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Unexpected Roles of Molecular Sieves in Palladium-Catalyzed Aerobic Alcohol Oxidation

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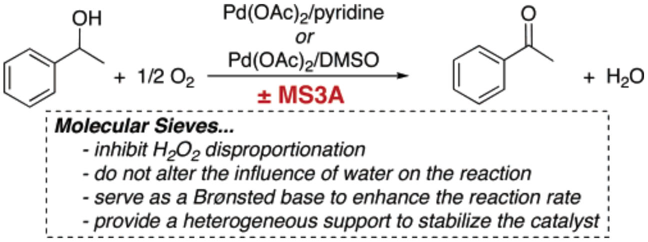

Methods for palladium-catalyzed aerobic oxidation of alcohols often benefit from the presence of molecular sieves. This report explores the effect of molecular sieves on the Pd(OAc)$_2$/pyridine and Pd(OAc)$_2$/DMSO (DMSO = dimethyl sulfoxide) catalyst systems by performing kinetic studies of alcohol oxidation in the presence and absence of molecular sieves. Molecular sieves enhance the rate of the Pd(OAc)$_2$/pyridine-catalyzed oxidation of alcohols, and the effect is attributed to the ability of molecular sieves to serve as a Brønsted base. In contrast, no rate enhancement is observed for the Pd(OAc)$_2$/DMSO-catalyzed reaction. Both catalyst systems exhibit improved catalyst stability in the presence of molecular sieves, manifested by higher catalytic turnover numbers. Control experiments indicate that neither of these beneficial effects is associated with the ability of molecular sieves to absorb water, a stoichiometric byproduct of these reactions. Finally, the use of simultaneous gas-uptake and in-situ IR spectroscopic studies reveal that molecular sieves inhibit the disproportionation of H$_2$O$_2$, an observation that contradicts a previous suggestion that the beneficial effect of molecular sieves may arise from their ability to promote H$_2$O$_2$ disproportionation.

Introduction

Over the past 10 years, the development of aerobic palladium-catalyzed oxidation reactions has advanced significantly.[1] These methods are particularly effective for aerobic alcohol oxidation (Scheme 1), including examples of kinetic resolution of racemic secondary alcohols.[2−9] The catalyst systems developed for these reactions (Chart 1) have been the subject of extensive experimental and computational investigation,[10−17] and both mechanistic and empirical screening studies have contributed to these developments.

For a number of these catalyst systems, including **B**−**D**, **F**, and **H**, molecular sieves (3 or 4 Å) were found to have a significant beneficial effect on the catalytic reactions.[3−5,7,9] Because water forms as the stoichiometric byproduct of dioxygen reduction (Scheme 1), it is reasonable to expect that

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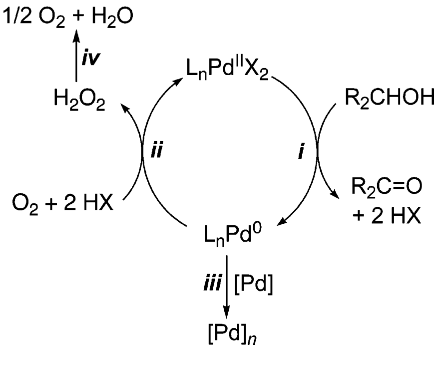
SCHEME 1. Simplified Catalytic Cycle for Palladium-Catalyzed Aerobic Oxidation of Alcohols



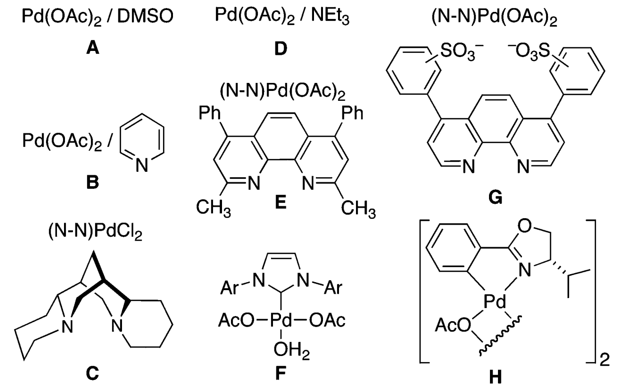
molecular sieves improve the reactions by sequestering water in the organic reaction medium.[18] Additionally, Uemura and co-workers have proposed that molecular sieves enhance catalytic turnover by promoting the hydrogen peroxide disproportionation (eq 1).[3b] If hydrogen peroxide is present, it might inhibit formation of a Pd(II)−alkoxide species (eq 2).[19]

$$H_2O_2 \rightarrow {}^{1}/_{2}O_2 + H_2O \tag{1}$$

$$L_2(X)Pd{-}OOH + RCH_2OH \overset{K}{\rightleftharpoons} L_2(X)Pd{-}OCH_2R + H_2O_2 \tag{2}$$

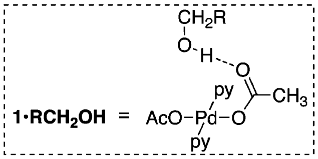
The $Pd(OAc)_2$/pyridine catalyst system is effective for aerobic alcohol oxidation even in the absence of molecular sieves,[3b] and we recently reported a mechanistic study of benzyl alcohol oxidation under such conditions.[11] Kinetic studies revealed the principle features of the catalytic mechanism (eqs 3−6). In-situ ^1H NMR spectroscopic studies enabled us to characterize the catalyst resting state, which consists of an equilibrium mixture of $(py)_2Pd(OAc)_2$, **1**, and an intermediate in which the alcohol is hydrogen-bonded to an acetate ligand of $(py)_2Pd(OAc)_2$, **1**·RCH_2OH (eq 3). Alcohol oxidation proceeds via subsequent formation of a Pd(II)−alkoxide intermediate, **2**, with release of acetic acid (eq 4), dissociation of pyridine (eq 5), and β-hydride elimination (eq 6).

