Supporting Information

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Toward an Improved Understanding of the Unusual Reactivity of Pd(0)/Trialkylphosphine Catalysts in Cross-Couplings of Alkyl Electrophiles.

I. Quantifying the Factors that Determine the Rate of Oxidative Addition

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I. General

All reactions were carried out under an atmosphere of nitrogen or argon in oven-dried glassware with magnetic stirring, unless otherwise indicated.

Toluene and THF were purified by passage through a neutral alumina column, and t-amyl alcohol was purified by distillation from CaH₂. All other solvents were used as received: hexane (Aldrich; Sure/Seal); NMP (Aldrich; Sure/Seal); DMF (Aldrich; Sure/Seal).

All alkyl halides were purified by either distillation or vacuum transfer: n-nonyl iodide (Aldrich); n-nonyl bromide (Aldrich); n-nonyl chloride (Aldrich); n-nonyl fluoride (Aldrich); 1-bromo-3-methylbutane (Aldrich); isobutylbromide (Aldrich); isopropylbromide (Aldrich). n-Nonyl tosylate was prepared by tosylation of n-nonyl alcohol.

P(t-Bu)₂Me (Strem) and Pd(P(t-Bu)₃)₂ (Strem) were used without further purification. Pd(PCy₃)₂ (Strem) was purified by recrystallization from toluene/methanol. P(t-Bu)₂Et was prepared as previously described.[1]

¹H and ¹³C NMR resonances are referenced to the solvent. ³¹P NMR resonances are referenced to external 85% H₃PO₄.
II. Preparation of PdL₂ Complexes

**General procedure:** Pd(\(\pi\)-allyl)(η⁵-Cp) (1.0 equiv), the trialkylphosphine (2.2 equiv), and toluene (amount required for a 0.10 M solution in Pd) were added to a Schlenk tube equipped with a stirbar. The tube was sealed and then heated at 75 °C for 3 hours. The reaction mixture was then cooled to r.t., and the solvent was removed under vacuum. The resulting red solid was dissolved in pentane, and the solution was filtered and concentrated, furnishing a semi-crystalline solid.

**Pd(P(t-Bu)₂Me)₂ [479210-19-0].** The general procedure was followed using 840 mg (3.9 mmol) of Pd(\(\pi\)-allyl)(η⁵-Cp), 1.4 g (8.7 mmol) of P(t-Bu)₂Me, and 39 mL of toluene. The product (1.69 g, 101%) was isolated as an orange-brown solid.

\(^{1}\)H NMR (300 MHz, THF-d₈) δ 1.12 (s, 36H), 1.26 (s, 6H). \(^{13}\)C NMR (300 MHz, THF-d₈) δ 7.4, 30.5, 33.6. \(^{31}\)P NMR (300 MHz, THF-d₈) δ 42.3.

**Pd(P(t-Bu)₂Et)₂.** The general procedure was followed using 250 mg (1.2 mmol) of Pd(\(\pi\)-allyl)(η⁵-Cp), 450 mg (2.6 mmol), P(t-Bu)₂Et, and 12 mL of toluene. The product (500 mg, 93% yield) was isolated as a brown-black solid.

\(^{1}\)H NMR (300 MHz, THF-d₈) δ 1.28 (m, 46H). \(^{13}\)C NMR (300 MHz, THF-d₈) δ 16.1, 16.6, 31.0, 34.8. \(^{31}\)P NMR (300 MHz, THF-d₈) δ 63.3. FTIR (thin film) 3402, 2894, 2864, 1469, 901 cm⁻¹.
III. Rates of Oxidative Addition[2]

**Kinetic Analysis.** Our kinetic analysis is based on an overall second-order rate law:

\[
\text{Rate} = k[PdL_2][RX]
\]

When \([PdL_2] = [RX]\), \(\text{Rate} = k[PdL_2]^2\)

\[
\frac{d[PdL_2]}{dt} = -k[PdL_2]^2 
\]

\[
\int_{t_0}^{t} \frac{1}{[PdL_2]^2} d[PdL_2] = -k \int_{t_0}^{t} dt
\]

\[
\frac{1}{[PdL_2]_t} - \frac{1}{[PdL_2]_0} = -k(t - t_0)
\]

\[
\frac{1}{[PdL_2]_t} - \frac{1}{[PdL_2]_0} = kt
\]

Thus, a plot of \(\frac{[PdL_2]}{[PdL_2]_0}\) versus time furnishes a linear plot, with a slope equal to the rate constant \(k\).

