds to 12.2 mL.

The use of quinones containing a sulfoxide moiety (**3** and **4**)[11] resulted in the most efficient reactions in this heteropolyacid-based triple catalytic system (Table 1, entries 4 and 5). Both reaction rate and yield (73%)

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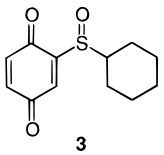
(40) Bäckvall, J.-E.; Gogoll, A. *Tetrahedron Lett.* **1988**, *29*, 2243.



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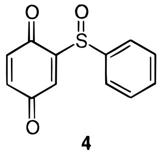

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were improved when **4** was used as activating ligand. Interestingly, it was found that this reaction can be carried out with the same yield and stereoselectivity by employing air instead of 1 atm of oxygen. This is an improvement of importance for safety reasons for work on a larger scale.

In contrast to earlier palladium-catalyzed aerobic systems employing metal macrocycles as oxygen activating catalysts,[11] no improvement of the reaction was observed with the use of *p*-benzoquinone together with a free sulfoxide such as DMSO (Table 1, entry 6).

The results of the study of the progress of the reaction are reported in Figure 5. The fastest reaction was obtained when 2-(phenylsulfinyl)-1,4-benzoquinone (**4**) was employed as ligand.

In the 1,4-diacetoxylation of 1,3-cyclohexadiene, formation of trans product is normally favored under chloride-free conditions.[1] This is the result of a favored internal migration of an acetate coordinated to palladium in the π-allyl complex (Figure 6). Also, in the aerobic reactions employing the heteropolyacid as catalyst, the predominant product is that with a trans relationship between the two added nucleophiles (trans:cis = 88:12). The lower stereoselectivity (trans:cis = 65:35) in the absence of an activating ligand (eq 2) is similar to that previously reported for quinone-free systems.[1] The stereoselectivity in these 1,4-diacetoxylations can be altered to give mainly cis product by addition of small amounts of chloride. The chloride coordinates strongly to palladium in the π-allyl complex, thus preventing the internal migration of an acetate ligand from palladium to the allyl ligand. A cis-selective reaction (trans:cis = 15:85) could be obtained also when using the heteropolyacid-based reoxidation conditions described in this paper, but for some reason which is not yet understood, the yield dropped dramatically under these conditions.[42,43]

The heteropolyacid-based aerobic reoxidation system can be used also for the 1,4-diacetoxylation of 1,3-cycloheptadiene. In this case the stereochemistry of the product (1,4-diacetoxy-2-cycloheptene (**5**)) is mainly cis, since the internal migration of acetate from palladium to the π-allyl ligand is hindered for steric reasons.[1] The stereoselectivity of the reaction is influenced by the reaction temperature (Table 2, entries 1, 4, and 5). The best selectivity (90% cis) was obtained at room temperature, whereas only 75% cis product was formed at 40 °C. Thus, when the temperature is raised, the rate of the internal nucleophilic attack on the palladium π-allyl complex (migration) increases relatively more than the

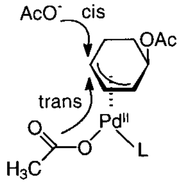
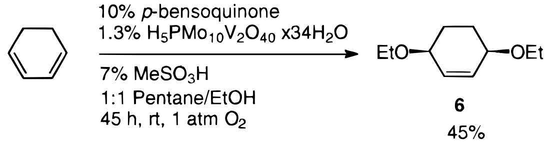


Figure 6. Second nucleophilic attack on the intermediate palladium π-allyl complex, determining the relative stereochemistry.

rate of external attack.[44] A lower than 20 mol % amount of *p*-benzoquinone gave a less efficient reaction. Thus, more quinone ligand has to be added than in the oxidation of 1,3-cyclohexadiene, which can be a result of a slower reaction of the seven-membered diene in general. The 1,4-diacetoxylation of 1,3-cycloheptadiene has to be carried out in a one-phase system in order to avoid an extremely slow reaction. As for the six-membered diene, this reaction can also be run using a double catalytic system (i.e. quinone-free conditions), but with lower yield (13%; Table 2, entry 2).

