

Supporting Information

Aerobic Dehydrogenation of Cyclohexanone to Phenol Catalyzed by Pd(TFA)₂/2-Dimethylaminopyridine: Evidence for the Role of Pd-Nanoparticles

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1. General Considerations.

$\text{Pd}(\text{TFA})_2$ was synthesized according to literature procedures.¹ All other commercially available compounds were purchased from Sigma-Aldrich and used as received. Gas chromatographic analysis of reactions was conducted with a Shimadzu GC-2010 Plus gas chromatograph with a RTX-5 column and referenced to an internal standard (1,4-dimethoxybenzene).

DLS samples were prepared by using filtered solvents (1 μm PTFE). The solution of palladium and/or the catalytic reaction mixture were filtered through a pad of glass wool into a dust free culture tube. DLS experiments were carried out with a 100 mW, 532 nm laser (Compass 315-100, Coherent, Santa Clara, CA) illuminating a temperature controlled glass cell at 25 °C filled with a refractive-index matching fluid (decahydronaphthalene, Fisher Scientific, Pittsburgh, PA) and the sample. The scattering of light was measured at 90° and the autocorrelation functions were obtained using a BI-9000AT digital autocorrelator (Brookhaven Instruments, Holtsville, NY). A calibration procedure was carried out on a diluted monodispersed suspension of polystyrene beads dissolved in water. Several observations suggest the DLS experiments are not complicated by the presence of dust particles. In cases that provide evidence of large particle sizes, the DLS experiments were performed with several independent catalytic reaction mixtures, and bulk Pd black is visibly evident in each of these mixtures. In contrast, when using identical sample preparation methods, no Pd particles (or dust) were detected by DLS analysis of the initial Pd-containing solutions or from solutions of a complementary homogeneous $\text{Pd}(\text{DMSO})_2(\text{TFA})_2$ -catalyzed dehydrogenation of cyclohexanone to cyclohexenone (see Section 14).

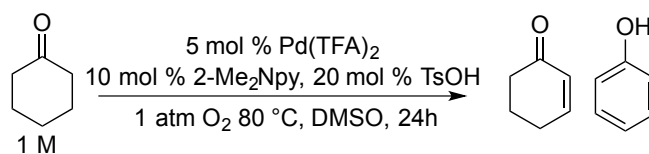
TEM samples were prepared by removing approx 10 μL aliquots from the catalytic reaction mixture and diluting with 1 mL of methanol. 5 μL of this solution was added to a TEM grid (EMS, holey carbon, 300 mesh, copper) and allowed to dry. TEM imaging was carried out on a Tecnai T12 instrument, equipped with energy dispersive X-ray (EDX) capability.

2. General Protocol for Acquisition of Kinetic Data.

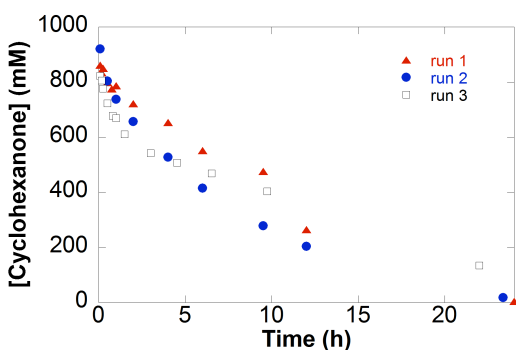
Appropriate quantities of DMSO stock solutions of $\text{Pd}(\text{TFA})_2$, *p*-toluenesulfonic acid, 2-dimethylaminopyridine, and 1,4-dimethoxybenzene (int. std.) were added to oven-dried disposable 13 mm culture tubes. The tubes were then placed in a 48-well aluminum block mounted on a Large Capacity Mixer (Glas-Col). This apparatus enables several reactions to be performed simultaneously under a constant pressure of O_2 (approx 1 atm) with controlled temperature and orbital agitation. The headspace above the tubes was purged with oxygen gas for ca. 5 min. The reactions were heated to 80 °C while vortexing under 1 atm of O_2 . Upon reaching 80 °C, stock solutions of substrate and other appropriate additives (e.g. phenol, water, PVPy, Hg, or phenathroline) were added into the reaction vessel. Aliquots (~ 10 μL) were removed periodically and analyzed by gas chromatography.

3. Assessment of Kinetic Reproducibility.

There are challenges associated with obtaining reliable kinetic data if the experiments are performed on different days or with different stock solutions (e.g., Figure S1A). Kinetic time courses suitable for quantitative comparisons could be achieved by performing a series of parallel experiments on the same day, and using the same stock solutions and in the same reaction apparatus (Figure S1B).



(A) Cyclohexanone Consumption - Different Reactions



(B) Cyclohexanone Consumption - Reactions in Parallel

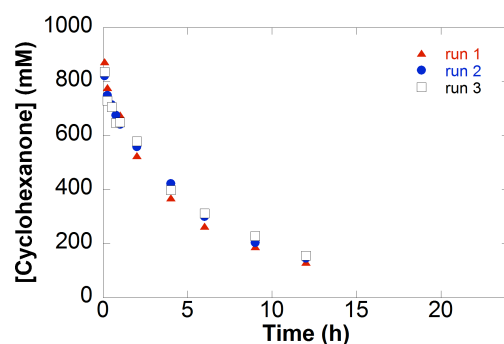


Figure S1. Comparison of kinetic time courses for the dehydrogenation of cyclohexanone to phenol (A) between different reactions on different days and (B) trials in parallel reactions. [cyclohexanone] = 1 M (0.5 mmol), [Pd(TFA)₂] = 0.05 M (0.025 mmol), [2-Me₂Npy] = 0.1 M (0.05 mmol), [TsOH] = 0.2 M (0.1 mmol), DMSO for V_{Total} of 0.5 mL, 1 atm O₂, 80 °C.

4. Dehydrogenation of Cyclohexanone to Cyclohexenone: Examination of Early Time Points.

The kinetic order of the palladium was obtained to probe the nature of the catalyst. Palladium concentrations, $[\text{Pd}(\text{TFA})_2]$, of 0, 1, 2.5, 5, 7.5, and 10 mM were used and the initial rates of the reactions were monitored by GC through 10 % conversion of the substrate (Figure S2.).

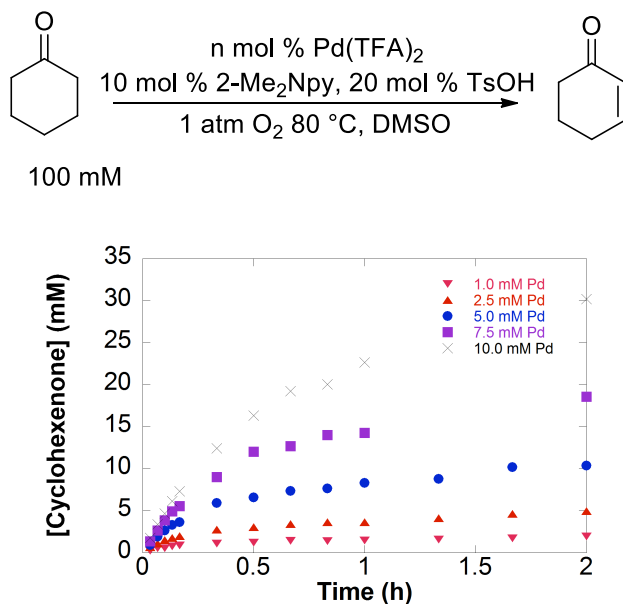


Figure S2. Initial kinetic timecourses for the formation of cyclohexenone from cyclohexanone at varying $[\text{Pd}(\text{TFA})_2]$. Reaction conditions: $[\text{cyclohexanone}] = 100 \text{ mM}$ (0.05 mmol), $[\text{Pd}(\text{TFA})_2] = 0 - 10 \text{ mM}$ (0 - 5 mmol), $[\text{2-Me}_2\text{Npy}] = 0.01 \text{ M}$ (0.005 mmol), $[\text{TsOH}] = 0.02 \text{ M}$ (0.01 mmol), DMSO for V_{Total} of 0.5 mL, 1 atm O_2 , $80 \text{ }^\circ\text{C}$.

5. Dehydrogenation of Cyclohexenone to Phenol: Examination of the Induction Period

The kinetic order of the cyclohexenone was obtained in the cyclohexenone-to-phenol dehydrogenation reaction. Cyclohexenone concentrations of 25, 50, 100, 200, 300, and 400 mM were used and the kinetic time courses were monitored (Figure S3) by GC.

