

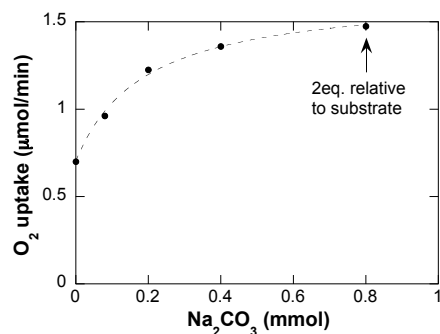
# Mechanistic Studies of Wacker-Type Amidocyclization of Alkenes Catalyzed by (IMes)Pd(TFA)<sub>2</sub>(H<sub>2</sub>O): Kinetic and Stereochemical Implications of Proton Transfer

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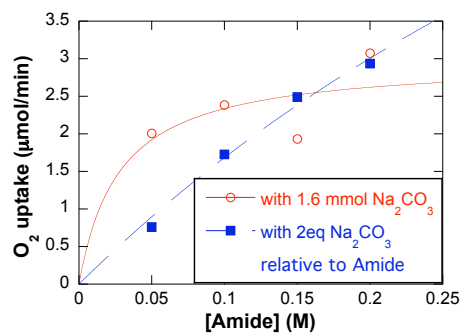
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## Supplemental rate dependence data obtained from gas-uptake kinetic studies.



**Figure S1.** Dependence of the initial rate on amount of exogenous base  $\text{Na}_2\text{CO}_3$ . The curve fit results from a nonlinear least-squares fit to a hyperbolic function of mols of exogenous base  $\text{Na}_2\text{CO}_3$ . Conditions:  $[(\text{IMes})\text{Pd}(\text{TFA})_2(\text{H}_2\text{O})] = 2 \text{ mM}$ ,  $[\mathbf{4}] = 100 \text{ mM}$ ,  $0 - 0.8 \text{ mmol Na}_2\text{CO}_3$ ,  $4.0 \text{ ml}$  of toluene, initial  $p\text{O}_2 = 700 \text{ torr}$ ,  $80 \text{ }^\circ\text{C}$ .



**Figure S2.** Comparison of [amide] dependences in the presence of fixed amount of  $\text{Na}_2\text{CO}_3$  and in the presence of 2 equivalent of  $\text{Na}_2\text{CO}_3$  relative to amide. Conditions:  $[(\text{IMes})\text{Pd}(\text{TFA})_2(\text{H}_2\text{O})] = 2 \text{ mM}$ ,  $[\text{amide } \mathbf{4}] = 0\text{-}200 \text{ mM}$ ,  $4.0\text{ml}$  of toluene, initial  $p\text{O}_2 = 700 \text{ torr}$ ,  $80 \text{ }^\circ\text{C}$ .

### Derivation of the rate law.

In the presence of added base:

The rate of product **5** formation is described by the following rate law.

$$\frac{d[\mathbf{5}]}{dt} = k_2^{cis} [\mathbf{7}] \quad (\text{S1})$$

Applying equilibrium approximation on **7**.

$$K_1^{cis} = \frac{[\text{H}_2\text{O}] \cdot [\mathbf{7}]}{[\text{IMesPd}(\text{TFA})_2(\text{H}_2\text{O})] \cdot [\mathbf{4}]} \quad (\text{S2})$$

$$[7] = \frac{K_1^{cis} \cdot [\text{IMesPd}(\text{TFA})_2(\text{H}_2\text{O})] \cdot [4]}{[\text{H}_2\text{O}]} \quad (\text{S3})$$

The total palladium concentration has contributions from  $\text{IMesPd}(\text{TFA})_2(\text{H}_2\text{O})$  and **7**.

$$[\text{Pd}]_T = [\text{IMesPd}(\text{TFA})_2(\text{H}_2\text{O})] + [7] \quad (\text{S4})$$