The half-life is found by setting \([PdL_2] = \frac{1}{2}[PdL_2]_0\) and \(t = t_{1/2}\), giving:

\[
t_{1/2} = \frac{1}{k[PdL_2]_0}
\]

Using the Eyring equation:

\[
k = \frac{kT}{h} e^{-\frac{-\Delta G^\ddagger}{RT}}
\]

The free energy of activation (\(\Delta G^\ddagger\)) can be solved for by rearrangement:

\[
\Delta G^\ddagger = -RT \ln \left( \frac{kh}{\kappa T} \right)
\]

\(R = 1.9872 \text{ cal} \cdot \text{mol}^{-1} \cdot \text{K}^{-1}\)

\(T = \text{temperature in Kelvin}\)

\(k = \text{rate constant}\)

\(h = 6.62608 \times 10^{-34} \text{ J} \cdot \text{s}\)

\(\kappa = 1.3806 \times 10^{-23} \text{ J} \cdot \text{K}^{-1}\)
**General procedure:** In a vial in a glovebox, PdL₂ (0.040 mmol) was dissolved in the appropriate solvent (0.20 mL), and the resulting solution was transferred to a screw-cap NMR tube. The vial was then washed with additional solvent (2 x 0.10 mL), and the washings were added to the NMR tube. The NMR tube was closed with a Teflon-lined cap and removed from the glovebox. A solution of the alkyl electrophile (0.16 mmol) in the solvent (0.40 mL) was prepared in a glovebox. Outside of a glovebox, 0.10 mL of this solution was added through the septum of the cap of the NMR tube.

The reaction was monitored by ³¹P NMR, and the percent conversion of PdL₂ was determined by integrating the resonances for PdL₂, PdL₂RX, and, in some cases, PdL₂HX. All experiments were performed twice. The data for a single run are provided below.

The ³¹P NMR shifts (δ) for species of interest are listed below.

<table>
<thead>
<tr>
<th>L</th>
<th>PdL₂</th>
<th>PdL₂RX</th>
<th>PdL₂HX</th>
</tr>
</thead>
<tbody>
<tr>
<td>P(t-Bu)₂Me</td>
<td>42.3</td>
<td>27.6</td>
<td>53.1</td>
</tr>
<tr>
<td>P(t-Bu)₂Et</td>
<td>63.3</td>
<td>–⁵</td>
<td>63.9</td>
</tr>
<tr>
<td>PCy₃</td>
<td>39.7</td>
<td>22.0</td>
<td>42.0</td>
</tr>
<tr>
<td>P(t-Bu)₃</td>
<td>85.9</td>
<td>–⁵</td>
<td>–⁵</td>
</tr>
</tbody>
</table>

Note: PdL₂HX is sometimes formed as a secondary reaction product.

**Activation Parameters (eq 1).** All experiments were conducted according to the general procedure, with 17.1 mg of Pd(P(t-Bu)₂Me)₂ and 8.3 mg of n-nonyl bromide. Prior to the addition of n-nonyl bromide, the NMR tubes were equilibrated to the appropriate temperature.

Rate constants were determined for reactions conducted from 263-303 K. Free energies of activation (ΔGᵢ) were determined from the rate constants and plotted versus reaction temperature.
These data indicate: $\Delta H^\ddagger = 2.4 \text{ kcal/mol}$ and $\Delta S^\ddagger = -63 \text{ eu}$.

**Solvent Effect (Table 1).** All experiments were conducted according to the general procedure, with 17.1 mg of Pd(P(t-Bu)$_2$Me)$_2$ and 8.3 mg of $n$-nonyl bromide. Prior to the addition of $n$-nonyl bromide, the NMR tubes were equilibrated to 0 °C. The reactions were monitored by $^{31}$P NMR spectroscopy at 0 °C.
**Hexane (Table 1, entry 1).** An initial experiment showed no reaction (<2%) after 3 hours at 0 °C. This indicates: $k < 2.36 \times 10^{-5} \text{ M}^{-1}\text{s}^{-1}$ and $\Delta G^\ddagger > 21.7 \text{ kcal/mol}$.

An additional experiment was performed at 60 °C. The reaction proceeded to 13.9% conversion after 15 min ($k = 0.00224 \text{ M}^{-1}\text{s}^{-1}$ and $\Delta G^\ddagger = 23.6 \text{ kcal/mol}$) and 27.5% conversion after 30 minutes ($k = 0.00263 \text{ M}^{-1}\text{s}^{-1}$ and $\Delta G^\ddagger = 23.5 \text{ kcal/mol}$).

**Toluene (Table 1, entry 2).**

These data indicate: $k = 0.000588 \text{ M}^{-1}\text{s}^{-1}$ and $\Delta G^\ddagger = 20.0 \text{ kcal/mol}$.
THF (Table 1, entry 3).