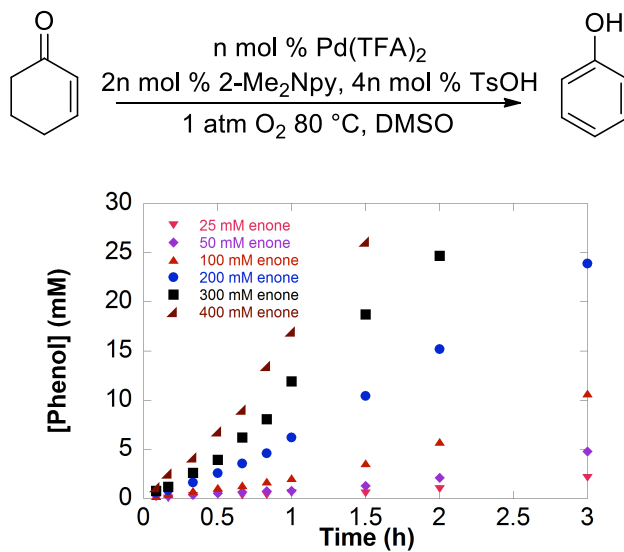


Figure S3. Initial kinetic time courses for the formation of phenol from cyclohexenone at varying [cyclohexenone]. Reaction conditions: $[\text{Pd}(\text{TFA})_2] = 0.005$ M (0.0025 mmol), $[2\text{-Me}_2\text{Npy}] = 0.01$ M (0.005 mmol), $[\text{TsOH}] = 0.02$ M (0.01 mmol), DMSO for V_{Total} of 0.5 mL, 1 atm O_2 , 80 °C. $[\text{cyclohexenone}] = 25, 50, 100, 200, 300, 400$ mM

6. Assessment of Autocatalysis.

The cyclohexenone-to-phenol dehydrogenation step exhibits an induction period. This induction period could arise from autocatalysis, where the product (e.g. phenol or water) accelerates the reaction. Addition of 12 mol % of phenol or 10 mol % H_2O^2 to the initial reaction mixture did not increase the rate of the reaction (Figure S4); the rates are all identical to the experiment lacking addition of products. This observation suggests that rate acceleration from the products is not the case.

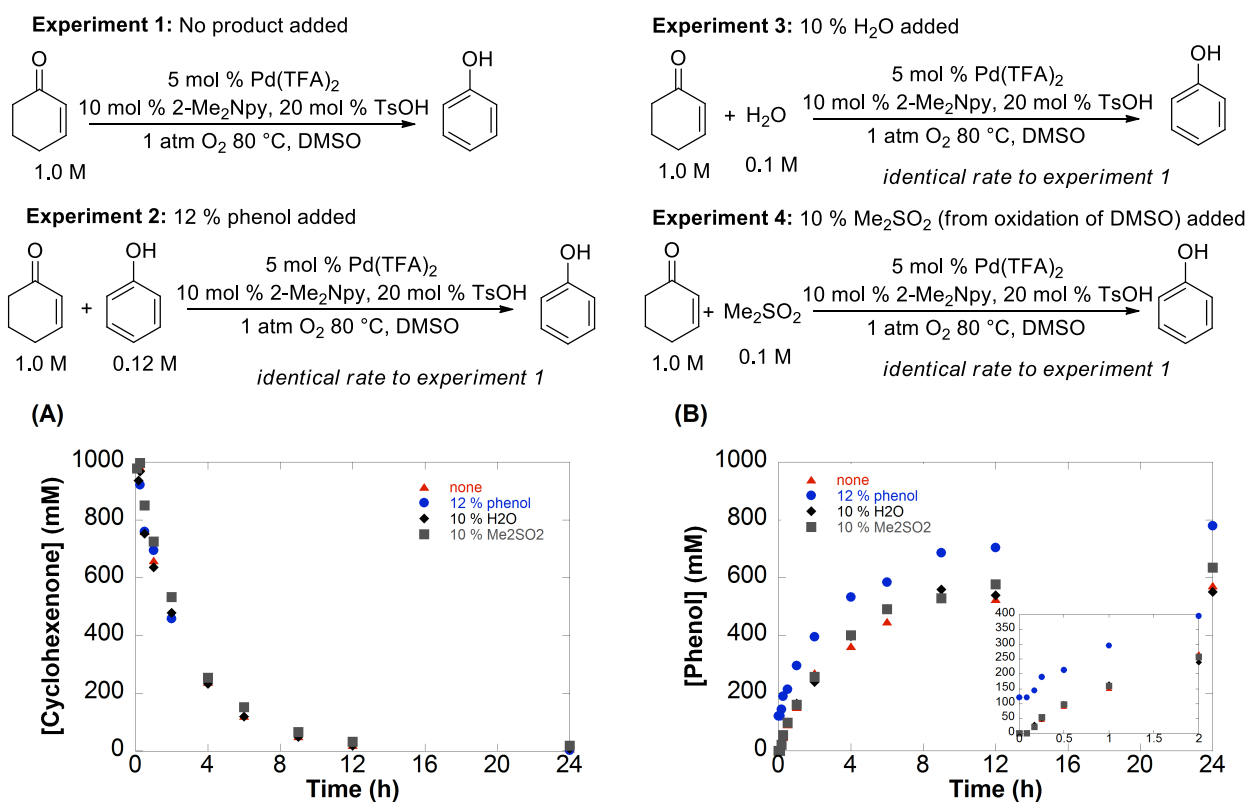


Figure S4. Plot phenol formation in the presence of 12 mol % phenol, 10 mol % H_2O or Me_2SO_2 shows no rate acceleration. Inset shows a blow up of the initial 2 hours, where the induction period is still observable. Reaction conditions: [substrate] = 1 M (0.5 mmol), $[\text{Pd(TFA)}_2]$ = 0.05 M (0.025 mmol), $[\text{2-Me}_2\text{Npy}]$ = 0.1 M (0.05 mmol), $[\text{TsOH}]$ = 0.2 M (0.1 mmol), phenol/ H_2O = 0.07M (0.04 mmol), DMSO for V_{Total} of 0.5 mL, 1 atm O_2 , 80 °C.

7. Filtration Tests: Analysis of the Precipitate and Supernatant After a Catalytic Reaction.

Palladium black and mirror are often observed after the dehydrogenation reactions. After the independent 24 h dehydrogenations of cyclohexanone, 3-methylcyclohexanone, cyclohexenone, and 3-methylcyclohexenone, the catalytic activity of the supernatants and the precipitates were assessed. In all instances, the supernatant retains catalytic activity, albeit with variability in yields (Tables S1 and S2, compare entries 1 and 2). Meanwhile, the precipitates show negligible catalytic activity (entries 3, $\leq 5\%$ yield).

Table S1. Analysis of Reaction Supernatants and Precipitates from the Dehydrogenation of Cyclohexanones.

1.0 M

1.0 M

Entry	Catalytic solution	% Enone	% Phenol
1	Fresh Catalyst	3(2)	72(8)
2	Catalyst Supernatant ^a	1(1)	74(11)
3	Catalyst Precipitate ^a	4(4)	3(2)

Entry	Catalytic solution	% Enone	% Phenol
1	Fresh Catalyst	4(1)	79(1)
2	Catalyst Supernatant ^a	1(1)	61(7)
3	Catalyst Precipitate ^a	1(1)	4(1)

^aSupernatant of entry 1 was removed by pipette, the remaining precipitate was washed with 50 μ L of solvent and fresh substrate was added to test for the activity of the precipitate. Reaction conditions for fresh catalyst: [substrate] = 1 M, [Pd(TFA)₂] = 0.05 M, [2-Me₂Npy] = 0.1 M, [TsOH] = 0.2 M, DMSO for V_{Total} of 0.5 mL, 1 atm O₂, 80 °C.

Table S2. Analysis of Reaction Supernatants and Precipitates from the Dehydrogenation of Cyclohexenones.

1.0 M

1.0 M

Entry	Catalytic solution	% Phenol
1	Fresh Catalyst	92(5)
2	Catalyst Supernatant ^a	83(3)
3	Catalyst Precipitate ^a	5(4)

Entry	Catalytic solution	% Phenol
1	Fresh Catalyst	67(6)
2	Catalyst Supernatant ^a	96(3)
3	Catalyst Precipitate ^a	3(2)

^a Supernatant of entry 1 was removed by pipette, the remaining precipitate was washed with 50 μ L of solvent and fresh substrate was added to test for the activity of the precipitate. Reaction conditions for fresh catalyst: [substrate] = 1 M, [Pd(TFA)₂] = 0.05 M, [2-Me₂Npy] = 0.1 M, [TsOH] = 0.2 M, DMSO for V_{Total} of 0.5 mL, 1 atm O₂, 80 °C.