CHART 1. Catalyst Systems for Palladium-Catalyzed Aerobic Oxidation of Alcohols

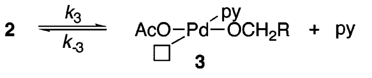


$$(py)_2Pd(OAc)_2 + RCH_2OH \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} (py)_2Pd(OAc)_2{\cdot}RCH_2OH \tag{3}$$

1 **1·RCH₂OH**



$$\mathbf{1{\cdot}RCH_2OH} \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \underset{\mathbf{2}}{(py)_2Pd(OAc)(OCH_2R)} + AcOH \tag{4}$$



$$\mathbf{2} \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} \underset{\mathbf{3}}{AcO{-}\overset{py}{Pd}{-}OCH_2R} + py \tag{5}$$

$$\mathbf{3} \xrightarrow{k_4} [(py)Pd(H)(OAc)] + RCHO \tag{6}$$

In the present study, we have examined the effect of molecular sieves on the mechanism of $Pd(OAc)_2$/pyridine-catalyzed alcohol oxidation. These studies confirm that molecular sieves significantly enhance the reaction rate,[3b] but the data do not support either of the aforementioned roles for molecular sieves. Specifically, molecular sieves are not needed as a dehydrating agent because water does not inhibit the reaction under the conditions tested, and they *inhibit*, rather than promote, hydrogen peroxide disproportionation. Molecular sieves instead appear to benefit the reaction by serving as a basic "buffer" to promote formation of the Pd(II)−alkoxide intermediate (eq 4) and by enhancing catalyst stability, either by promoting catalyst reoxidation or by hindering palladium(0) aggregation (steps ii and iii, Scheme 1, respectively). This catalyst-stabilizing effect is reproduced, and is even more profound, in the $Pd(OAc)_2$/DMSO-catalyzed alcohol oxidation. The use of molecular sieves has not been reported previously for this catalyst system, which is particularly susceptible to catalyst decomposition. We propose that molecular sieves arrest catalyst decomposition by providing a heterogeneous surface for site isolation of metastable palladium(0) species. These results have important implications for future developments in palladium-catalyzed oxidation reactions because the traditional method for improving catalyst

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(19) This proposal does not explain why water, one of the products of hydrogen peroxide disproportionation, would not inhibit formation of the Pd(II)−alkoxide intermediate.

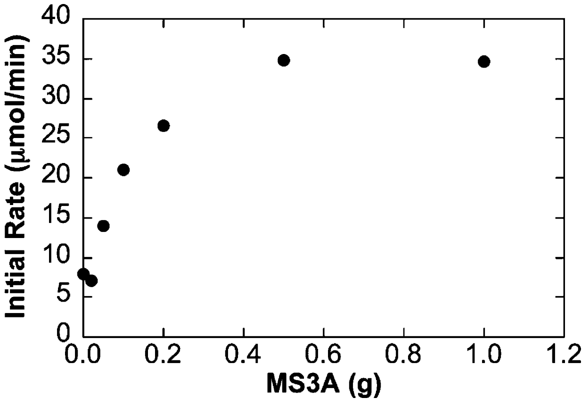
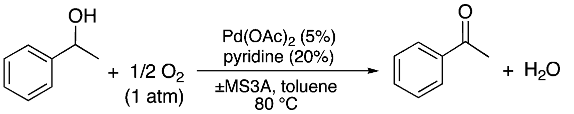


FIGURE 1. Dependence of the initial rate of gas uptake on the quantity of 3 Å molecular sieves in the aerobic oxidation of benzyl alcohol. Conditions: 5.00 mM $Pd(OAc)_2$, 20.0 mM pyridine, 100 mM benzyl alcohol, 700 Torr O_2, 0.02−1.00 g of 3 Å molecular sieves, 80 °C, 10 mL of toluene.

stability in nonoxidative palladium catalysis via the use of soft donor ligands (especially phosphines) is generally not compatible with oxidizing reaction conditions.

Results and Discussion

Kinetic Studies of the $Pd(OAc)_2$/Pyridine System in the Presence of 3 Å Molecular Sieves (MS3A).[20] A catalyst consisting of $Pd(OAc)_2$/pyridine at 5:20 mol % loading promotes the aerobic oxidation of 1-phenylethanol in toluene (eq 7). The gas-uptake rate increases significantly in the presence of MS3A, and the effect maximizes at a loading of 50 mg/mL toluene (Figure 1).



(7)

Molecular sieves are commonly used as a drying (i.e., water sequestering) agent for organic solvents; however, two observations indicate the beneficial effect of molecular sieves does not arise from this property. First, the gas-uptake time course obtained for alcohol oxidation performed in the absence of molecular sieves exhibits clean exponential decay (Figure 2). This result suggests that water formed during the reaction does not interfere with catalytic turnover. Furthermore, intentional addition of water to the reaction mixture prior to initiation of the reaction has no effect on the turnover rate, both in the presence and absence of 3 Å molecular sieves (Figure 3).

Further studies to probe the effect of molecular sieves focused on evaluating the dependence of the rate on the concentration of the individual reaction components, including [benzyl alcohol], pO_2, [pyridine], and [catalyst] (catalyst = 1:4 ratio of $Pd(OAc)_2$/pyridine). The effect of [AcOH] was also tested. The results of these studies are compared directly to those obtained in the absence of molecular sieves[11] in Figure 4.