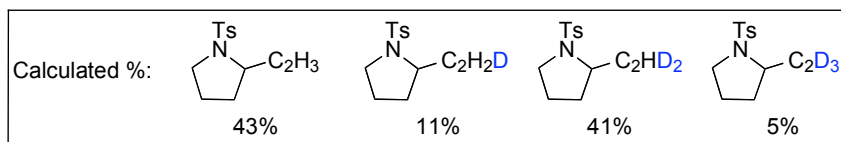
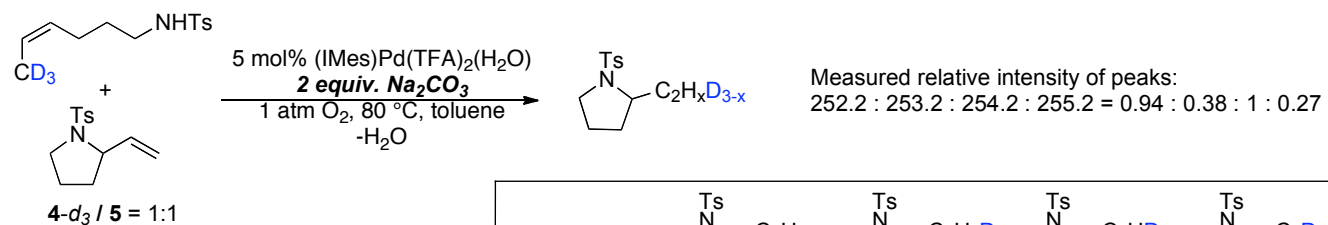
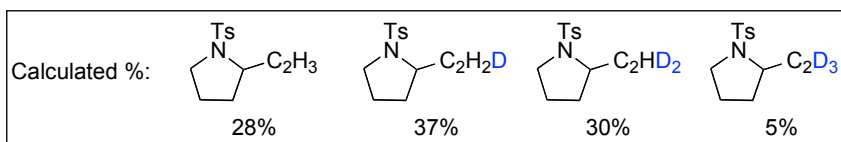
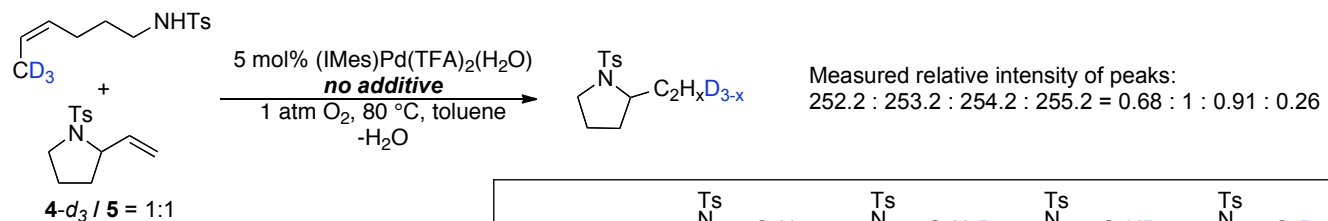
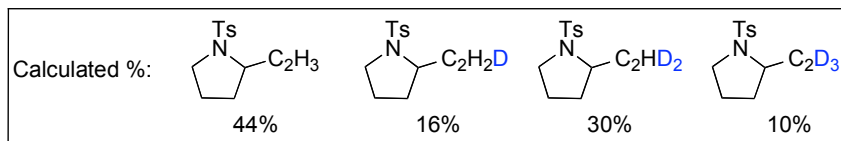
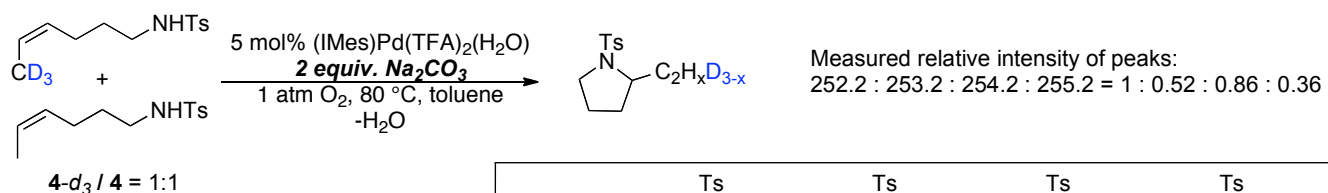
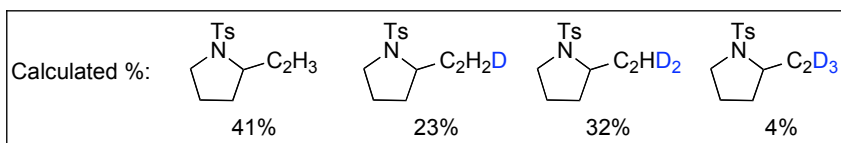
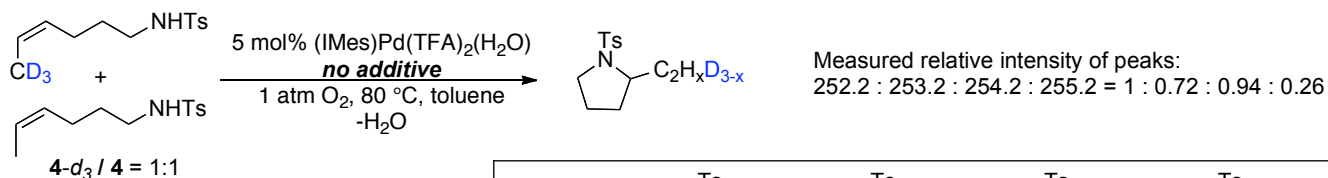
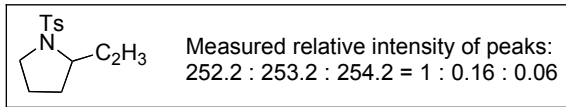
By substituting eq S3 into eq S4, one obtains