8. Hot Filtration Tests

Hot filtration tests of the reaction mixtures were employed according to the protocol of Maitlis.³ Independent dehydrogenation reactions of cyclohexanone and cyclohexenone were carried out to low ($\leq 20\%$) conversion, and the hot reaction mixtures were filtered through a layer of Celite 535 or through a 200 nm PTFE filter to remove particles greater than approximately 3.3⁴ and 200 nm, respectively. While the filtrand shows no catalytic activity, the filtrate continues to catalyze the reaction, with reduced yields of phenol relative to the unfiltered reaction after 24 h (Table S3, entries 1, 2, 5). The control reactions of Celite addition without filtration shows the yield reduction is not attributed to the presence of Celite (entry 4). Reaction time course is presented in Figure S5.

Procedure for Hot Filtration Tests: Four oven-dried culture tubes were charged with 450 μL of a stock solution containing $\text{Pd}(\text{TFA})_2$ (93.2 mg, 0.28 mmol; each vessel: 0.025 mmol), *p*-toluenesulfonic acid (216.7 mg, 1.14 mmol; each vessel: 0.103 mmol), 2-dimethylaminopyridine (67.6 mg, 0.55 mmol; each vessel: 0.050), and 1,4-dimethoxybenzene as the internal standard in 5 mL of DMSO and placed with 3 empty oven-dried culture tubes in the parallel-reaction apparatus described above. The headspace above the tubes was purged with oxygen gas for ca. 5 min. The reactions were heated to 80 $^\circ\text{C}$ while vortexing under 1 atm of O_2 . Upon reaching 80 $^\circ\text{C}$, stock solutions of substrate (0.5 mmol) were added. Aliquots ($\sim 10 \mu\text{L}$) were removed periodically and analyzed by gas chromatography. After $< 20\%$ conversion, Celite (25 mg) was added to two reactions and allowed to vortex for 2 min, after which one Celite containing mixture was filtered through a plug of glass wool, washing with 200 μL of DMSO into another clean culture tube. Meanwhile, a third reaction was filtered through a 0.2 μm PTFE filter syringe, washing with 300 μL of DMSO into a clean culture tube. Aliquots of both filtrates were removed immediately after filtration to ensure little change to the dehydrogenation activity. To the remaining clean culture tube, the Celite filtrand, 450 μL DMSO, 1,4-dimethoxybenzene internal standard, and substrate were added. The reactivity of these final five reaction mixtures were monitored by GC.

Table S3. Hot Filtration Data for the Dehydrogenation of Cyclohexanone after Filtration with Celite 535 and 0.2 μm PTFE Filter.

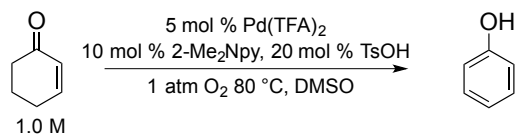
1.0 M

Filtration through Celite/0.2 μm PTFE filter after 15 min

Entry	Catalytic solution	% Product at Time								
		0.25 h	0.5 h	1 h	4 h		8 h		24 h	
		% enone	% enone	% enone	% enone	% phenol	% enone	% phenol	% enone	% phenol
1	no filtration	20(3)	20(3)	27(8)	23(1)	17(6)	11(4)	41(8)	0	49(5)
2	Celite filtrate	18(4)	// 19(10)	27(3)	20(3)	5(3)	16(1)	16(2)	5(1)	35(6)
3	Celite layer	0	0	1(1)	3(3)	0	5(5)	0	3(3)	0
4	add Celite, no filtration	18(4)	// 18(1)	23(4)	18(2)	14(4)	11(2)	30(2)	0	52(1)
5	PTFE filtrate	23(11)	// 29(24)	36(15)	28(9)	2(2)	20(5)	8(2)	9(4)	38(23)

// Denotes that the reaction mixture was manipulated between the adjacent time points.

Table S4. Hot Filtration Data for the Dehydrogenation of Cyclohexenone after Filtration with Celite 535 and a 0.2 μm PTFE Filter.



Filtration through Celite/0.2 μm PTFE filter after 30 min

Entry	Catalytic solution	% Phenol at Time				
		0.5 h	1 h	4 h	8 h	24 h
1	no filtration	10(1)	15(1)	36(5)	44(3)	50(2)
2	Celite filtrate	10(1) //	12(1)	35(4)	53(4)	63(3)
3	Celite layer	0	0	0	1(1)	4(4)
4	add Celite, no filtration	10(1) //	16(1)	37(3)	53(11)	59(11)
5	PTFE filtrate	11(3) //	15(6)	33(1)	56(5)	65(5)

// Denotes that the reaction mixture was manipulated between the adjacent time points.

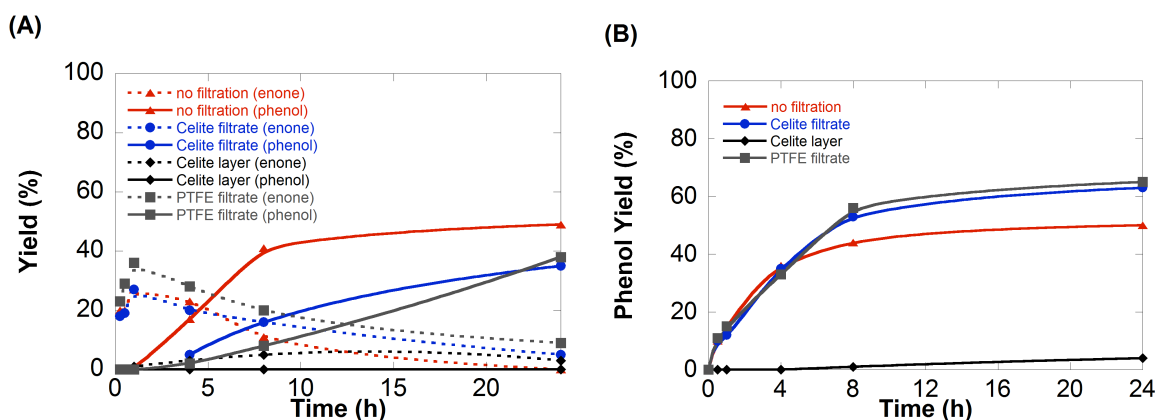


Figure S5. Catalytic activity after filtration through Celite 535 using the following starting substrate: (A) cyclohexenone at $t = 0.25$ h and (B) cyclohexenone at $t = 0.5$ h. (Dash lines represent cyclohexenone and solid lines represent phenol formation.) Reaction conditions: [substrate] = 1 M (0.5 mmol), $[\text{Pd(TFA)}_2]$ = 0.05 M (0.025 mmol), $[\text{2-Me}_2\text{Npy}]$ = 0.1 M (0.05 mmol), $[\text{TsOH}]$ = 0.2 M (0.1 mmol), DMSO for V_{Total} of 0.5 mL, 1 atm O_2 , 80 $^\circ\text{C}$. Similar results with 200 nm PTFE filters and the control reaction in the presence of Celite without filtration.

9. Hg Poisoning Study with the Pd(DMSO)₂(TFA)₂ Catalyst System.

A Hg poisoning study was performed with the Pd(DMSO)₂(TFA)₂-catalyzed aerobic dehydrogenation of cyclohexanone to cyclohexenone. This catalyst system has been proposed to proceed via a homogeneous Pd^{II} to Pd⁰ cycle. Figure S6 shows the continued reactivity for several hours after Hg addition.

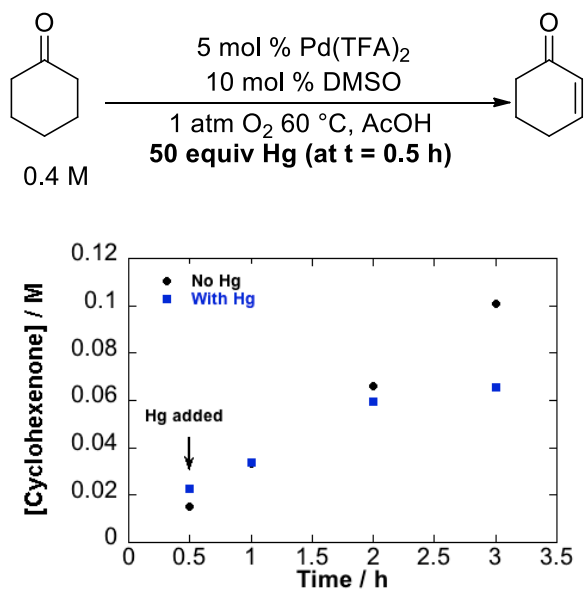
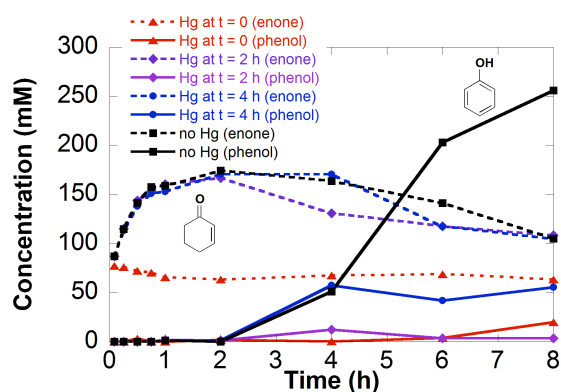
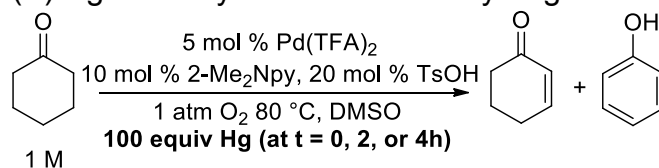


Figure S6. Continued reactivity for 3 turnovers for the dehydrogenation of cyclohexanone to cyclohexenone with the addition of 50 equiv of Hg at t = 0.5 h using Pd(TFA)₂(DMSO)₂ catalyst system. Reaction conditions: [substrate] = 0.4 M (0.2 mmol), [Pd(TFA)₂] = 0.02 M (0.01 mmol), [DMSO] = 0.04 M (0.02 mmol), Hg = 100 mg (0.5 mmol), AcOH for V_{Total} of 0.5 mL, 1 atm O₂, 60 °C.