2. 1,4-Dialkoxylation. The palladium-catalyzed 1,4-oxidations can be extended to the use of alcohols as nucleophiles.[45] These 1,4-dialkoxylations are carried out in the appropriate alcoholic solvent. As acidic conditions have been shown to be necessary for a *p*-benzoquinone-mediated reoxidation of Pd(0),[46] catalytic amounts of methanesulfonic acid are normally added to the reaction mixtures. In diethoxylation of 1,3-cyclohexadiene employing the aerobic reoxidation system described in this paper, it has been shown that the heteropolyacid can, in addition to being an oxidation catalyst, also act as an acid. However, a more efficient reaction was observed upon addition of small amounts of methanesulfonic acid. When the diethoxylation was performed under similar triple catalysis as described above for 1,4-diacetoxylations, but with ethanol−pentane (1:1) as reaction medium and 7 mol % $MeSO_3H$ as acid, a 45% yield of 1,4-diethoxy-2-cyclohexene (**6**) could be isolated (eq 4).



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Benzene is a likely side product in the 1,4-oxidations of 1,3-cyclohexadiene. It can be formed via different mechanisms, catalyzed either by the heteropolyacid as described by Neumann[28,29] or by zerovalent palladium. Under the reaction conditions described in this paper with 5 mol % PhSOQ (**4**) as ligand (Table 1, entry 5), 5−20% of benzene[47] was normally formed in addition to the desired 1,4-diacetoxy-2-cyclohexene (**1**). The reaction was best performed by employing a two-phase

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[41] Grennberg, H.; Langer, V.; Bäckvall, J.-E. *J. Chem. Soc., Chem. Commun.* **1991**, 1190.

[42] The heteropolyacid should not be sensitive toward chloride, as in the Wacker process developed by Catalytica, Inc., chloride is present.[34]

[43] The oxidation potential of the heteropolyacid is not strong enough for oxidation of chloride ions to molecular chlorine: Kozhevnikov, I. V.; Matveev, K. I. *Appl. Catal.* **1983**, *5*, 135.

[44] One possible explanation for this is the difference in $\Delta S^{\ddagger}$ for the two pathways. The entropy change for the migration pathway should be relatively smaller than for the external attack ($\Delta S^{\ddagger} < 0$).

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[47] Determined by GC using *n*-heptane as internal standard.

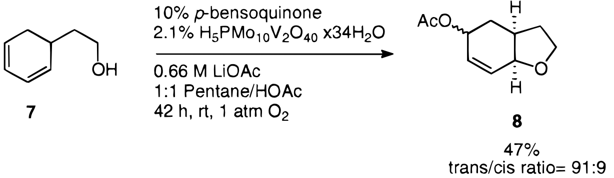
Table 2. 1,4-Diacetoxylation of Cycloheptadiene Using the Triple Catalytic System $Pd^{II}-BQ-H_5PMo_{10}V_2O_{40}\cdot 34H_2O$

entry no.	reacn temp (°C)	reacn time (h)	amt of BQ (mol %)[a]	cis:trans	yield (%)
1	25	24	20	90:10	40
2	30	24		60:40	13
3	30	24	5	67:33	25
4	30	24	20	89:11	48
5[b]	40	6.5	20	75:25	40

[a] *p*-Benzoquinone. [b] The shorter reaction time can probably explain the lower yield obtained at this temperature.

system (2:1 pentane−HOAc) to minimize nonselective reactions between the heteropolyacid and the diene.

3. Intramolecular Oxidations. 1,4-Oxidations of conjugated dienes employing the aerobic reoxidation system described here can be extended to the use of substrates for intramolecular reactions, which have the nucleophile on a tether. In the reaction of the alcohol **7** the fused tetrahydrofuran **8** is formed in 47% yield, via intramolecular attack on the palladium-diene complex by the alcohol function in the substrate (eq 5). In this case 11% of the starting material was aromatized.