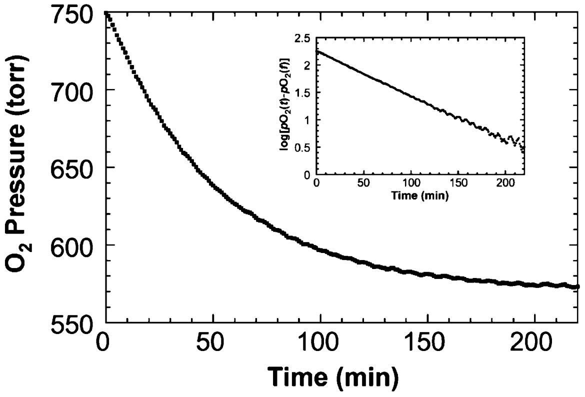


FIGURE 2. Typical reaction time course for the oxidation of 1-phenylethanol by the $Pd(OAc)_2$/pyridine system. Inset: Logarithmic plot of the alcohol concentration over time. Conditions: 5.0 mM $Pd(OAc)_2$, 20.0 mM pyridine, 100 mM 1-phenylethanol, 750 Torr O_2, 80 °C, 10 mL of toluene.

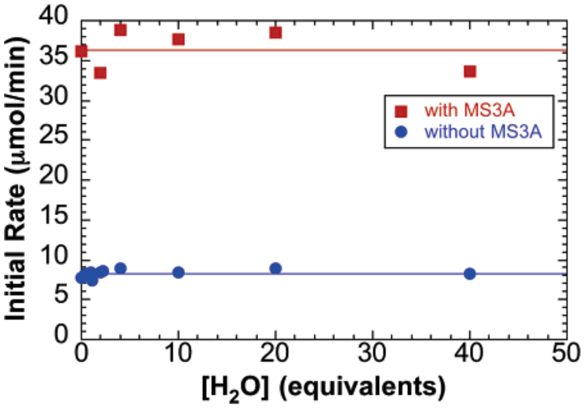


FIGURE 3. Dependence of the initial rate of gas uptake on the equivalents of water in the aerobic oxidation of benzyl alcohol. Conditions: 5.00 mM $Pd(OAc)_2$, 20.0 mM pyridine, 100 mM benzyl alcohol, 0−40 equiv of H_2O relative to [Pd], 700 Torr O_2, 0.50 g of 3 Å molecular sieves, 80 °C, 10 mL of toluene.

Overall, the data suggest that reactions conducted in the presence of molecular sieves proceed significantly faster; however, the qualitative kinetic features are very similar to the reactions conducted in the absence of molecular sieves. The [alcohol] dependence (Figure 4A) displays saturation behavior and the O_2 pressure dependence (Figure 4B) is zero order above a minimum pressure threshold. Variation of [pyridine] reveals that the optimal initial rate under both conditions is obtained at a 1:1 Pd/pyridine ratio (Figure 4C). Below 1 equiv of pyridine, the catalyst is extremely prone to decomposition and the rate suffers, and when the ratio of pyridine to palladium is increased beyond 1 equiv, the rate decreases. Finally, the reaction rate is inversely proportional to the acetic acid concentration (Figure 4E).

Deuterium kinetic isotope effect (KIE) data provide further evidence that molecular sieves do not dramatically affect the reaction mechanism. Comparison of the initial rates of oxidation of $PhC(H)(CH_3)OH$ and $PhC(D)(CH_3)OH$ reveals kinetic isotope effects of $k_H/k_D = 1.5 \pm 0.2$ and 1.7 ± 0.2 in the absence[11b] and presence of MS3A, respectively. If monodeuterated benzyl alcohol, PhCHDOH, is oxidized, an intrinsic isotope effect of 2.6 ± 0.2 is obtained, both in the absence and presence of MS3A.

One significant effect of molecular sieves is their ability to promote catalytic turnover in the absence of pyridine (Figure 4C). $Pd(OAc)_2$ promotes only stoichiometric oxidation of alcohol with concomitant formation of palladium black if

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[20] MS3A are molecular sieves of the A-type zeolite with 3 Å pores arising from the partial substitution of potassium for sodium ions in the aluminosilicate lattice. For detailed descriptions of molecular sieves and other zeolites, see ref 18.