These data indicate: $k = 0.00151 \text{ M}^{-1}\text{s}^{-1}$ and $\Delta G^\ddagger = 19.5 \text{kcal/mol}$. 
$t$-Amyl Alcohol (Table 1, entry 4).

These data indicate: $k = 0.0189 \text{ M}^{-1}\text{s}^{-1}$ and $\Delta G^\ddagger = 18.1 \text{ kcal/mol}$. 
NMP (Table 1, entry 5).

These data indicate: \( k = 0.0203 \text{ M}^{-1}\text{s}^{-1} \) and \( \Delta G^\ddagger = 18.0 \text{ kcal/mol} \).
DMF (Table 1, entry 6).

These data indicate: \( k = 0.0301 \text{ M}^{-1}\text{s}^{-1} \) and \( \Delta G^\ddagger = 17.8 \text{ kcal/mol} \).

**Leaving-Group Effect (Table 2).** All experiments were conducted according to the general procedure, with 17.1 mg of Pd(P(t-Bu)_2Me)_2 and 0.040 mmol of \( n \)-nonyl-X.
Prior to the addition of the electrophile, the NMR tubes were equilibrated to the appropriate temperature. The reactions were monitored by $^{31}$P NMR spectroscopy.

**Iodide (Table 2, entry 1).**

These data indicate: $k = 0.00158 \text{ M}^{-1}\text{s}^{-1}$ and $\Delta G^\dagger = 15.1 \text{ kcal/mol}$. This corresponds to a half-life of 2.20 hours at $-60 ^\circ\text{C}$. 
Bromide (Table 2, entry 2).

These data indicate: \( k = 0.00151 \text{ M}^{-1}\text{s}^{-1} \) and \( \Delta G^\ddagger = 19.5 \text{ kcal/mol} \). This corresponds to a half-life of 2.30 hours at 0 °C.
Chloride (Table 2, entry 3).

These data indicate: $k = 0.0000722 \text{ M}^{-1}\text{s}^{-1}$ and $\Delta G^\ddagger = 25.9 \text{ kcal/mol}$. This corresponds to a half-life of 2.00 days at 60 °C.

Fluoride (Table 2, entry 4).

Addition of $n$-nonyl fluoride gave no (< 2%) PdL$_2$RF or PdL$_2$HF after 43 hours at 60 °C. This corresponds to $k < 1.64 \times 10^{-6} \text{ M}^{-1}\text{s}^{-1}$ and $\Delta G^\ddagger > 28.4 \text{ kcal/mol}$. 
Tosylate (Table 2, entry 5).

These data indicate: $k = 0.000334 \text{ M}^{-1} \text{s}^{-1}$ and $\Delta G^\ddagger = 23.3 \text{ kcal/mol}$. This corresponds to a half-life of 10.4 hours at 40 °C.

**Steric Effect of R (Table 3).** All experiments were conducted according to the general procedure, with 17.1 mg of Pd(P(t-Bu)₂Me)₂ and 0.040 mmol of the alkyl
bromide. Prior to the addition of the electrophile, the NMR tubes were equilibrated to 0 °C. The reactions were monitored by $^{31}$P NMR spectroscopy.

_n-Nonyl bromide (Table 3, entry 1)._  

![Graph](Image)

These data indicate: $k = 0.00151 \text{ M}^{-1}\text{s}^{-1}$, $\Delta G^\ddagger = 19.5 \text{ kcal/mol}$, and $k_{rel} = 1.0$. 
1-Bromo-3-methylbutane (Table 3, entry 2).

These data indicate: $k = 0.000294 \text{ M}^{-1}\text{s}^{-1}$, $\Delta G^\ddagger = 20.3 \text{ kcal/mol}$, and $k_{\text{rel}} = 0.19$. 
Isobutyl bromide (Table 3, entry 3).

\[ y = -0.21 + 8.18 \times 10^{-5}x \quad R = 0.962 \]

These data indicate: \( k = 0.0000818 \text{ M}^{-1}\text{s}^{-1} \), \( \Delta G^\ddagger = 21.0 \text{ kcal/mol} \), and \( k_{rel} = 0.0542 \).

Isopropyl bromide (Table 3, entry 4). An initial experiment showed no reaction (<2%) after 3 hours at 0 °C. This indicates: \( k < 2.36 \times 10^{-5} \text{ M}^{-1}\text{s}^{-1} \) and \( \Delta G^\ddagger > 21.7 \text{ kcal/mol} \).

