

## Supporting Information

### **Aerobic Dehydrogenation of Cyclohexanone to Cyclohexenone Catalyzed by Pd(DMSO)<sub>2</sub>(TFA)<sub>2</sub>: Evidence for Ligand-Controlled Chemoselectivity**

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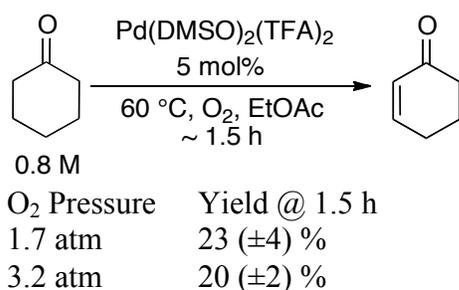
## 1. General Considerations

All commercially available compounds were used as received and purchased from Sigma-Aldrich. Cyclohexanone- $d_{10}$  was purchased from CDN Isotopes. The deuterated substrates, 2,2,6,6- $d_4$ -Cyclohexanone, 2,4,4,6,6- $d_5$ -cyclohexenone and 2,6,6- $d_3$ -cyclohexenone, were prepared according to literature procedures.<sup>12</sup>

$^1\text{H}$  NMR spectra were recorded on a Bruker AC-300 MHz or a Varian Mercury-300 MHz spectrometer. The chemical shifts ( $\delta$ ) are given in parts per million and referenced to residual solvent peaks or a TMS internal standard. Gas chromatography was performed on a Shimadzu GC-17A using a Stabilwax®-DB column or a RTX-5MS column and referenced to an internal standard (tetradecane). Flash column chromatography was performed on an Isco Combiflash system using silica gel 60 (Silicycle) and eluted with ethyl acetate/hexane.

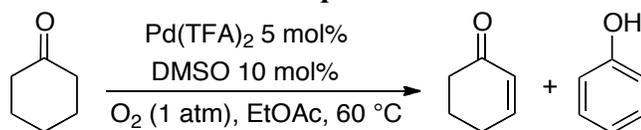
## 2. O<sub>2</sub> Dependence of Pd(DMSO)<sub>2</sub>(TFA)<sub>2</sub>-Catalyzed Dehydrogenation of Cyclohexanone

Dehydrogenation reactions at various O<sub>2</sub> pressures above 1 atm were performed on a HEL high pressure (HP) ChemSCAN 8-reactor platform with controlled temperature, pressure, and mechanical overhead stirring. A 20 mL Hastelloy reactor was charged with a stock solution containing Pd(TFA)<sub>2</sub> (26.6 mg, 0.08 mmol) and DMSO (13.5 mg, 0.16 mmol) in 1 mL of EtOAc and mounted on the HEL HP ChemSCAN. The headspace was purged with oxygen gas three times, and the reactions were heated to 60 °C while stirring under 1 atm of O<sub>2</sub>. Upon reaching 60 °C, each reactor was pressurized to a set pressure of O<sub>2</sub> (e.g. 1.7 atm). Then 1 mL of a stock solution containing cyclohexanone (1.6 mmol) and tetradecane internal standard was fed at a rate of 2 mL/min through pre-flushed tubing. After 1 h of catalysis, the reactors were cooled (30 min), vented to ambient air, quenched with dichloromethane, and the yields and conversion were analyzed by gas chromatography with tetradecane as the internal standard.



**Figure S1.** Yield of Pd(DMSO)<sub>2</sub>(TFA)<sub>2</sub>-catalyzed cyclohexanone-to-cyclohexenone dehydrogenation at two different O<sub>2</sub> pressures. Reaction conditions: [Pd(TFA)<sub>2</sub>] = 0.04 M (0.08 mmol), [DMSO] = 0.08 M (0.16 mmol), [cyclohexanone] = 0.8 M (0.16 mmol), EtOAc (2 mL), 60 °C. O<sub>2</sub> = 1.7 and 3.2 atm.