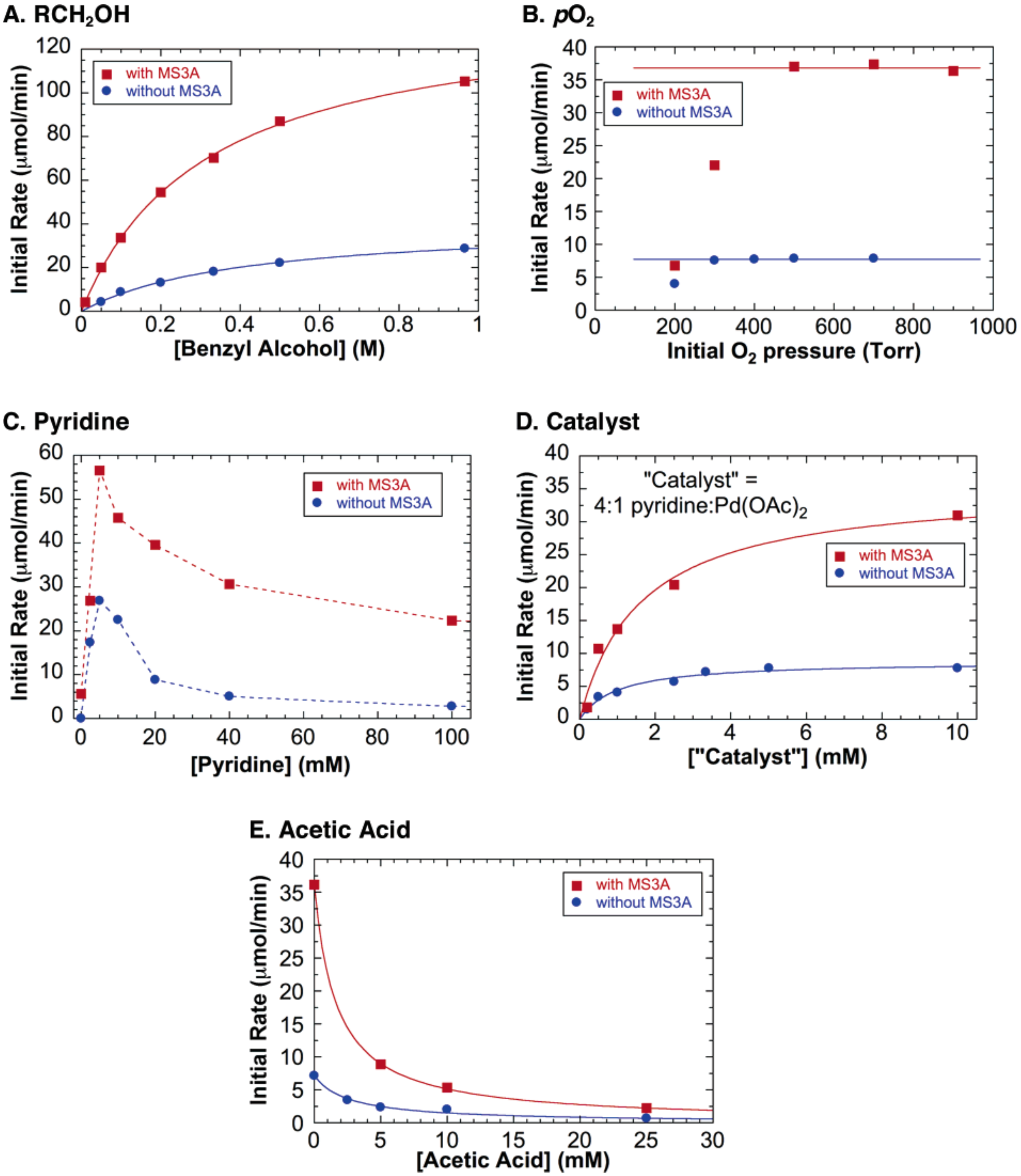

FIGURE 4. Kinetic dependences with the $Pd(OAc)_2$/pyridine system. Standard conditions: 5.0 mM $Pd(OAc)_2$, 20.0 mM pyridine, 100 mM benzyl alcohol, 700 Torr O_2, with or without 0.50 g of 3 Å molecular sieves, 80 °C, 10 mL of toluene.

pyridine and molecular sieves are both absent from the reaction mixture. The addition of 0.50 g of MS3A to the reaction mixture, however, enables catalytic turnover to proceed with a rate similar to that observed under standard conditions (i.e., $Pd(OAc)_2$: pyridine = 1:4) in the absence of molecular sieves. This result suggests that molecular sieves either enhance the rate of Pd(0) oxidation by the molecular oxygen or reduce the rate of Pd(0) decomposition, steps ii vs iii, respectively, in Scheme 1 (see further discussion below).

Simultaneous Gas-Uptake/in-Situ FTIR Spectroscopic Studies. Analysis of the gas-uptake kinetic traces for reactions conducted in the presence and absence of molecular sieves reveal distinct differences over the course of the reaction (Figure 5). In the absence of MS3A, the O_2 pressure decreases monotonically with an exponential decay. In contrast, the reaction containing molecular sieves rapidly consumes dioxygen, reaching a pressure minimum in approximately 90 min, and beyond this time, the pressure slowly rises, approaching a plateau at an oxygen pressure corresponding to the theoretical stoichiometry of $ROH/O_2 = 2:1$.

These observations can be explained by noting that the initial product of dioxygen reduction is hydrogen peroxide (Scheme

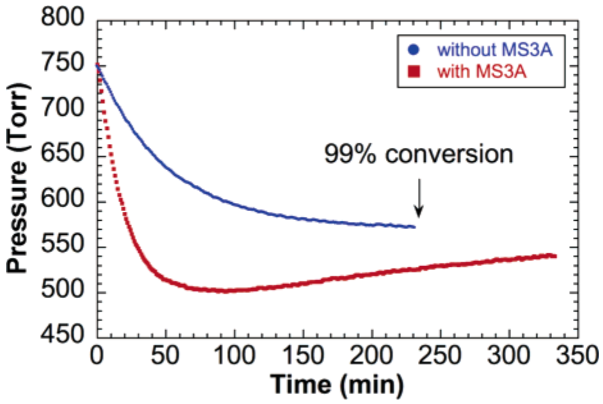

FIGURE 5. Typical reaction time course for the oxidation of 1-phenylethanol by the Pd(OAc)$_2$/pyridine system. Conditions: 5.0 mM Pd(OAc)$_2$, 20.0 mM pyridine, 100 mM 1-phenylethanol, 750 Torr O$_2$, either with or without 3 Å molecular sieves, 80 °C, 10 mL of toluene.

1). Slow hydrogen peroxide disproportionation could cause >0.5 equiv (up to 1.0 equiv) of dioxygen to be consumed during oxidation of the alcohol substrate. The data suggest that molecular sieves *inhibit* hydrogen peroxide disproportionation under the present reaction conditions.

To probe the H_2O_2 disproportionation hypothesis further, we performed the reaction in a manner that enabled us to monitor simultaneously the dioxygen consumption and alcohol oxidation via gas-uptake and in-situ FTIR spectroscopy, respectively. The product, acetophenone, exhibits a diagnostic infrared absorption at 1691 cm^{-1} that can be monitored conveniently throughout the reaction. The results of this study are shown in Figure 6. In the absence of molecular sieves, dioxygen consumption and acetophenone formation track together throughout the time course in a 1:2 ratio (Figure 6A) as predicted by the reaction stoichiometry (eq 7). In the presence of molecular sieves, however, the stoichiometry of dioxygen consumption and acetophenone production initially exhibits a 1:1 ratio. The theoretical reaction stoichiometry of 1:2 is achieved only after extended reaction times (Figure 6B). These results are best rationalized by proposing that molecular sieves stabilize hydrogen peroxide under the reaction conditions or otherwise inhibit its disproportionation.[21]

Effects of Molecular Sieves on the Pd(OAc)$_2$/DMSO System. The Pd(OAc)$_2$/DMSO catalyst system has been employed in the aerobic oxidation of numerous organic substrates,[1,22] including alcohols.[2] Molecular sieves are generally not used in these reactions. In our prior kinetic studies of Pd(OAc)$_2$/DMSO-catalyzed aerobic alcohol oxidation, we noted the propensity of this catalyst system to decompose via palladium aggregation.[10] On the basis of our observation that molecular sieves promote catalyst reoxidation in the Pd(OAc)$_2$/pyridine-catalyzed reaction (cf. Figure 4C at [py] = 0 mM), we decided to probe the effect of molecular sieves on Pd(OAc)$_2$/DMSO-catalyzed oxidation of 1-phenylethanol.