An additional experiment was performed at 60 °C. The reaction proceeded to 3.0% conversion after 15 min (\( k = 0.000430 \text{ M}^{-1}\text{s}^{-1} \) and \( \Delta G^\ddagger = 24.7 \text{ kcal/mol} \)) and 6.0% after
30 min (k = 0.000443 M^{-1}s^{-1} and \Delta G^\ddagger = 24.7 \text{ kcal/mol}). Assuming a \Delta G^\ddagger of 24.7 \text{ kcal/mol at 0 °C,} these data correspond to k = 9.0 \times 10^{-8} \text{ M}^{-1}\text{s}^{-1} and k_{rel} = 6.0 \times 10^{-6}.

**Ligand Effect (Table 4).** All experiments were conducted according to the general procedure, with 0.040 mmol of PdL_2 and 8.3 mg of n-nonyl bromide. Prior to the addition of the electrophile, the NMR tubes were equilibrated to the appropriate temperature. The reactions were monitored by \(^{31}\text{P} \text{ NMR spectroscopy.} \)
P(t-Bu)$_2$Me (Table 4, entry 1).

These data indicate: $k = 0.00151 \text{ M}^{-1}\text{s}^{-1}$ and $\Delta G^\ddagger = 19.5 \text{ kcal/mol}$.
PCy$_3$ (Table 4, entry 2).

These data indicate: $k = 0.000596$ M$^{-1}$s$^{-1}$ and $\Delta G^\dagger = 20.0$ kcal/mol.
$P(t\text{-}Bu)_2\text{Et}$ (Table 4, entry 3).

These data indicate: $k = 0.000144 \text{ M}^{-1}\text{s}^{-1}$ and $\Delta G^\ddagger = 25.4 \text{ kcal/mol}$.

$P(t\text{-}Bu)_3$ (Table 4, entry 4). The reaction showed no product (<2%) after 43 hours at 60 °C. This gives an estimate of: $k < 1.63 \times 10^{-6} \text{ M}^{-1}\text{s}^{-1}$ and $\Delta G^\ddagger > 28.4 \text{ kcal/mol}$.
IV. Computations

All calculations were performed using Gaussian 98 Rev. A.11.4. Optimization of free-phosphine structures was performed using the B3LYP method and 6-31G* basis-set. Optimization of structures containing palladium was performed using the B3LYP method and LanL2DZ basis-set. Frequency calculations were performed on all solutions, and each stationary point was determined to be a local minimum (i.e., no imaginary frequencies were determined). All solutions were also checked for stability and were found to be stable under the perturbations considered.

The absolute electronic energies in hartrees are given below, along with corrected energies taking into account thermal energy (i.e., calculated zero-point vibrational energy and thermal energy at 298.15 K).

<table>
<thead>
<tr>
<th>Picture</th>
<th>Description</th>
<th>Electronic Energy (hartrees)</th>
<th>Thermally Corrected Energy (hartrees)</th>
<th>Relative Energy$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="P(t-Bu)2Et/eclipsed" /></td>
<td>P(t-Bu)2Et/eclipsed</td>
<td>-736.269658</td>
<td>-735.940378</td>
<td>0.0 kcal/mol$^b$</td>
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<tr>
<td><img src="image2" alt="P(t-Bu)2Et/gauche" /></td>
<td>P(t-Bu)2Et/gauche</td>
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<td>-735.938657</td>
<td>+1.1 kcal/mol$^b$</td>
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<tr>
<td><img src="image3" alt="P(t-Bu)2Et/anti" /></td>
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<td>-735.935191</td>
<td>+3.3 kcal/mol$^b$</td>
</tr>
<tr>
<td><img src="image4" alt="P(t-Bu)2EtPd/eclipsed" /></td>
<td>(P(t-Bu)2Et)Pd/ eclipsed</td>
<td>-528.109929</td>
<td>-527.777394</td>
<td>0.0 kcal/mol$^c$</td>
</tr>
<tr>
<td>Structure</td>
<td>Formula</td>
<td>Energy (a.u.)</td>
<td>Energy (eV)</td>
<td>Relative Energy (kcal/mol)</td>
</tr>
<tr>
<td>-----------</td>
<td>---------</td>
<td>---------------</td>
<td>-------------</td>
<td>---------------------------</td>
</tr>
<tr>
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<tr>
<td><img src="image4.png" alt="Structure" /></td>
<td>(P(t-Bu)2Me)Pd</td>
<td>-488.806647</td>
<td>-488.504342</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) Relative energies are based on thermally corrected energies. \(^b\) Relative energies are with respect to the various conformations of P(t-Bu)2Et. \(^c\) Relative energies are with respect to various conformations of (P(t-Bu)2Et)Pd.
References