$$[7] = \frac{K_1^{cis} \cdot [4] \cdot [\text{Pd}]_T}{K_1^{cis} \cdot [4] + [\text{H}_2\text{O}]} \quad (\text{S5})$$

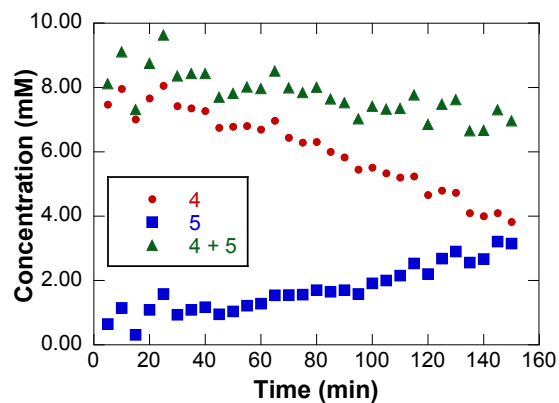
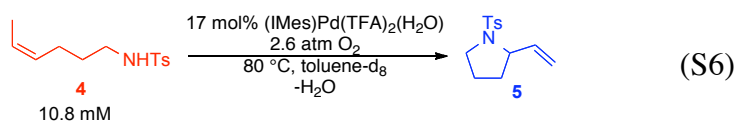
Substitution of eq S5 into eq S1 yields the rate law (eq 4).

$$\frac{d[5]}{dt} = \frac{k_2^{cis} K_1^{cis} \cdot [4] \cdot [\text{Pd}]_T}{K_1^{cis} \cdot [4] + [\text{H}_2\text{O}]} \quad (4)$$

# Analysis of crossover experiments via mass-spectroscopy.



## Kinetic time course generated from monitoring catalytic reaction by $^1\text{H}$ NMR spectroscopy.



**Figure S3.** A kinetic time course for (IMes)Pd(TFA)<sub>2</sub>(H<sub>2</sub>O)-catalyzed oxidative amidocyclization of **4** monitored by  $^1\text{H}$  NMR spectroscopy. Condition: [(IMes)Pd(TFA)<sub>2</sub>(H<sub>2</sub>O)] = 1.8 mM, [**4**] = 10.8 M, [1,3,5-trimethoxybenzene] = 6.0 mM, in toluene-*d*<sub>8</sub>, 80 °C. Data sampling occurred at every 5 min.