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C. Mechanistic Aspects. We studied the effect of the amount of heteropolyacid catalyst on the reaction rate employing hydroquinone and sulfoxyquinone **4** as ligands to palladium. In both cases only a small increase in reaction rate was observed when larger amounts of the catalyst were used. In these reactions the color of the reaction mixture was brown during most of the reaction time, indicating that the heteropolyacid is present in its oxidized form.[48] In the control reaction (Figure 1), 1 mmol of hydroquinone was oxidized aerobically in less than 1 h when 2 mol % of the heteropolyacid was employed as catalyst. This corresponds to a turnover frequency (TOF) on the heteropolyacid of more than 50 h^{-1}. The color of the heteropolyacid is in this case blue until the theoretical amount of oxygen has been consumed, in contrast to the diacetoxylations employing the whole triple catalytic system. Probably, the rate-limiting step in the control reaction is the reoxidation of reduced heteropolyacid by molecular oxygen, whereas in the diacetoxylations this step is faster than the other steps involved (Figures 3 and 4).

Table 3. Yield and Stereoselectivity in 1,4-Diacetoxylation of 1,3-Cyclohexadiene Using Different Amounts of PhSOQ (4)[a]

entry no.	amt of PhSOQ (mol %)	yield (%)	trans:cis
1[b]		30	65:35
2	1	36	83:17
3	5	73	88:12
4	10	74	88:12
5	17	67	88:12

[a] Reaction conditions: 5 mol % $Pd(OAc)_2$, 1−17 mol % PhSOQ (**4**), 2 mol % $H_5PMo_{10}V_2O_{40}\cdot 34H_2O$, 0.66 M LiOAc, 2:1 Pentane−HOAc, 1 atm of O_2, 5 h 30 min at room temperature. [b] 10 mol % $Pd(OAc)_2$ was used. The reaction was run 24 h at room temperature.

In an early version of the 1,4-diacetoxylation of 1,3-cyclohexadiene with MnO_2 as terminal oxidant, the amount of benzoquinone should be 20−25 mol % in order to get a reaction that proceeds smoothly.[1] It has been shown that the reaction in an aerobic reoxidation system is more efficient when a sulfoxyquinone instead of *p*-benzoquinone is employed as ligand (Figure 5).[49] When using the aerobic reoxidation system described in this paper for oxidation of 1,3-cyclohexadiene, the reaction is efficient with amounts of PhSOQ (**4**) as low as 5 mol % (Table 3, entry 3). No significant differences concerning rate or yield could be detected between reactions using either 5 or 10 mol % of **4**, indicating that the quinone **4** is probably not involved in the rate-limiting step. In fact, an increase of the amount of **4** to 17 mol % resulted in a lower yield of the desired product **1**. This is probably due to a greater extent of the competing Diels−Alder reaction between the quinone and the diene.

When the amount of palladium was varied between 2 and 10 mol %, an effect on the rate was observed. This observation, taken together with the observed color differences and the fact that the amounts of heteropolyacid and quinone do not affect the rate, suggests that most likely the palladium part of the system (Figure 4) is the slow step in this complex triple catalytic system. Although the rate is as high as in the best of the previously developed systems,[10,11,50] there is a slight decrease in yield and selectivity which can be explained by the direct interaction between palladium and the heteropolyacid (cf. Table 1, entry 1).

Conclusion

The use of a heteropolyacid as oxygen-activating agent has been extended to different 1,4-oxidations of conjugated dienes. An active heteropolyacid catalyst is more easily accessible than the previously employed iron phthalocyanine and more stable toward degradation than other metal macrocycles. In addition, extractive workup procedures are much simplified since the heteropolyacid is very soluble in water. For 1,4-diacetoxylations a direct electron transfer from Pd(0) to the oxidized form of the heteropolyacid takes place at a reasonable rate in the presence of maleic anhydride. However, the reactions are faster and more selective in the presence of a benzoquinone as coordinating ligand and additional electron transfer mediator. The stability of the catalyst enables 1,4-dialkoxylation in the presence of a strong organic acid such as methanesulfonic acid. It has been shown that this triple catalytic system can be extended also to intramolecular 1,4-oxidations.

Experimental Section

General Comments. All NMR spectra were recorded for $CDCl_3$ solutions on a Varian XL-300 spectrometer (^1H at 300

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(48) Cotton, F. A.; Wilkinson, G. *Advanced Inorganic Chemistry*, 5th ed.; Wiley: New York, 1988; p 818.