10. Hg Poisoning Study with the Pd(TFA)₂/2-Me₂Npy Catalyst System.

Excess Hg (100 equiv) was added to the Pd(TFA)₂/2-Me₂Npy-catalyzed dehydrogenation of cyclohexanone and cyclohexenone. Presented below in Figures S7A and S7B are the full data for Hg addition to cyclohexanone and cyclohexenone dehydrogenation, respectively.

(A) Hg Test: Cyclohexanone Dehydrogenation



(B) Hg Test: Cyclohexenone Dehydrogenation

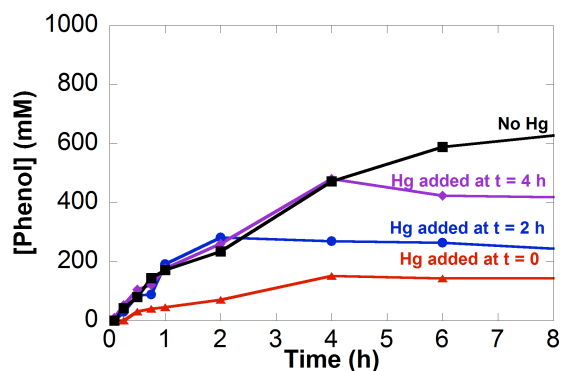
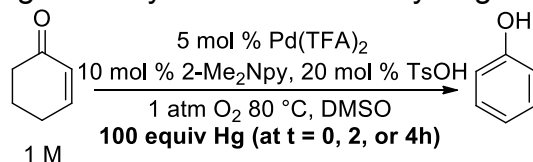
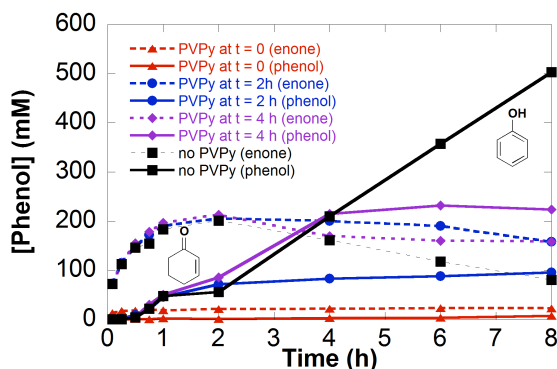
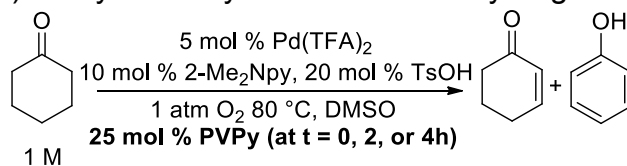


Figure S7. Reaction inhibition of phenol formation with the addition of 100 equiv of Hg at $t = 0$, 2, and 4 h using (A) cyclohexanone and (B) cyclohexenone. Dashed lines indicate cyclohexenone and solid lines indicate phenol formation. Reaction conditions: [substrate] = 1 M (0.5 mmol), [Pd(TFA)₂] = 0.05 M (0.025 mmol), [2-Me₂Npy] = 0.1 M (0.05 mmol), [TsOH] = 0.2 M (0.1 mmol), Hg = 500 mg (2.49 mmol), DMSO for V_{Total} of 0.5 mL, 1 atm O₂, 80 °C.

11. Poly(4-vinyl-pyridine) Poisoning Study with Pd(TFA)₂/2-Me₂Npy Catalyst System.

Excess PVPy (25 equiv) was added to the Pd(TFA)₂/2-Me₂Npy-catalyzed dehydrogenation of cyclohexanone and cyclohexenone. Presented below in Figures S8A and S8B are the full data for PVPy addition to cyclohexanone and cyclohexenone dehydrogenation, respectively.

(A) PVPy Test: Cyclohexanone Dehydrogenation



(B) PVPy Test: Cyclohexenone Dehydrogenation

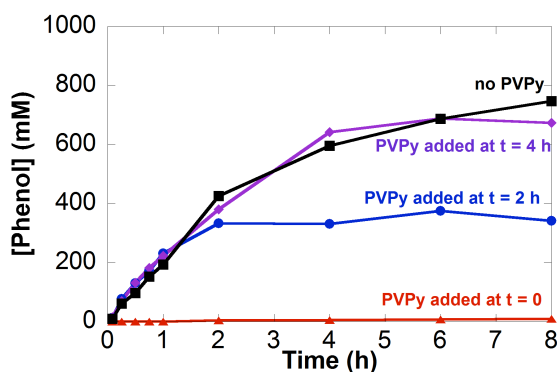
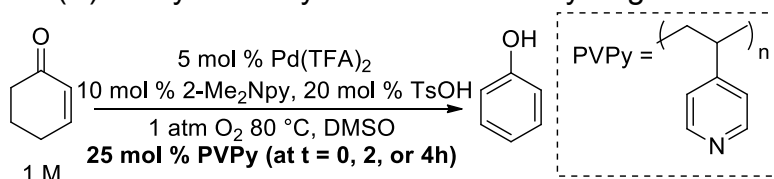


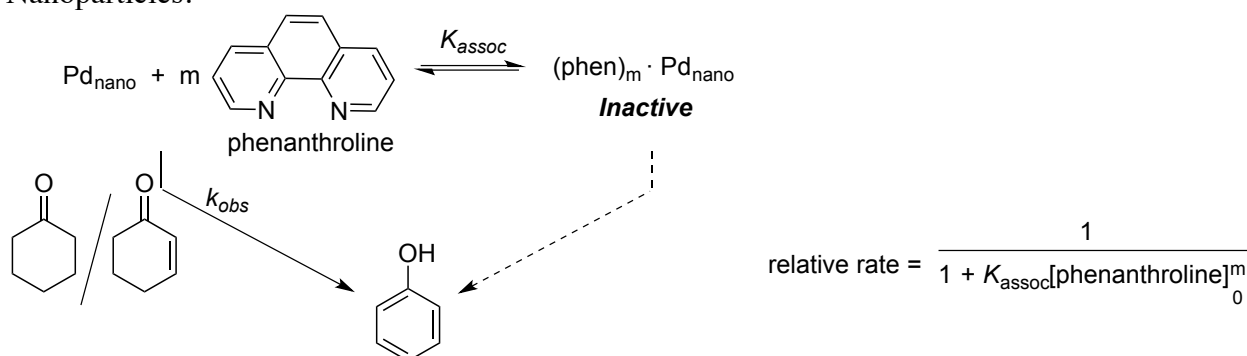
Figure S8. Reaction inhibition of phenol formation with the addition of 25 equiv of poly(4-vinylpyridine) at $t = 0, 2,$ and 4 h using (A) cyclohexanone and (B) cyclohexenone. Dashed lines indicate cyclohexenone and solid lines indicate phenol formation. Reaction conditions: [substrate] = 1 M (0.5 mmol), [Pd(TFA)₂] = 0.05 M (0.025 mmol), [2-Me₂Npy] = 0.1 M (0.05 mmol), [TsOH] = 0.2 M (0.1 mmol), PVPy = 65 mg, DMSO for V_{Total} of 0.5 mL, 1 atm O₂, 80 °C.