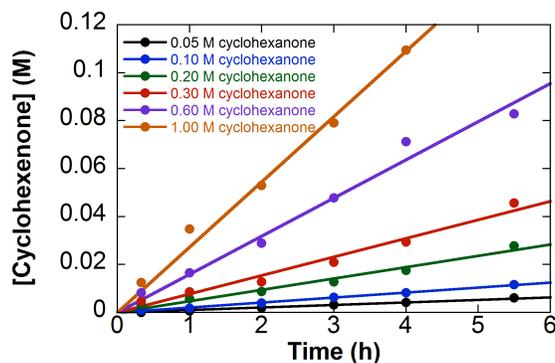
### 3. General Procedure for Kinetic Data Acquisition.



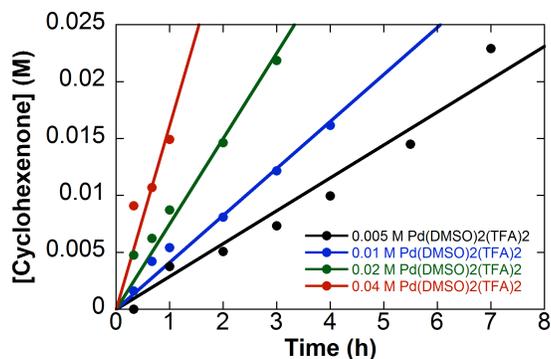
Catalytic aerobic oxidation reactions were performed using a custom reaction apparatus that enabled several reactions to be performed simultaneously under a constant pressure of O<sub>2</sub> (approx. 1 atm) with controlled temperature and orbital agitation. To a disposable 13 mm thick-walled culture tube was added Pd(TFA)<sub>2</sub> (13.2 mg, 0.04 mmol, 0.05 equiv.), DMSO (5.6 mL, 0.04 mmol, 0.1 equiv.), and 1 mL EtOAc, resulting in a bright yellow solution. The reaction tube was placed in a 48-well parallel reactor mounted on a Glas-Col large capacity mixer. The headspace was purged with O<sub>2</sub> for 10 min, after which tetradecane (20 mL, 0.077 mmol) was added via syringe. The reactor temperature was set to 60 °C and allowed to equilibrate for 5 min. Injection of cyclohexanone (80 mL, 0.8 mmol) established the *t* = 0 point. After various time intervals, 10 μL aliquots were removed, quenched/diluted with dichloromethane and analyzed by GC.

### 4. Raw Kinetic Data.

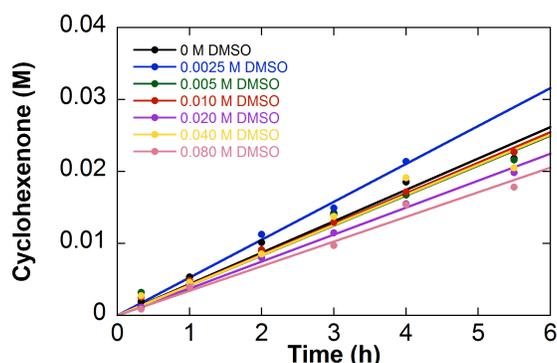
Most kinetic data and orders presented were derived from the initial rates of the reactions. Unless specified, the initial rate was defined as the slope of [cyclohexenone] versus time from *t* = 0 up to 10% conversion. Figures S2 - S6, representing the reaction time courses under different conditions, are the raw data for Figures 2-4 and 6-7. Experiments in each figure were performed in parallel using the same stock solutions and in the same large capacity mixer.