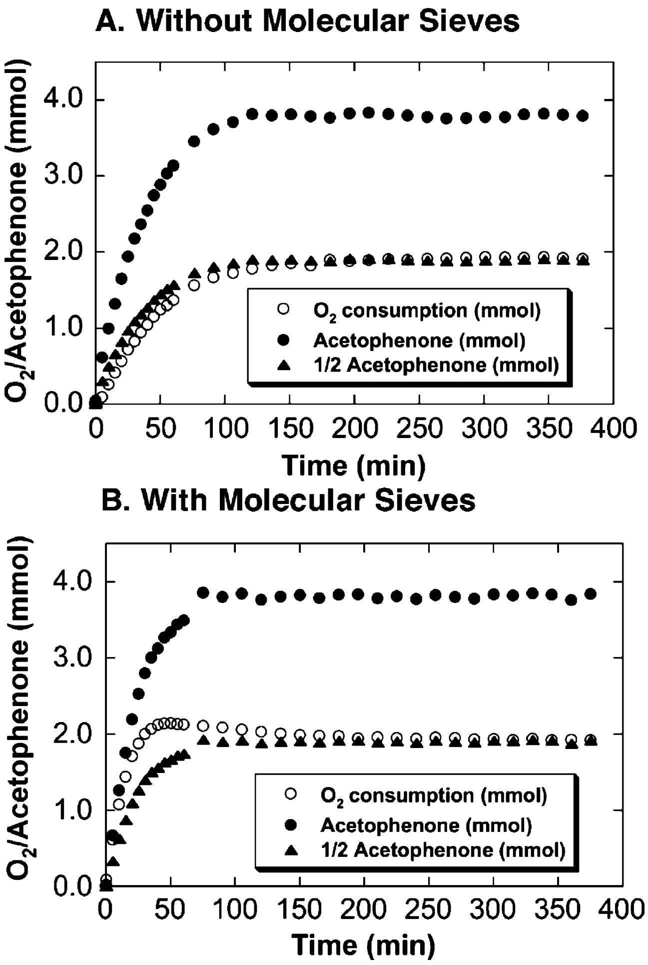

FIGURE 6. Comparison of dioxygen consumption and acetophenone production during Pd(OAc)$_2$/pyridine-catalyzed oxidation of 1-phenylethanol in the absence (A) and presence (B) of 3 Å molecular sieves present. Conditions: 12.5 mM Pd(OAc)$_2$, 50.0 mM pyridine, 250 mM 1-phenylethanol, 800 Torr O$_2$, 80 °C, 15 mL of toluene, ±0.750 g of 3 Å molecular sieves.

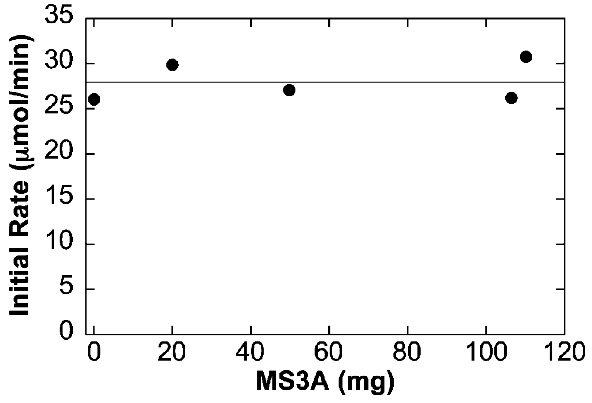

FIGURE 7. Dependence of the initial rate on 3 Å molecular sieves. Conditions: 2.5 mM Pd(OAc)$_2$, 730 Torr O$_2$, 0.52 M 1-phenylethanol, 0−116 mg of 3 Å molecular sieves, 2 mL of DMSO, 80 °C.

In contrast to the Pd(OAc)$_2$/pyridine system, molecular sieves have no effect on the initial rate of catalytic turnover (Figure 7). Another distinction between the two reactions is the fact that water inhibits the Pd(OAc)$_2$/DMSO-catalyzed reaction. This inhibitory effect is evident both in the absence and presence of activated MS3A (Figure 8; cf. Figures 1 and 3).

Whereas molecular sieves appear to have little effect on the rate of Pd(OAc)$_2$/DMSO-catalyzed alcohol oxidation, they do

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[21] This proposal contrasts with the earlier suggestion by Uemura that MS3A *promote* hydrogen peroxide disproportionation. In their study of benzyl alcohol oxidation,[3b] the O$_2$:benzaldehyde ratio was 1:1 in the absence of molecular sieves and 2:3 in the presence of molecular sieves. The theoretical value of 1:2 was not obtained in either case. Presently, we do not have an explanation for the conflicting data.