(49) This effect has also been observed in aerobic oxidations employing iron phthalocyanine as ligand.[11]

(50) Grennberg, H.; Bäckvall, J.-E. *J. Chem. Soc., Chem. Commun.* **1993**, 1331.

MHz). The trans:cis ratios of the products obtained in diacetoxylation reactions of dienes were determined by ^{1}H NMR spectroscopy. GC was carried out on an SE 54 column (25 m, 250 μm) using a 25 °C isotherm (5 min) and then a gradient of 10 °C/min with *n*-heptane as internal standard. Slow additions of substrates were performed using a Sage Instruments Model 355 syringe pump. 1,3-Cyclohexadiene was distilled at reduced pressure before use. π-Allyl complex **2** was prepared from the corresponding chloro complex,[51] followed by exchange of the chloride to an acetate ligand.[41] Quinones **3** and **4**[11] and 2-(2,4-cyclohexadienyl)ethanol (**7**)[52] were prepared according to literature procedures. Other chemicals and solvents were obtained from commercial sources and used as received.

Synthesis of $H_5PMo_{10}V_2O_{40}\cdot 34H_2O$.[36] $NaVO_3$ (6.05 g, 49.6 mmol) was dissolved in 25 mL of H_2O at 100 °C. Na_2HPO_4 (1.76 g, 12.4 mmol) dissolved in 25 mL of H_2O was added to the warm solution. After the mixture had cooled to room temperature, 1.25 mL of concentrated H_2SO_4 was added, and the solution developed a dark red color. Na_2MoO_4 (30.0 g, 146 mmol) in 50 mL of H_2O was added, followed by a dropwise addition of 21.1 mL of concentrated H_2SO_4 over a period of 15 min, whereby the color changed to bright red. The hot solution was allowed to reach room temperature. Upon extraction with ether (5 × 40 mL), the heteropolyacid formed a dark red etherate (oil) which was insoluble in both the organic and aqueous phases. The liquid etherates were combined, and N_2 was bubbled through to make them free from ether. The orange solid that remained was dissolved in H_2O and crystallized by concentration of the solution under vacuum over H_2SO_4. The ^{31}P NMR of the prepared catalyst was compared to data reported in the literature.[29]

Oxidation of Hydroquinone (Test of Catalytic Activity of the Heteropolyacid). Hydroquinone (110 mg, 1.00 mmol), $H_5PMo_{10}V_2O_{40}\cdot 34H_2O$ (46 mg, 0.020 mmol), and $LiOAc\cdot 2H_2O$ (341 mg, 3.35 mmol) were dissolved in 5 mL of HOAc. The blue mixture was stirred at room temperature under 1 atm of O_2. The O_2 uptake ceased after 55 min. The theoretical amount of O_2 had then been consumed, and the color of the mixture had changed from dark blue to brown-green.

General Procedure for Aerobic 1,4-Diacetoxylation of Conjugated Dienes Catalyzed by Pd(II)−Quinone−$H_5PMo_{10}V_2O_{40}\cdot 34H_2O$. 1,4-Diacetoxy-2-cyclohexene (1). $Pd(OAc)_2$ (11.6 mg, 0.052 mmol, 5 mol %), 2-(phenylsulfinyl)-1,4-benzoquinone (11.9 mg, 0.051 mmol, 5 mol %), $H_5PMo_{10}V_2O_{40}\cdot 34H_2O$ (51 mg, 0.022 mmol, 2.1 mol %), and $LiOAc\cdot 2H_2O$ (168 mg, 1.65 mmol, 0.66 M) were dissolved in HOAc (2.5 mL) and pentane (5 mL). The reaction atmosphere was changed to O_2 (1 atm), and 1,3-cyclohexadiene (100 μL, 1.0 mmol) was added with a syringe, giving a color change from brown to blue-green. The oxygen consumption was measured with a gas buret. The reaction mixture was stirred at room temperature for 5.5 h (the color changed to brown and remained so during most of the reaction), after which time the theoretical amount of O_2 (12.2 mL) had been consumed. The reaction mixture was then worked up by diluting it with aqueous saturated NaCl (10 mL), followed by extraction with pentane−ether (4:1, 3 × 10 mL). The combined organic layers were washed with NaOH (2 M, 2 × 10 mL), H_2O (2 × 10 mL), and aqueous saturated NaCl (1 × 10 mL) and dried over $MgSO_4$. Evaporation of the solvents yielded 147 mg (73%) of 1,4-diacetoxy-2-cyclohexene (**1**; 88% trans) as white crystals. The ^{1}H NMR of the product was identical with that reported in the literature.[1]