12. Attempted Quantitative Poisoning Study with Pd(TFA)₂/2-Me₂Npy Catalyst System.

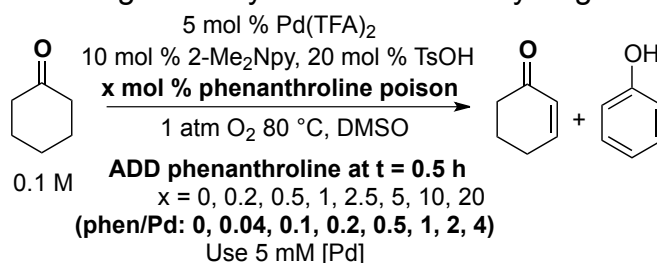
Phenanthroline (phen) has been used as a quantitative poison to probe the number of active sites with nanoparticle catalysts. A thorough presentation of this methodology has been elaborated by Finke and coworkers and will not be reproduced here.⁵ The catalytic activity of Pd(TFA)₂/2-Me₂Npy-catalyzed dehydrogenation of cyclohexanone and cyclohexenone was assessed as a function of the concentration of added phen, with phen:Pd ratios of 0.04, 0.1, 0.2, 0.5, 1.0, 2.0, and 4.0. The time-course data for dehydrogenation reactions of cyclohexanone and cyclohexenone in the presence of varying quantities of phen are shown in Figures S9 and S10, respectively. Phen was added to the reaction mixtures at $t = 0.5$ (cyclohexanone) and 1.5 h (cyclohexenone), after the kinetic burst and induction periods, respectively. The experiment was repeated for the cyclohexenone dehydrogenation reaction, with phen added at $t = 5$ h (Figure S11), when the particles were expected to be larger than those at $t = 1.5$ h.

Plots of the relative initial rates (after addition of the phenanthroline poison) as a function of [phen] afforded sigmoidal poisoning curves (Figures S9C, S10B and S11B). Finke has attributed sigmoidal plots of this type to the involvement of a reversible, weak-binding poison,⁵ for which the mechanistic model is depicted in Scheme S1. The relative reaction rate is a function of the binding equilibrium constant (K_{assoc}), [phen], and the phen:Pd stoichiometry in the deactivated form of the catalyst (m). Application of the rate equation to fit the sigmoidal curves yielded $m = 1.6$ for cyclohexanone dehydrogenation and $m = 1.3$ and 1.8 for cyclohexenone dehydrogenation with phen addition at $t = 1.5$ and 5 h, respectively. The latter apparent increase in phen:Pd stoichiometry suggests that more catalytic active sites are present with larger Pd nanoparticles. This result is unexpected because the number of active sites should decrease with increasing nanoparticle size. The origin of this anomaly was not fully elucidated, but several considerations suggest that the "weak binding" model is not appropriate in this case. Phen-stabilized Pd nanoparticles have been the focus of extensive investigation by Moiseev and coworkers, including in aerobic oxidation reactions.⁶ Analysis of a ¹H NMR spectrum of a phen poisoned (phen:Pd = 4.0) reaction mixture does not show any free (unbound) phen present in solution. We speculate that phen binds sufficiently tightly to Pd in the nanoparticles that it perturbs the Pd speciation under the reaction conditions and results in unreliable quantitative poisoning data.

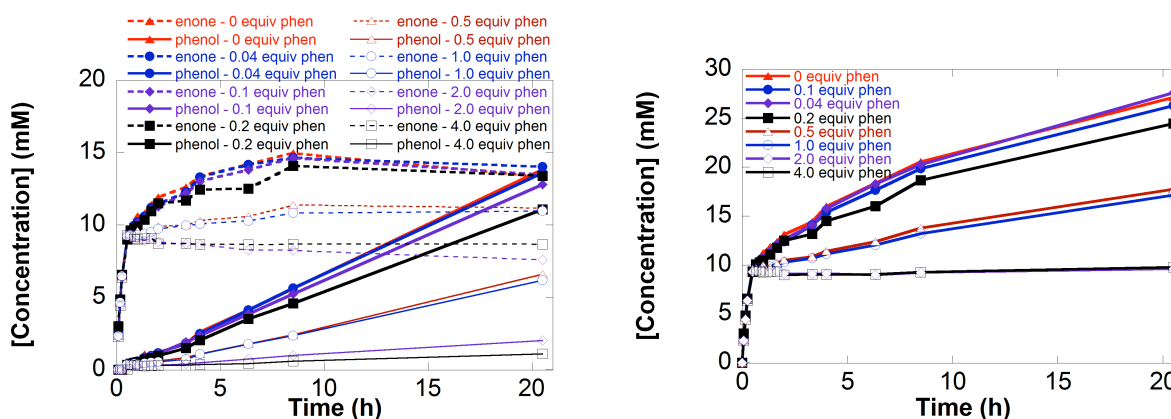
Scheme S1. Weak-Binding Poison Kinetic Model for Phenanthroline Poisoning of Pd Nanoparticles.⁵



Quantitative Poisoning Test: Cyclohexanone Dehydrogenation at t = 0.5 h



(A) Time Courses of Individual Products (B) Time Course of Total Products (Cyclohexenone + Phenol)



(C) Determination of m (phen: Pd stoichiometry in the poisoned catalyst)

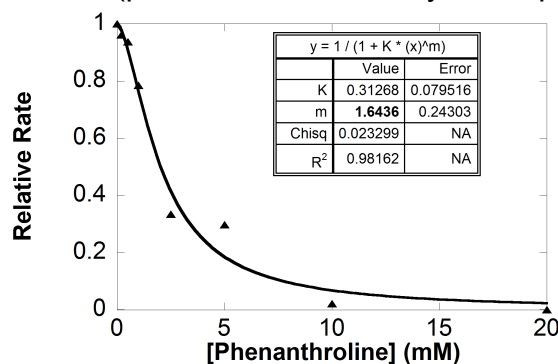


Figure S9. Reaction time course plots showing inhibition of cyclohexanone dehydrogenation upon addition of varying [phen] at t = 0.5 h, showing (A) the full time course with cyclohexenone and phenol product formation separately and (B) the full time course with the sum of both cyclohexenone and phenol products. Dashed lines in (A) correspond to cyclohexenone and solid lines indicate phenol. (C) Use of the kinetic model and equation in Scheme S1 to fit relative initial rates ($d[\text{cyclohexenone} + \text{phenol}]/dt$) after phen addition as a function of [phen]. The fit reveals $m = 1.6$. Reaction conditions: [substrate] = 0.1 M (0.05 mmol), $[\text{Pd(TFA)}_2] = 0.005 \text{ M}$ (0.0025 mmol), $[\text{2-Me}_2\text{Npy}] = 0.01 \text{ M}$ (0.005 mmol), $[\text{TsOH}] = 0.02 \text{ M}$ (0.01 mmol), [phen] = 0.0002, 0.0005, 0.001, 0.0025, 0.005, 0.010, 0.020 M, DMSO for V_{Total} of 0.5 mL, 1 atm O_2 , 80 $^\circ\text{C}$.

Quantitative Poisoning Test: Cyclohexenone Dehydrogenation at t = 1.5 h

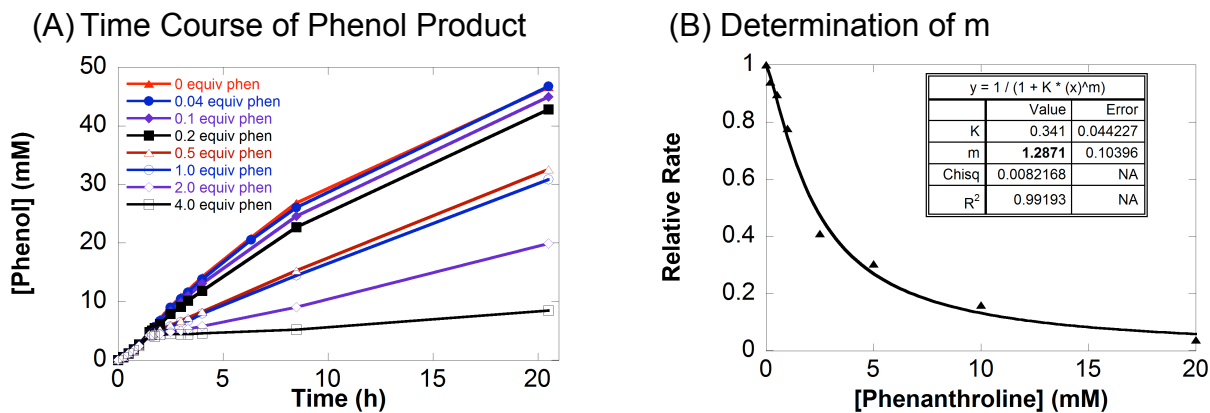
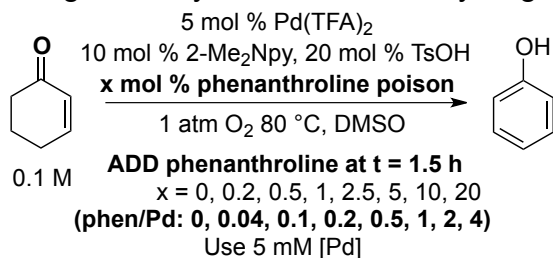


Figure S10. Reaction time course plots showing inhibition of cyclohexenone dehydrogenation upon addition of varying [phen] at t = 1.5 h, showing (A) the full time course with phenol product formation. (B) Use of the kinetic model and equation in Scheme S1 to fit relative initial rates ($d[\text{phenol}]/dt$) after phen addition as a function of [phen]. The fit reveals $m = 1.3$. Reaction conditions: [substrate] = 0.1 M (0.05 mmol), [Pd(TFA)₂] = 0.005 M (0.0025 mmol), [2-Me₂Npy] = 0.01 M (0.005 mmol), [TsOH] = 0.02 M (0.01 mmol), [phen] = 0.0002, 0.0005, 0.001, 0.0025, 0.005, 0.010, 0.020 M, DMSO for V_{Total} of 0.5 mL, 1 atm O₂, 80 °C.