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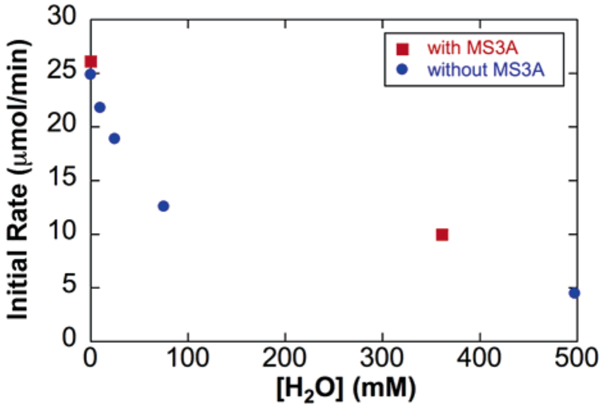

FIGURE 8. Dependence of the initial rate on water concentration. Conditions: (a) 2.5 mM $Pd(OAc)_2$, 730 Torr O_2, 0.52 M 1-phenylethanol, 0−500 mM H_2O, 2 mL of DMSO, 80 °C; (b) 2.5 mM $Pd(OAc)_2$, 730 Torr O_2, 0.52 M 1-phenylethanol, 0−360 mM H_2O, 116 mg of 3 Å molecular sieves, 2 mL of DMSO, 80 °C.

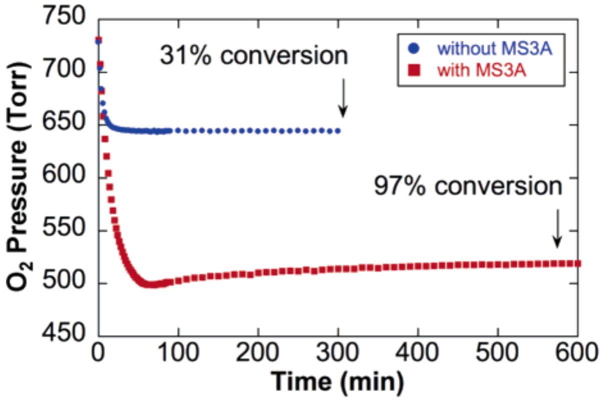

FIGURE 9. Typical reaction time courses with the $Pd(OAc)_2$/DMSO system. Conditions: (a) 2.5 mM $Pd(OAc)_2$, 730 Torr O_2, 520 mM 1-phenylethanol, 2 mL of DMSO, 80 °C; (b) 2.5 mM $Pd(OAc)_2$, 730 Torr O_2, 0.52 M 1-phenylethanol, 110 mg of 3 Å molecular sieves, 2 mL of DMSO, 80 °C.

impact the catalyst stability. With the use of 5 mol % $Pd(OAc)_2$ in DMSO, the oxidation of 1-phenylethanol proceeds to complete conversion, corresponding to 20 catalytic turnovers. At lower catalyst loading (0.5 mol % $Pd(OAc)_2$), higher total turnover numbers (TON = 62) are obtained, but the reaction does not proceed to completion (Figure 9). With the inclusion of MS3A, however, the reaction yield increases to 97% (TON = 194; Figure 9). Once again, molecular sieves appear to inhibit hydrogen peroxide disproportionation. The gas-uptake time course reveals that >0.5 equiv of dioxygen are consumed in the first 50−60 min of the reaction, after which the pressure equilibrates to a value corresponding to an O_2/acetophenone stoichiometry of 0.5.

In previously published control experiments, we demonstrated that hydrogen peroxide disproportionates rapidly under the catalytic reaction conditions;[23] however, the prior studies did not assess the effect of molecular sieves on the disproportionation rate. To address this question directly, $Pd(OAc)_2$ was added to a dimethyl sulfoxide (DMSO) solution of hydrogen peroxide attached to the gas-uptake apparatus. Rapid and quantitative evolution of molecular oxygen was observed (blue data, Figure 10). If the same experiment is conducted with MS3A present, the rate of disproportionation is significantly slower, reaching completion only after 25−30 h (red data, Figure 10). No hydrogen peroxide disproportionation is observed for several hours if $Pd(OAc)_2$ is not added to the solution. Although the origin of MS3A-induced retardation of the rate is not known, the data are consistent with the observations made during catalytic turnover (Figures 5, 6, and 9).

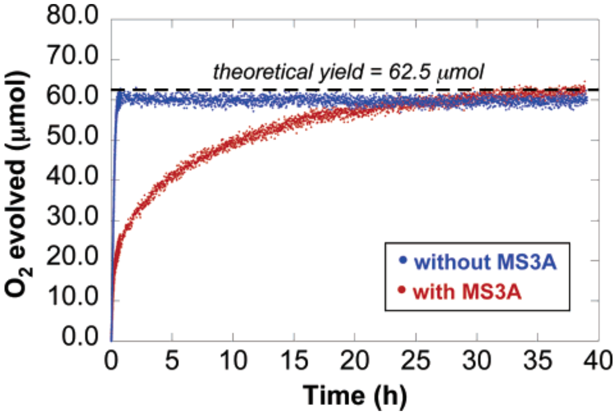

FIGURE 10. Effect of 3 Å molecular sieves on the rate of $Pd(OAc)_2$-catalyzed disproportionation of hydrogen peroxide in DMSO. See Experimental Section for reaction conditions.

Analysis of the Roles for Molecular Sieves in Pd-Catalyzed Aerobic Alcohol Oxidation. The data outlined above fail to support either of the previously proposed roles for molecular sieves in palladium-catalyzed aerobic oxidation reactions, namely, water sequestration and promotion of hydrogen peroxide disproportionation. In fact, the gas-uptake data for both $Pd(OAc)_2$/pyridine- and $Pd(OAc)_2$/DMSO-catalyzed reactions indicate that molecular sieves *stabilize* hydrogen peroxide and slow its disproportionation under catalytic conditions. Thus, the beneficial effect of molecular sieves must have a different origin. Any mechanistic proposal to explain the observations must account for two different phenomena: (1) MS3A enhance the rate of the $Pd(OAc)_2$/pyridine-catalyzed reactions and (2) they improve catalyst stability and lead to higher turnover numbers for both the $Pd(OAc)_2$/pyridine and $Pd(OAc)_2$/DMSO catalyst systems.[24]

The faster rates measured for the $Pd(OAc)_2$/pyridine system (Figure 4) can be partly attributed to the different O_2/product stoichiometry. Specifically, if H_2O_2 does not disproportionate, an apparent 2-fold rate enhancement will be obtained if the reaction rate is measured by gas-uptake methods because more gas is consumed per equivalent of alcohol. The rates of $Pd(OAc)_2$/pyridine-catalyzed alcohol oxidation, however, are more than a factor of 2 faster in the presence of molecular sieves. Therefore, another mechanistic explanation is needed.