1,4-Diacetoxy-2-cycloheptene (5). $Pd(OAc)_2$ (9.2 mg, 0.041 mmol, 5 mol %), *p*-benzoquinone (17.8 mg, 0.165 mmol, 20 mol %), $H_5PMo_{10}V_2O_{40}\cdot 34H_2O$ (34 mg, 0.015 mmol, 1.8 mol %), and $LiOAc\cdot 2H_2O$ (1.068 g, 10.5 mmol, 3.0 M) were dissolved in HOAc (3.5 mL). After the reaction atmosphere was changed to 1 atm of O_2, 1,3-cycloheptadiene (90 μL, 0.83 mmol) was added with a syringe. The reaction mixture was stirred for 24 h at 30 °C, during which time the oxygen consumption was measured. Then the reaction mixture was worked up as above. An 84 mg amount (48%) of 1,4-diacetoxy-2-cycloheptene (89% cis) was isolated as white crystals. The ^{1}H NMR of the product was identical with that reported in the literature.[1]

Diethoxylation of 1,3-Cyclohexadiene. 1,4-Diethoxy-2-cyclohexene (6). $Pd(OAc)_2$ (14.2 mg, 0.063 mmol, 6 mol %), *p*-benzoquinone (11.7 mg, 0.108 mmol, 10 mol %), and $H_5PMo_{10}V_2O_{40}\cdot 34H_2O$ (32.0 mg, 0.014 mmol, 1.3 mol %) were dissolved in EtOH (5 mL). A 5 mL amount of pentane was added. To the mixture were added $MeSO_3H$ (5 μL, 0.073 mmol, 7 mol %) and H_2O (0.2 mL). The atmosphere was changed to 1 atm of O_2, and 1,3-cyclohexadiene (100 μL, 1.0 mmol) was added slowly over a period of 4 h 30 min, with stirring at room temperature. The stirring was continued for another 40 h. The workup procedure was as described above for 1,4-diacetoxylations. The solvents were carefully evaporated. The crude product was purified by column chromatography (pentane−ether gradient 98:2 to 90:10), yielding 77 mg (45%) of *cis*-1,4-diethoxy-2-cyclohexene (**6**) as a colorless oil. The ^{1}H NMR spectrum was compared to previously reported data.[45]

Intramolecular 1,4-Oxidations. Fused Tetrahydrofuran 8. $Pd(OAc)_2$ (11.1 mg, 0.049 mmol, 5 mol %), *p*-benzoquinone (10.8 mg, 0.100 mmol, 10 mol %), $H_5PMo_{10}V_2O_{40}\cdot 34H_2O$ (47.1 mg, 0.020 mmol, 2.1 mol %), and $LiOAc\cdot 2H_2O$ (168 mg, 1.65 mmol, 0.66 M) were dissolved in HOAc (2.5 mL). The atmosphere was changed to O_2 (1 atm), and pentane (5 mL) was added. 2-(2,4-Cyclohexadienyl)ethanol (**7**; 133 mg, 0.97 mmol) and $LiOAc\cdot 2H_2O$ (168 mg, 1.65 mmol, 0.66 M) in HOAc (2.5 mL) was added over 10 h with stirring at room temperature. Stirring was continued for another 32 h. The reaction mixture was worked up by evaporation of HOAc, followed by dissolution of the residue in ether (30 mL). The organic phase was washed with H_2O (15 mL), 0.5 M NaOH (2 × 10 mL), and H_2O (10 mL). Back-extraction of the aqueous washes with ether (2 × 15 mL), followed by washing of the combined organic phases with aqueous saturated NaCl (10 mL) and drying ($MgSO_4$), gave 144 mg of product (91% trans) after evaporation of the solvents. Purification by column chromatography (pentane−ether 80:20) gave 83 mg (47%, 91% trans) of **8**. The ^{1}H NMR of the product was identical with that reported previously in the literature.[52]

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