

Computational mechanistic study of Suzuki coupling of an α -cyano-activated secondary alkyl
Supporting Information I

I. BENCHMARKS OF TRANSITION METAL COMPLEX GEOMETRIES

In this section, we benchmark the M06/6-31+G(d,p)/LANL08 method used in this work against experimental crystal structures of two transition metal complexes[1, 2]. Table 1 reports the calculated geometric parameters for the molybdenum acetonitrile complex of Ref. 1. The mean absolute errors of calculated bond lengths and bond angles 0.04 Å and 1.0° respectively. These small errors are consistent with crystal packing effects. Table 2 reports the the calculated geometric parameters for the palladium complex in Ref. 2. Bond lengths and bond angles have mean absolute errors 0.04 Å and 2.3°. Calculated geometries and atom indices are shown in Figure 1. M06 has also been shown to outperform most other DFT methods for agostic interactions in Nobium organometallic complexes.[3, 4] This suggests that M06 is appropriate for the geometry optimizations performed here.

FIG. 1. M06/6-31+G(d,p)/LANL08 geometries and atom labels. (a) Mo(II)-acetonitrile, Ref. 1 (b) Cl-Pd(II)En-(NO₂), Ref. 2.

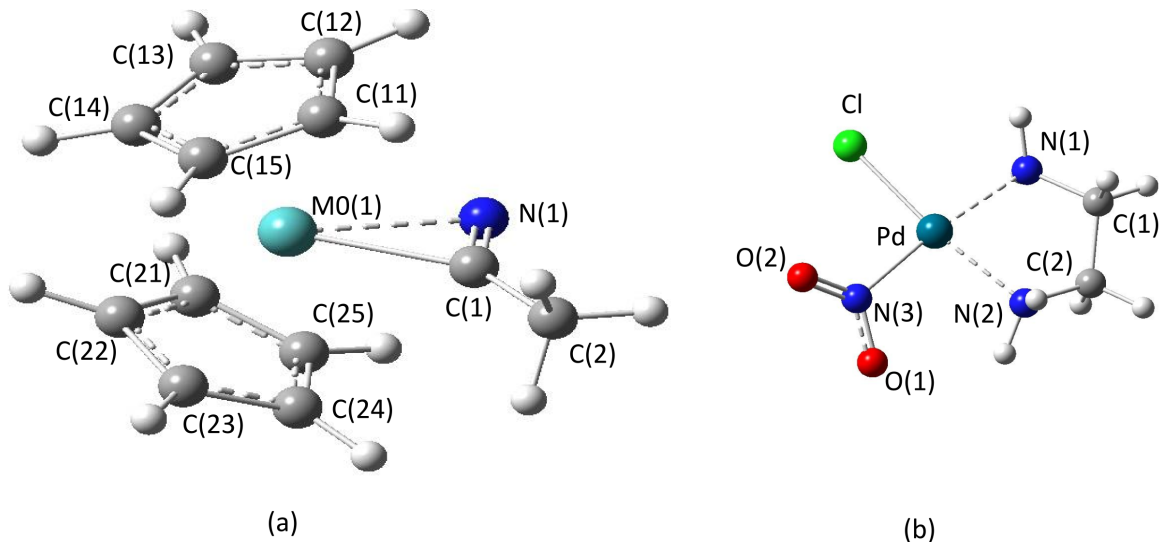


TABLE I. Calculated bond distances (\AA) and bond angles (degrees) of Cp_2Mo -Acetonitrile, and errors vs. Ref. 1.