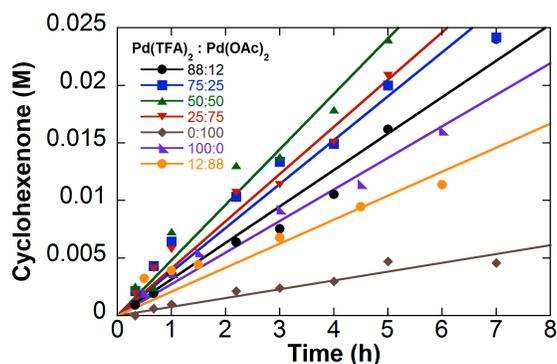
**Figure S2.** Time courses for the oxidation of cyclohexanone with varying concentrations in the presence of a fixed catalyst concentration. Reaction conditions: [Pd(TFA)<sub>2</sub>] = 0.01 M (0.01 mmol), [DMSO] = 0.02 M (0.02 mmol), EtOAc (1 mL), O<sub>2</sub> (1 atm), 60 °C, [cyclohexanone] = 0.05, 0.1, 0.2, 0.3, 0.6 and 1 M.



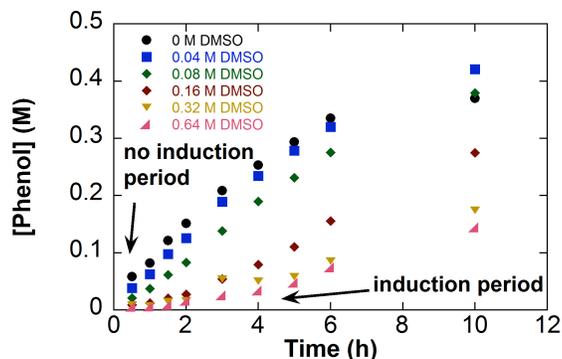
**Figure S3.** Time courses for oxidation of cyclohexanone in the presence of different catalyst loadings, where the “catalyst” is a 1:2 mixture of Pd(TFA)<sub>2</sub> and DMSO. Reaction conditions: [cyclohexanone] = 0.2 M (0.2 mmol), EtOAc (1 mL), O<sub>2</sub> (1 atm), 60 °C, [Pd(TFA)<sub>2</sub>] = 0.005, 0.01, 0.02 and 0.04 M, [DMSO] = 0.01, 0.02, 0.04 and 0.08 M, respectively.



**Figure S4.** Time courses for oxidation of cyclohexanone in the presence of different quantities of DMSO with fixed Pd(TFA)<sub>2</sub> concentration. Reaction conditions: [cyclohexanone] = 0.2 M (0.2 mmol), [Pd(TFA)<sub>2</sub>] = 0.01 M (0.01 mmol), EtOAc (1 mL), O<sub>2</sub> (1 atm), 60 °C, [DMSO] = 0, 0.0025, 0.005, 0.01, 0.02, 0.04 and 0.08 M.



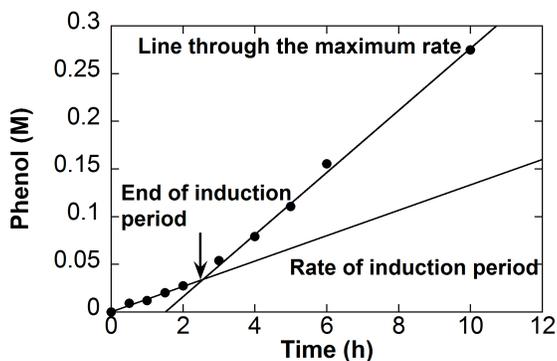
**Figure S5.** Time courses of Pd-catalyzed oxidation of cyclohexanone using different anionic ligands of Pd. Reaction conditions: [cyclohexanone] = 0.2 M (0.2 mmol), [Pd]<sub>total</sub> = 0.01 M (0.01 mmol), [Pd(TFA)<sub>2</sub>]:[Pd(OAc)<sub>2</sub>] = 0:100, 12:88, 25:75, 50:50, 75:25, 88:12, 100:0. [DMSO] = 0.02 M (0.02 mmol), EtOAc (1 mL), O<sub>2</sub> (1 atm), 60 °C.