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[23] For details of these control experiments, see the Supporting Information of ref 10. The precise mechanism of disproportionation is not known; however, the following qualitative observations have been made. Addition of aqueous hydrogen peroxide (30%) to a fresh solution of $Pd(OAc)_2$ (recrystallized from toluene) in DMSO results in rapid disproportionation. In contrast, if hydrogen peroxide is added to a suspension of palladium black obtained from a completed catalytic reaction, disproportionation is slow. These observations suggest that the Pd-catalyzed disproportionation mechanism may proceed via a Pd(II)/Pd(IV) cycle.

[24] Some of the observations made in this study are not fully understood and will require further study: (1) Why does water inhibit the $Pd(OAc)_2$/DMSO system but not the $Pd(OAc)_2$/pyridine system? (2) Why do molecular sieves enhance the rate of the $Pd(OAc)_2$/pyridine-catalyzed reaction but not the reaction conducted in DMSO?

Our prior mechanistic studies of $Pd(OAc)_2$/pyridine-catalyzed alcohol oxidation demonstrated that the catalytic rate in the absence of molecular sieves is defined by the half-reaction associated with Pd(II)-mediated alcohol oxidation (step i, Scheme 1), not dioxygen-coupled catalyst oxidation (step ii, Scheme 1). The similarity between the kinetic data (Figure 4) and isotope effects obtained in the absence and presence of MS3A reveal the stepwise mechanism for Pd(II)-mediated alcohol oxidation (eqs 3−6) is identical in the presence of molecular sieves. The enhanced catalytic rates in the presence of molecular sieves can be explained by recognizing that MS3A can serve as a weak Brønsted base. We have previously established that traditional Brønsted bases, such as acetate, enhance the catalytic turnover rate by reacting with acetic acid to favor preequilibrium formation of the Pd(II)−alkoxide intermediate **2** (eq 8, cf. eq 4).[11b] MS3A consist of aluminosilicate crystals with anionic charges localized on lattice oxygen atoms. Sodium and potassium ions are present to balance the charge. The Brønsted basic character of MS3A is widely recognized.[25] For example, a slurry of MS3A in deionized water registers a pH of 10.5.[26]

$$(\mathrm{py})_2\mathrm{Pd(OAc)}_2 + \mathrm{RCH_2OH} + \mathrm{B}\!: \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} (\mathrm{py})_2\mathrm{Pd(OAc)(OCH_2R)} + [\mathrm{BH}^+]\mathrm{OAc}^- \tag{8}$$

The other beneficial role of molecular sieves is their ability to enhance catalyst stability and increase the catalytic turnover numbers. This effect, which is evident for both the $Pd(OAc)_2$/pyridine and $Pd(OAc)_2$/DMSO catalyst systems, arises from the influence of molecular sieves on the relative rates of catalyst oxidation by O_2 and decomposition of the catalyst, V_{ii}/V_{iii} (i.e., steps ii and iii, Scheme 1). The $Pd(OAc)_2$/DMSO system is particularly susceptible to catalyst aggregation and formation of palladium black. We propose that molecular sieves provide a heterogeneous surface that can trap low nuclearity clusters or monomeric palladium species to inhibit bulk aggregation into inactive palladium metal. The low-nuclearity aggregates can potentially reenter the catalytic cycle via reaction with molecular oxygen to form soluble palladium(II) species. This hypothesis finds support from the recent literature in the field of palladium-catalyzed cross-coupling chemistry.[27] The latter reactions often utilize a colloidal or heterogeneous palladium source as the catalyst, but recent mechanistic studies indicate that aryl halides react with surface palladium atoms and generate soluble palladium species that perform the cross-coupling chemistry in solution.[28]

The ability of molecular sieves to stabilize the reduced palladium catalyst has important implications for palladium-catalyzed aerobic oxidation reactions. Whereas palladium-catalyzed cross-coupling reactions commonly feature soft donor ligands such as phosphines to stabilize palladium(0) and prevent aggregation of palladium metal, these ligands generally decompose rapidly under oxidizing reaction conditions such as those described here. Oxidatively stable ligands, for example, pyridine, enable catalytic turnover (cf. Figure 4C), but they are not as effective as phosphines in preventing catalyst decomposition. The inclusion of molecular sieves (and presumably other heterogeneous additives) in homogeneous palladium-catalyzed oxidation reactions provides an alternative strategy for achieving improved catalytic lifetimes and/or activities. Recently, several examples of heterogeneous palladium catalysts have been reported with very good activity for aerobic alcohol oxidation. Effective heterogeneous supports include carbon,[29] TiO_2,[30] pumice,[31] hydrotalcite,[32] and hydroxyapatite.[33]

Conclusion

In summary, we have gained mechanistic insights into the role of molecular sieves in $Pd(OAc)_2$/pyridine- and $Pd(OAc)_2$/DMSO-catalyzed aerobic alcohol oxidation. Quite unexpectedly, we found that the water-absorbing properties of MS3A are not associated with the improved catalytic reactivity. Nor do molecular sieves promote hydrogen peroxide disproportionation. The data suggest that molecular sieves enhance the rate of the $Pd(OAc)_2$/pyridine-catalyzed reaction by serving as a heterogeneous Brønsted base, and for both catalyst systems, molecular sieves increase the catalyst stability. The latter effect seems to arise from the ability of MS3A to provide a heterogeneous surface that hinders bulk aggregation of palladium metal.