Quantitative Poisoning Test: Cyclohexenone Dehydrogenation at t = 5.0 h

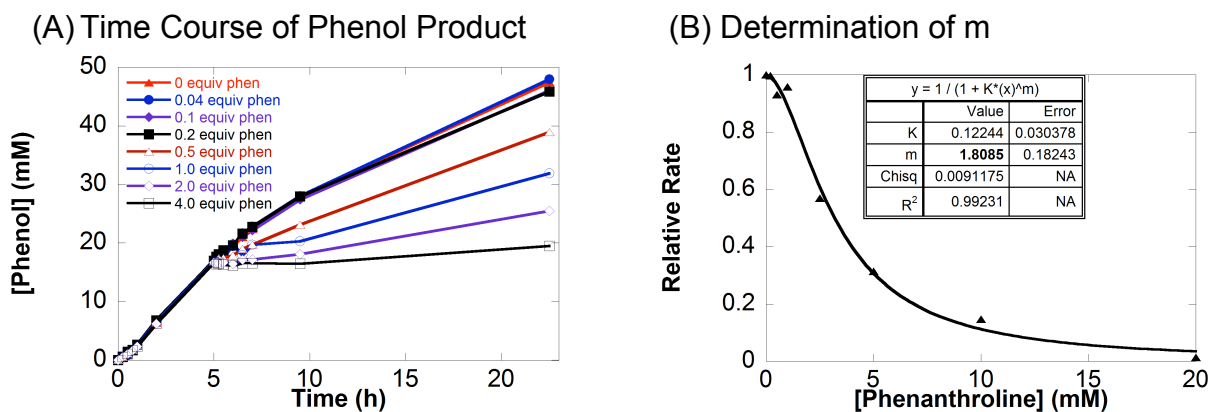
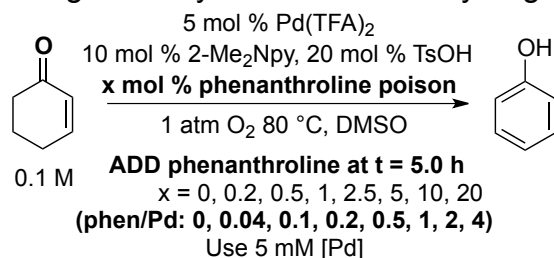
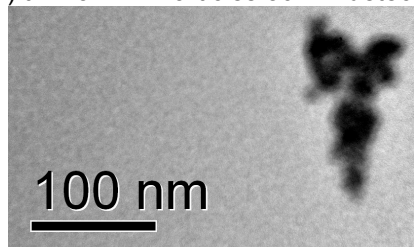


Figure S11. Reaction time course plots showing inhibition of cyclohexenone dehydrogenation upon addition of varying [phen] at t = 5 h, showing (A) the full time course with phenol product formation. (B) Use of the kinetic model and equation in Scheme S1 to fit relative initial rates ($d[\text{phenol}]/dt$) after phen addition as a function of [phen]. The fit reveals $m = 1.8$. Reaction conditions: [substrate] = 0.1 M (0.05 mmol), [Pd(TFA)₂] = 0.005 M (0.0025 mmol), [2-Me₂Npy] = 0.01 M (0.005 mmol), [TsOH] = 0.02 M (0.01 mmol), [phen] = 0.0002, 0.0005, 0.001, 0.0025, 0.005, 0.010, 0.020 M, DMSO for V_{Total} of 0.5 mL, 1 atm O₂, 80 °C.

13. Transmission Electron Microscopy (TEM) Images

Transmission electron microscopy (TEM) images were obtained from aliquots of a cyclohexanone dehydrogenation reaction mixture. The images obtained from a reaction at $t = 15$ min and $t = 4$ h reveal nanoparticles of approx 30 and > 100 nm, respectively (Figure S12).

(A) $t = 15$ min: Particles 30 nm detected



(B) $t = 4$ h: Particles 100 – 400 nm detected

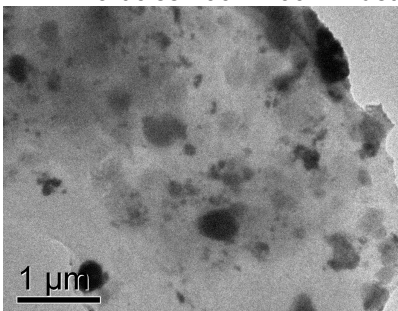
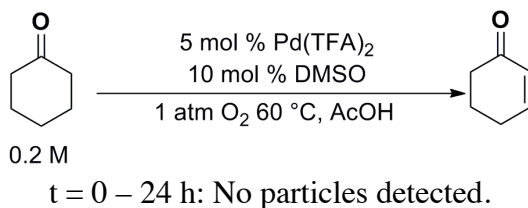


Figure S12. Use of transmission electron microscopy (TEM) images to analyze palladium particle sizes from the dehydrogenation of 3-methylcyclohexanone. TEM images after (A) 15 min, (B) 4 h. Reaction conditions: [ketone] = 2M (1 mmol), [Pd(TFA)₂] = 0.06 M (0.03 mmol), [2-Me₂Npy] = 0.12 M (0.06 mmol), [TsOH] = 0.24 M (0.12 mmol), DMSO for V_{Total} of 0.5 mL, 1 atm O₂, 80 °C.

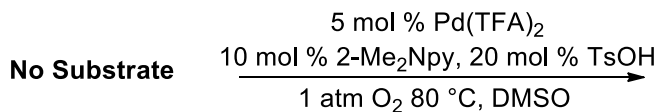
14. Dynamic Light Scattering (DLS) Data for the Pd(DMSO)₂(TFA)₂ Catalyst System.

The Pd(DMSO)₂(TFA)₂-catalyzed aerobic dehydrogenation of cyclohexanone to cyclohexenone was monitored by dynamic light scattering (DLS) for Pd nanoparticle formation. This catalyst system has been proposed to proceed via a homogeneous Pd^{II} to Pd⁰ cycle. For example, Figure S6 shows continued reactivity for several hours after Hg addition. No particles were evident by DLS throughout a 24 h reaction period, with time points at $t = 0.5, 1, 2, 4, 8.5,$ and 24 h.



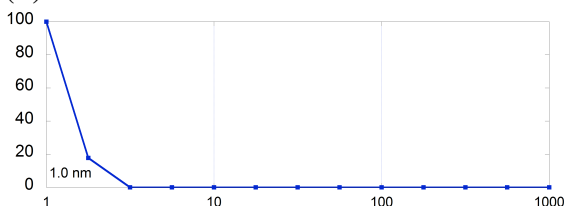
15. Dynamic Light Scattering (DLS) Data of Control Reaction

Dynamic light scattering data were obtained at different time points for the dehydrogenation of both 3-methylcyclohexanone and 3-methylcyclohexenone, where large Pd particle sizes (300 – 600 nm) were immediately observable (Figure 8). A control experiment where no substrate was added is shown in Figure S13, depicting Pd nanoparticle formation but no larger than 10 nm.