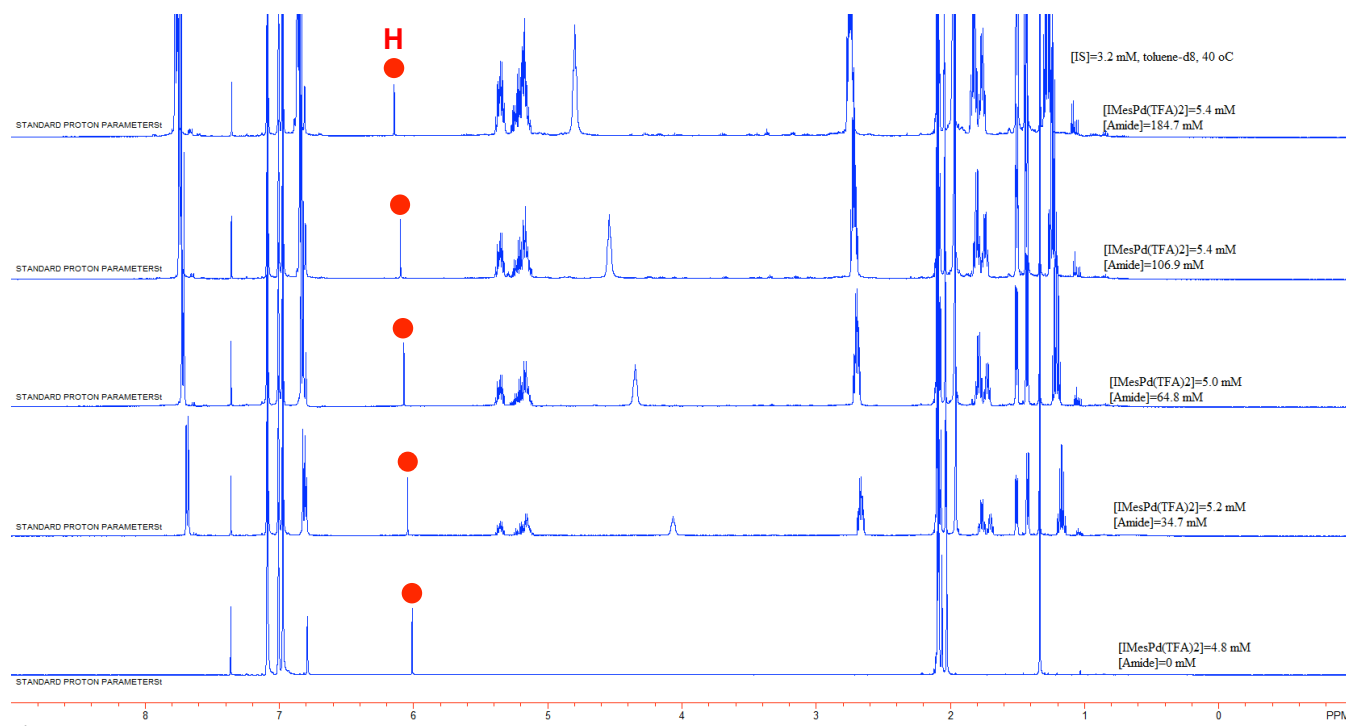
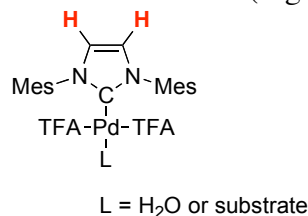
Note: Small amounts of starting material **4** are oxidized to the *N*-tosylimine, which hydrolyzes in situ into tosylamide (TsNH<sub>2</sub>) and 4-pentenal. This background reaction accounts for the slightly faster consumption of **4** relative to the formation of **5**, evident in Figure S3. This decomposition pathway does not significantly affect the initial rates measurements determined by gas-uptake methods.

## Titration of Catalyst Solution with Substrate **4** Monitored by $^1\text{H}$ NMR Spectroscopy.

The following five NMR samples were prepared in toluene- $d_8$  stock solution of 1,3,5-tri-tert-butylbenzene ( $[\text{IS}]=3.2$  mM). The following concentrations were calculated based on IS.

- #1.  $[(\text{IMes})\text{Pd}(\text{TFA})_2(\text{H}_2\text{O})] = 4.8$  mM
- #2.  $[(\text{IMes})\text{Pd}(\text{TFA})_2(\text{H}_2\text{O})] = 5.2$  mM;  $[\mathbf{4}] = 34.7$  mM
- #3.  $[(\text{IMes})\text{Pd}(\text{TFA})_2(\text{H}_2\text{O})] = 5.0$  mM;  $[\mathbf{4}] = 63.8$  mM
- #4.  $[(\text{IMes})\text{Pd}(\text{TFA})_2(\text{H}_2\text{O})] = 5.4$  mM;  $[\mathbf{4}] = 106.9$  mM
- #5.  $[(\text{IMes})\text{Pd}(\text{TFA})_2(\text{H}_2\text{O})] = 5.4$  mM;  $[\mathbf{4}] = 184.7$  mM

$^1\text{H}$  NMR Spectra of all five samples were taken on a 500 MHz spectrometer at five temperatures:  $-37$  °C,  $-20$  °C,  $0$  °C,  $24$  °C,  $40$  °C. The stacked plot of the five  $^1\text{H}$  NMR spectra measured at  $40$  °C is shown below to show the dependence of the chemical shift of the NHC proton on the concentration of **4** (Figure S4).



**Figure S4.** Titration of  $(\text{IMes})\text{Pd}(\text{TFA})_2(\text{H}_2\text{O})$  solution with substrate **4**. Condition:  $[(\text{IMes})\text{Pd}(\text{TFA})_2(\text{H}_2\text{O})] = 5$  mM,  $[\mathbf{4}] = 0 - 0.18$  M, in toluene- $d_8$ ,  $40$  °C.