Experimental Section

Palladium acetate was recrystallized prior to use from benzene/acetic acid.[34] Oxygen gas, anhydrous dimethyl sulfoxide, benzyl alcohol, 1-phenylethanol, 2,5-dimethoxybenzyl alcohol, pyridine, acetic acid, hexadecane, lithium aluminum deuteride, benzoic acid, and benzaldehyde were used without purification. Toluene and diethyl ether were purified by passage through a column of activated alumina and Q4. Powdered MS3A were activated by flowing N_2 through a glass tube of sieves maintained at 200 °C. Benzyl alcohol-d_1 and -d_2 (i.e., PhCH(D)OH and $PhCD_2OH$) were prepared by standard methods via reduction of benzaldehyde and benzoic acid, respectively, with lithium aluminum deuteride. In-situ FTIR spectroscopy was conducted with an FTIR spectrometer fitted with an immersion probe with a ZnSe ATR crystal.

Gas-Uptake Kinetics for the $Pd(OAc)_2$/Pyridine System. A typical reaction was conducted as follows. $Pd(OAc)_2$ (11.2 mg, 50 μmol) and MS3A (0.50 g) were added to a 25 mL round-bottom flask with a stir bar. A solution of pyridine (22.3 mM in toluene, 9.00 mL) was added to the flask containing $Pd(OAc)_2$. The flask was attached to an apparatus with a calibrated volume equipped

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with a computer-interfaced pressure transducer. The apparatus was evacuated to 300 Torr and filled with oxygen to 900 Torr, and this cycle was repeated 10 times. The pressure was set initially to 700 Torr, and the flask was heated to 80 °C. When the pressure stabilized in the apparatus, benzyl alcohol (1.0 M in toluene, 1.00 mL) was added via syringe through a septum. Data were acquired using custom software written within LabVIEW. Correlations between oxygen uptake and conversion were made by analysis by gas chromatography with hexadecane as an internal standard or by ^{1}H NMR spectroscopy.

Kinetic Experiments with the Addition of Water to the Pd$(OAc)_2$/Pyridine System. The typical procedure described above was followed except that the water ($\leq$36 μL) was added to the bottom of the reaction flask prior to adding the solution of pyridine.

Gas-Uptake Kinetics for the Pd$(OAc)_2$/DMSO System. A typical reaction was conducted as follows. Pd$(OAc)_2$ (5.4 mg, 24 μmol) was added to a 25 mL round-bottom flask with a stir bar, and a rubber septum was placed on the flask. The flask was evacuated completely and filled with nitrogen, and this cycle was repeated five times. Dimethyl sulfoxide (9.00 mL) was added to flask containing Pd$(OAc)_2$ under nitrogen and stirring was commenced. Separately, activated MS3A (0.11 g) was added to a separate flask, which was immediately attached to the volume-calibrated gas-uptake apparatus. The apparatus was immediately evacuated to 30 Torr and filled with oxygen to 900 Torr, and this cycle was repeated 10 times. The pressure was established at 670 Torr before Pd$(OAc)_2$ (2.67 mM in DMSO, 1.875 mL) was added via syringe through a septum. The flask was heated to 80 °C. When the pressure stabilized in the apparatus, 1-phenylethanol (0.125 mL, 1.04 mmol) was added via syringe through a septum. Data were acquired using custom software written within LabVIEW. Correlations between oxygen uptake and conversion were made by analysis by gas chromatography with hexadecane as an internal standard or by ^{1}H NMR spectroscopy.

Catalytic Reaction Monitored by Simultaneous Gas-Uptake/in-Situ FTIR Spectroscopy. Pd$(OAc)_2$ (42.0 mg, 187 μmol) and MS3A (0.75 g) were added to a three-necked 125 mL round-bottom flask with a stir bar. A solution of pyridine (53 mM in toluene, 14.00 mL) was added to Pd$(OAc)_2$. The flask was attached to the in-situ FTIR probe with a 24/40 adapter and an O-ring seal through one of the necks of the flask. The flask was also attached to the volume-calibrated gas-uptake apparatus through another neck of the flask. A glass stopper was added to the remaining neck of the flask. The apparatus was evacuated to 300 Torr and filled with oxygen to 900 Torr, and this cycle was repeated 10 times. The pressure was established at 700 Torr, and the flask was heated to 80 °C. When the pressure stabilized in the apparatus, 1-phenylethanol (3.73 M in toluene, 1.00 mL) was added via syringe through a septum. Gas-uptake data were acquired using custom software written within LabVIEW.

Monitoring the Effect of MS3A on the Rate of H_2O_2 Disproportionation. Solutions of H_2O_2 (30% aqueous) and Pd$(OAc)_2$ in DMSO were prepared (27.8 mM and 24.9 mM, respectively). Four 25 mL round-bottom flasks were attached to a multiwell gas-uptake apparatus, each equipped with a magnetic stir bar. Two of the flasks (A and B) contained 300 mg of MS3A. The other two flasks (C and D) contained only the stir bar. The four flasks were evacuated and back-filled with O_2 to an initial pressure of 650 Torr. To each vessel, 4.5 mL of the H_2O_2 solution were added. Subsequently, 0.5 mL of the Pd$(OAc)_2$ solution was added to vessels A and C, and the pressures in the sealed reaction vessels were monitored for 40 h. A summary of the reaction components in each vessel is as follows: vessel A, MS3A, 2.5 mM Pd$(OAc)_2$, 25 mM H_2O_2; vessel B, MS3A, 27.8 mM H_2O_2; vessel C, 2.5 mM Pd$(OAc)_2$, 25 mM H_2O_2; vessel D, 27.8 mM H_2O_2.

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