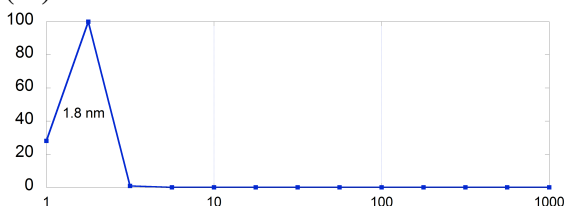


(i) t = 0: No particles detected

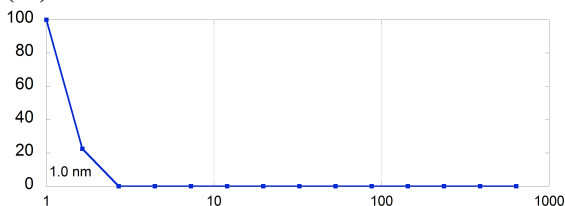
(ii) t = 0.5 h: Particles 1.0 – 1.8 nm detected



(iii) t = 4 h: Particles 1.8 – 3.2 nm detected



(iv) t = 8 h: Particles 1.0 – 1.6 nm detected



(v) t = 24 h: Particles 1.8 – 17.8 nm detected

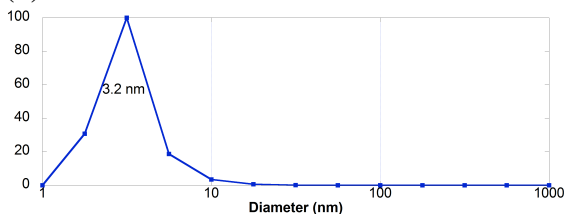


Figure S13. Palladium particle sizes at under the catalytic reaction conditions but without any substrate to reduce the Pd^{II}. Reaction conditions: [Pd(TFA)₂] = 0.06 M, [2-Me₂Npy] = 0.12 M, [TsOH] = 0.24 M, DMSO for V_{Total} of 0.5 mL, 1 atm O₂, 80 °C.

16. Correlation of Pd Particle Sizes with Phenol Formation

The role of the TsOH and 2-Me₂Npy additives was investigated by both GC for product yields and for Pd particle formation by DLS. The conversion of 3-methylcyclohexanone, **1a**, to 3-cresol, **2**, was monitored under the following catalytic conditions: (A) without TsOH nor 2-Me₂Npy additives, (B) with 2-Me₂Npy, without TsOH, (C) with TsOH, without 2-Me₂Npy, and (D) with both TsOH and 2-Me₂Npy. Phenol yields are shown with denotation of when particle formation occurs in Figure S14. In the absence of both additives (Exp A), Pd nanoparticles take at least 2 h to become detectable by DLS (Figure S15A), and this time period correlates with the initial detection of phenol in the reaction mixture. The presence of 2-Me₂Npy in the reaction mixture without TsOH (Exp B) completely inhibits Pd nanoparticle formation (Figure S15B) over the first 4 h of the reaction, and no phenol formation is observed over this time period. In the presence of TsOH, both in the absence (Exp C) and in the presence of 2-Me₂Npy (Exp D), Pd nanoparticles and phenol production are detected immediately after initiating the reactions (Figures S15C and D). These data suggest Pd nanoparticles are important for phenol formation.

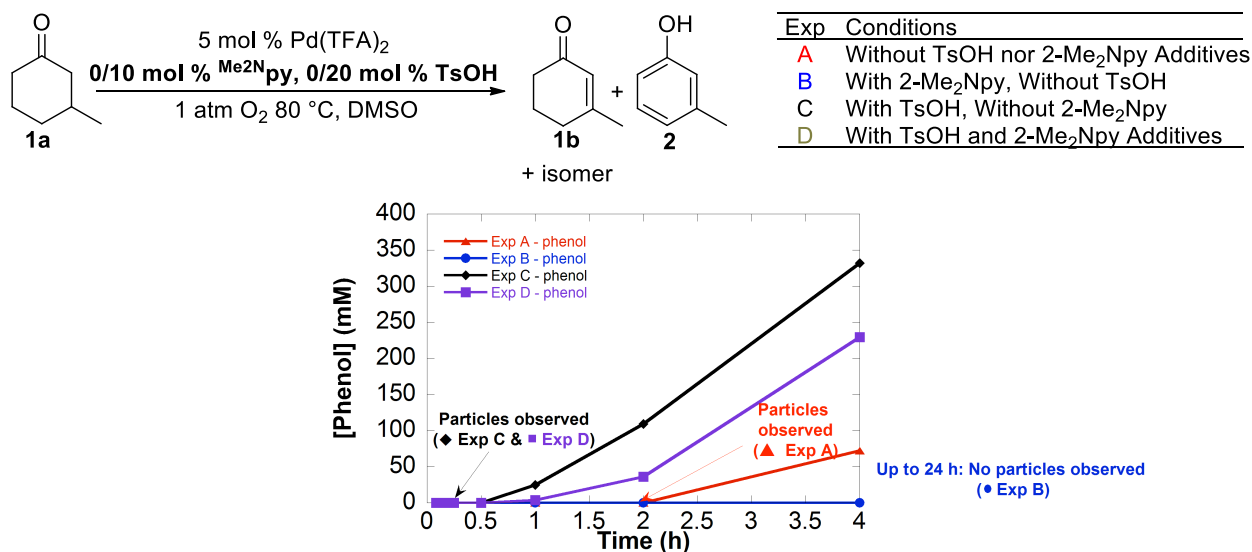
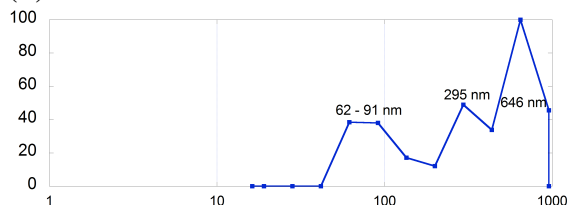


Figure S14. Palladium particle sizes at different reaction times for the conversion of **1a** to **2** with the following conditions: (A) without TsOH nor 2-Me₂Npy additives, (B) with 2-Me₂Npy, without TsOH, (C) with TsOH, without 2-Me₂Npy, and (D) with both TsOH and 2-Me₂Npy. Reaction conditions for experiment A: [3-methylcyclohexanone] = 2 M (1 mmol), [Pd(TFA)₂] = 0.06 M (0.03 mmol), [2-Me₂Npy] = 0.12 M (0.06 mmol), [TsOH] = 0.24 M (0.12 mmol), DMSO for V_{Total} of 0.5 mL, 1 atm O₂, 80 °C.

(A) DLS: Catalyst Conditions Without TsOH nor 2-Me₂Npy Additives

(i) t = 0: No particles detected

(ii) t = 2 h: 62 – 1000 nm detected



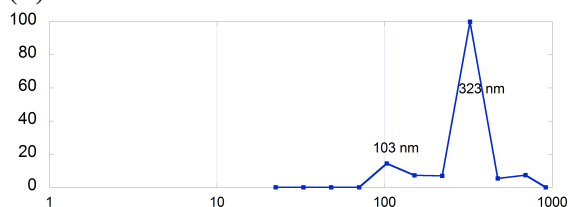
(B) DLS: Catalyst Conditions With 2-Me₂Npy, Without TsOH

(i) t = 0 to 24 h: No particles detected

(C) DLS: Catalyst Conditions With TsOH, Without 2-Me₂Npy

(i) t = 0: No particles detected

(ii) t = 1 h: Particles 100 – 700 nm detected



(D) DLS: Catalyst Conditions With Both TsOH and 2-Me₂Npy

(i) t = 0: No particles detected

(ii) t = 1 h: Particles 93 – 800 nm detected

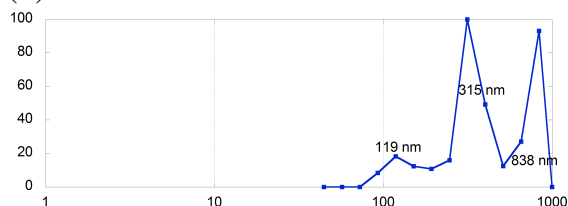
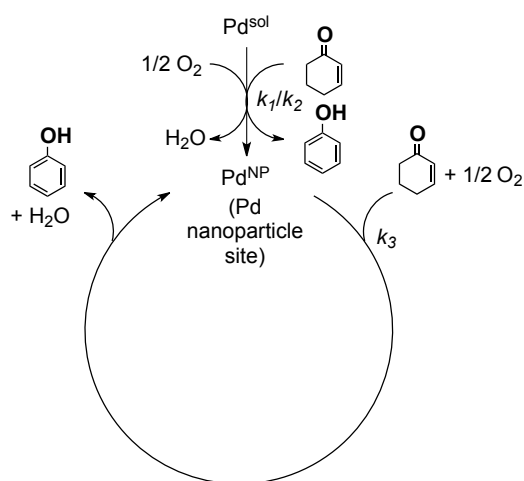


Figure S15. Palladium particle sizes at different reaction times for the conversion of **1a** to **2** with the following conditions: (A) without TsOH nor 2-Me₂Npy additives, (B) with 2-Me₂Npy, without TsOH, (C) with TsOH, without 2-Me₂Npy, and (D) with both TsOH and 2-Me₂Npy. Reaction conditions for experiment A: [3-methylcyclohexanone] = 2 M (1 mmol), [Pd(TFA)₂] = 0.06 M (0.03 mmol), [2-Me₂Npy] = 0.12 M (0.06 mmol), [TsOH] = 0.24 M (0.12 mmol), DMSO for V_{Total} of 0.5 mL, 1 atm O₂, 80 °C.