**Figure S6.** Dependence of the initial rate of Pd-catalyzed oxidation of cyclohexenone to phenol on the DMSO/Pd ratio. Reaction conditions: [cyclohexenone] = 0.8 M (0.8 mmol), [Pd(TFA)<sub>2</sub>] = 0.08 M (0.08 mmol), EtOAc (1 mL), O<sub>2</sub> (1 atm), 60 °C, [DMSO] = 0, 0.04, 0.08, 0.16, 0.32 and 0.64 M.

### 5. Estimated Induction Periods

Based on the time courses shown in Figure S6, there are clearly induction periods with increasing DMSO concentration. The length of the induction period was estimated from the intersection of lines corresponding to the initial rate (i.e., during the induction period) and the maximum rate after the induction period. A representative plot illustrating this method is shown in Figure S7. Table S1 shows the induction periods estimated for each [DMSO] used to prepare Figure 8 in the manuscript.



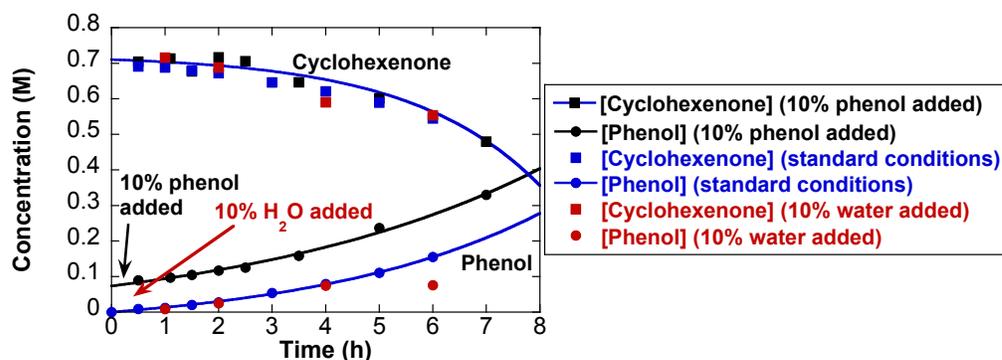
**Figure S7.** Depiction of method for induction period length estimation.

**Table S1.** Estimated Induction Periods for Varying [DMSO].

[DMSO] (M)	Estimated Induction Period (h)
0.00	0.0
0.04	0.5
0.08	1.8
0.16	2.4
0.32	3.4
0.64	3.7

## 6. Assessment of Autocatalysis on Pd(DMSO)<sub>2</sub>(TFA)<sub>2</sub>-Catalyzed Oxidation of Cyclohexenone to Phenol

The Pd(DMSO)<sub>2</sub>(TFA)<sub>2</sub>-catalyzed dehydrogenation of cyclohexenone to phenol exhibits an induction period and a sigmoidal time course for formation of phenol. To probe the possibility of product-induced autocatalysis, three parallel reactions of cyclohexenone were initiated under the standard conditions; 10 mol% of H<sub>2</sub>O and phenol relative to the cyclohexenone substrate were added into two reactions, respectively, at  $t = 0$ . The time courses for three reactions were recorded as shown in Figure S8.



**Figure S8.** Effect of products on the induction period in Pd(DMSO)<sub>2</sub>(TFA)<sub>2</sub>-catalyzed oxidation of cyclohexenone to phenol. Reaction conditions: [cyclohexenone] = 0.8 M (0.8 mmol), [Pd(TFA)<sub>2</sub>] = 0.04 M (0.04 mmol), ([DMSO] = 0.08 M (0.08 mmol)), EtOAc = 1 ml, 1 atm O<sub>2</sub>, 60 °C.

## References

1. Wanat, R. A.; Collum, D. B. *Organometallics* **1986**, *5*, 120.
2. Lambert, J. B.; Clikeman, R. R. *J. Am. Chem. Soc.* **1976**, *98*, 4203-4211.