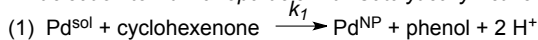
17. Simplified Mechanism for Pd Nanoparticle Nucleation and Growth from a Molecular Pd Precatalyst (Pd^{sol}) for Cyclohexenone Dehydrogenation.

The sigmoidal reaction kinetics observed in the dehydrogenation of cyclohexenone can be explained by in situ transformation of a molecular Pd precatalyst (Pd^{sol}) into a catalytically active site (Pd^{NP}) on a Pd nanoparticle. This mechanism, which involves nucleation and autocatalytic growth of the nanoparticles, has been well studied and documented in the literature.⁷ A simplified mechanism corresponding to this sequence in the dehydrogenation of cyclohexenone to phenol is shown in Figure S16. Nucleation of a Pd nanoparticle involves reaction of a Pd^{sol} species and cyclohexenone, resulting in formation of a catalytically active site, Pd^{NP} (step 1). Autocatalytic growth of the nanoparticle (step 2) forms more catalytically active Pd^{NP} sites. The overall catalytic aerobic dehydrogenation reaction of cyclohexenone to phenol mediated by Pd^{NP} corresponds to step 3. Inactive Pd black and/or mirror (Pd^{bulk}) are observed in the reactions, and a catalyst deactivation pathway arising from nanoparticle aggregation is also included (step 4, not shown in the catalytic cycle). Experimental time courses obtained at two different initial cyclohexenone concentrations (430 and 220 mM) have been fit to this kinetic model and are shown in Scheme S16B and S16C. (Note: A similar mechanism can be envisioned for the two-step dehydrogenation from cyclohexanone but would need to incorporate the sequential reaction kinetics for cyclohexanone \rightarrow cyclohexenone \rightarrow phenol and the kinetic burst associated with the initial cyclohexanone dehydrogenation step, as shown in Figure 2A in the manuscript).

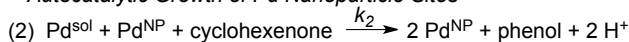
(A) Mechanism for Cyclohexenone Dehydrogenation to Phenol



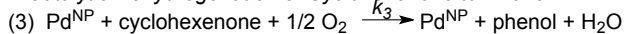
Nucleation to Pd Nanoparticle with Catalytically Active Sites (Pd^{NP})



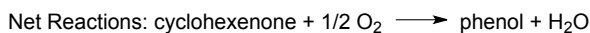
Autocatalytic Growth of Pd Nanoparticle Sites



Catalytic Dehydrogenation of Cyclohexenone to Phenol



Catalyst Aggregation to Inactive Heterogeneous Pd



Based on Fit of Experimental Data (assuming pO₂ is zero-order):

Plot B

$$k_1 = 5.3 \times 10^{-4} \text{ M}^{-1} \text{ s}^{-1}$$

$$k_2 = 4.4 \times 10^{-4} \text{ M}^{-2} \text{ s}^{-1}$$

$$k_3 = 1.6 \times 10^{-3} \text{ M}^{-1} \text{ s}^{-1}$$

$$k_4 = 1.5 \times 10^{-4} \text{ M}^{-1} \text{ s}^{-1}$$

Plot C

$$k_1 = 6.0 \times 10^{-4} \text{ M}^{-1} \text{ s}^{-1}$$

$$k_2 = 5.9 \times 10^{-4} \text{ M}^{-2} \text{ s}^{-1}$$

$$k_3 = 2.2 \times 10^{-3} \text{ M}^{-1} \text{ s}^{-1}$$

$$k_4 = 4.7 \times 10^{-4} \text{ M}^{-1} \text{ s}^{-1}$$

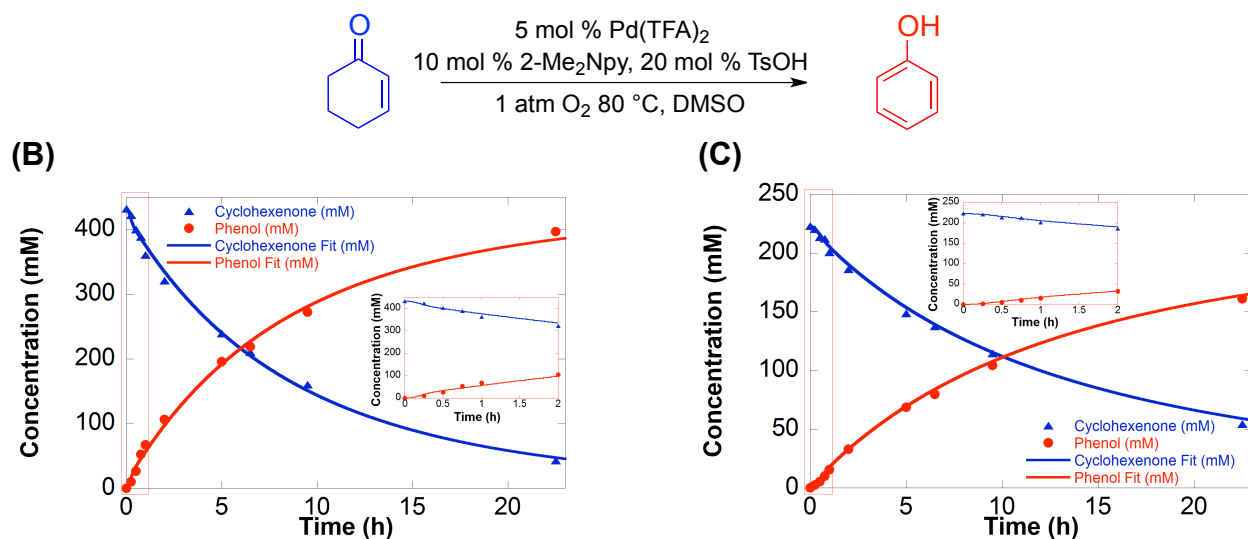


Figure S16. (A) Proposed mechanism for in situ transformation (nucleation and nanoparticle autocatalytic growth) of a molecular Pd precatalyst (Pd^{sol}) into a catalytically active site (Pd^{NP}) on a Pd nanoparticle for the dehydrogenation of cyclohexenone to phenol. The kinetically modeled rate constants, from fitting experimental time courses with [cyclohexenone]₀ of (B) 430 and (C) 220 mM are provided. Reaction conditions for experiment B: [cyclohexenone] = 430 mM (0.86 mmol), [Pd(TFA)₂] = 0.02 M (0.01 mmol), [2-Me₂Npy] = 0.04 M (0.02 mmol), [TsOH] = 0.08 M (0.04 mmol), DMSO for V_{Total} of 0.5 mL, 1 atm O₂, 80 °C. Reaction conditions for experiment C: [cyclohexenone] = 220 mM (0.44 mmol), [Pd(TFA)₂] = 0.01 M (0.005 mmol), [2-Me₂Npy] = 0.02 M (0.01 mmol), [TsOH] = 0.04 M (0.02 mmol), DMSO for V_{Total} of 0.5 mL, 1 atm O₂, 80 °C. Concentrations of cyclohexenone and phenol with respect to time were fitted using the kinetic simulation software COPASI⁸ according to the kinetic model presented in A.

18. Procedure for Dehydrogenation with Well-Defined Pd Nanoparticles.

Pd nanoparticles were synthesized using a modified procedure from the report of Sheldon and coworkers.⁹ To a 25 mL round bottom flask charged with Pd(TFA)₂ (17.0 mg, 0.05 mmol) and neocuproine (11.4 mg, 0.05 mmol) was added 0.5 mL H₂O, and the orange slurry was stirred for 1 h under air. Ethylene carbonate (44 mg) was added and the slurry stirred for another 10 min, when the solution was purged with a balloon of H₂ with a vent needle for 5 min, resulting in a dark red slurry. The vent needle and balloon were replaced with a new H₂ balloon and stirred for another 10 minutes resulting in a black slurry. Dynamic light scattering measurements of the solution revealed the presence of Pd nanoparticles with a diameter of 1.7 nm (Figure S17).

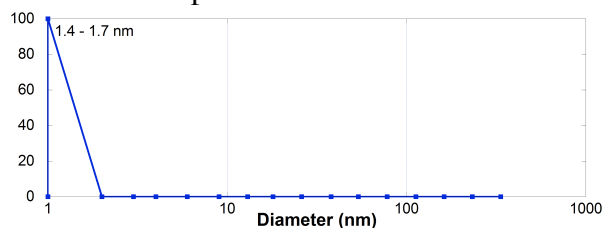


Figure S17. Dynamic light scattering data for Pd nanoparticles prepared according to the protocol above.

References.

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