Distance	Calculated(\AA)	Err.(\AA)	Angle	Calculated($^\circ$)	Err.($^\circ$)
N(1)-Mo(1)	2.216	0.001	C(1)-Mo(1)-N(1)	32.7	-0.5
C(1)-Mo(1)	2.147	-0.030	C(2)-C(1)-Mo(1)	144.0	-0.3
C(11)-Mo(1)	2.336	-0.063	C(2)-C(1)-N(1)	139.3	-1.6
C(12)-Mo(1)	2.350	-0.043	C(15)-C(11)-C(12)	108.7	0.0
C(13)-M0(1)	2.326	-0.035	C(13)-C(12)-C(11)	109.0	-2.4
C(14)-Mo(1)	2.273	0.020	C(14)-C(13)-C(12)	106.6	3.2
C(15)-Mo(1)	2.304	-0.023	C(15)-C(14)-C(13)	109.2	-1.4
C(21)-Mo(1)	2.326	-0.033	C(14)-C(15)-C(1 1)	106.5	0.6
C(22)-Mo(1)	2.273	-0.008	C(25)-C(2 1)-C(22)	106.6	0.5
C(23)-Mo(1)	2.304	-0.025	C(23)-C(22)-C(21)	109.2	-0.5
C(24)-Mo(1)	2.336	-0.025	C(24)-C(23)-C(22)	106.5	0.2
C(25)-Mo(1)	2.350	-0.037	C(25)-C(24)-C(23)	108.7	-0.7
C(1)-N(1)	1.228	0.125	C(24)-C(25)-C(21)	109.0	0.6
C(2)-C(1)	1.481	-0.036			
C(12)-C(11)	1.425	-0.011			
C(15)-C(11)	1.418	-0.021			
C(13)-C(12)	1.410	-0.015			
C(14)-C(13)	1.435	-0.055			
C(15)-C(14)	1.433	-0.023			
C(22)-C(21)	1.435	-0.042			
C(25)-C(21)	1.410	-0.013			
C(23)-C(22)	1.435	-0.0243			
C(24)-C(23)	1.433	-0.027			
C(25)-C(24)	1.425	-0.122			

TABLE II. Calculated bond distances (\AA) and bond angles (degrees) of En-PdCl-NO₂, and errors vs. Ref. 2.

Distance	Calculated \AA	Err	Angle ⁰	Calculated	Err
Pd-N(1)	2.154	-0.12	N2-Pd-N1	81.8	1.9
Pd-N(2)	2.147	-0.12	N3-Pd-Cl	96.3	-4.5
Pd-N(3)	2.014	0.01	N3-Pd-N2	91.7	0.2
Pd-Cl	2.315	0.00	N1-Pd-Cl	90.1	2.5
N(1)-C(1)	1.475	0.01	N2-Pd-Cl	171.7	4.1
C(1)-C(2)	1.519	-0.05	N3-Pd-N1	173.2	2.2
N(2)-C(2)	1.475	0.02	C1-N1-Pd	108.3	0.6
N(3)-O(2)	1.208	-0.01	C2-C1-N1	109.3	0.5
N(3)-O(1)	1.236	0.00	C1-C2-N2	109.3	-1.4
Cl-N(1)	3.16	0.00	C2-N2-Pd	107.1	2.1
Cl-N(3)	3.23	-0.11	O2-N3-O1	124.2	-3.8
N(3)-N(2)	2.98	-0.07	O2-N3-Pd	122.7	-1.2
N(2)-N(1)	2.81	-0.10	O1-N3-Pd	113.0	4.9

II. BENCHMARKS OF TRANSITION METAL REACTION BARRIERS

This section benchmarks M06 against *ab initio* calculations for the barriers to β -hydride elimination from the model oxidative addition products **2H-cis-beta** and **2H-trans-beta**, *via* transition states **TS23-cis-beta** and **TS23-trans-beta**. These are two conformations of (C₂H₅)Pd(Cl)PMe₃. Calculations use M06/6-31+G(d,p)/LANL08 geometries. Results are reported in Table 3. All three DFT methods give the same barrier for **TS23-trans-beta**, slightly overestimating the accurate CCSD(T) result. M06 somewhat overestimates the **TS23-cis-beta** barrier. The error is acceptable given its aforementioned good performance for transition metal complex geometries.

TABLE III. Calculated β -hydride elimination barriers (kcal mol⁻¹)

Method	TS23-cis-beta	TS23-trans-beta
CCSD(T)/pVTZ	1.1	13.6
CCSD(T)/pVQZ*	1.1	13.7
M06/LB	4.5	15.9
M06/HB	4.1	15.0
B3LYP/LB	3.2	15.5
B3LYP/HB	2.5	15.0
PBE0/HB	1.7	15.1
HF/pVQZ	5.1	22.1

*- energy approximated as $E_{HF/Aug-cc-pvQZ} - E_{HF/cc-pvTZ} + E_{CCSD(T)/cc-pvTZ}$

Notes on Basis sets combinations:

LB: - Lanl08 on Pd, 6-31+G(d,p) on other atoms

HB :- Lanl08 on Pd, 6-311+G(d,p) on other atoms

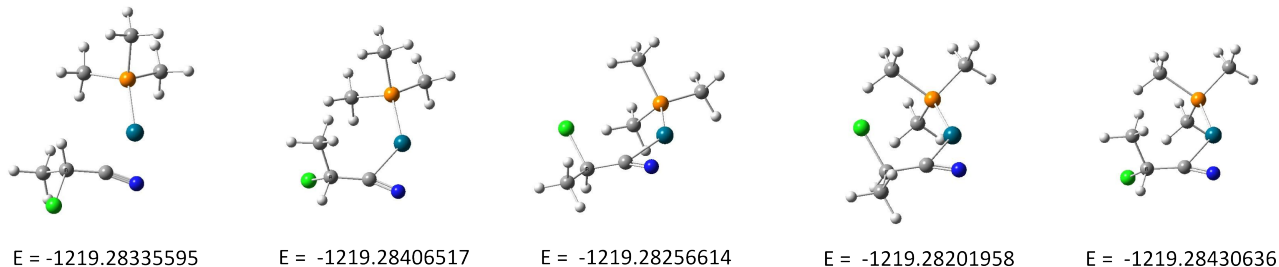
pvQZ : -Aug-cc-pvQZ-pp on Pd, Aug-cc-pvQZ on other atoms

pvTZ :- cc-pvQZ-pp on Pd, cc-pvTZ on other atoms

III. EXAMPLE CONFORMATIONAL ANALYSIS

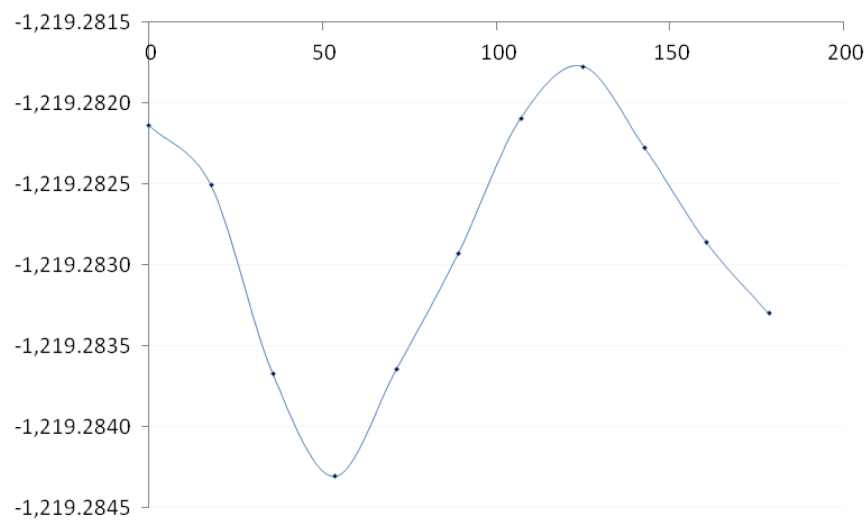
This section presents a conformational analysis of the initial reactant complex between 2-chloropropane nitrile and Pd(0)-PMe₃ complex. Figure 2 shows the calculated initial side bonded complexations of the reactant cyano to the Pd(0)-PMe₃.

FIG. 2. Conformers of η^2 complexation of 2-Chloropropane nitrile. Energies of the conformers are in Hartrees. (1 hartree = 627.5095 kcal mol⁻¹)



We choose the lowest energy geometry in 2 for conformational analysis. We created ~ 10 initial geometries by manually (or automatically) varying the Pd-C(*sp*)-C(*sp*³)-Cl dihedral angle. We then reoptimized each of these initial geometries. In this case, the geometry optimizations converged to one of two different conformers, **1-CN_a** and **1-CN_b**. These conformers influence the guesses in the geometries of the transition states (**TS12-CN_b-SN2** and **TS12-CN_a-I**) and their corresponding products. Often, the optimized products and transition states also go through a similar conformational search procedure. IRC calculations verify the reactants and products are connected to the transition via a minimal energy pathway. The molecular mechanics force field method and the semi-empirical methods proved not very useful in conformational searches for the coordinatively unsaturated Pd complexes.

FIG. 3. PES of dihedral scan of the lowest energy conformer in figure 2. The abscissa is the Pd-C(*sp*)-C(*sp*³)-Cl dihedral angle (°) and the ordinate is the energy (a.u) of the conformer. (1 a.u =627.5095 kcal/mol)



IV. HALIDE EFFECTS ON *CIS-TRANS* ISOMERIZATION IN MODEL OXIDATIVE ADDITION PRODUCTS

Here we study the *cis-trans* isomerization of a simple model for a coordinatively unsaturated oxidative addition product, $\text{MePd}(\text{PMe}_3)\text{-X}$, where X is a halide (figure 4). We calculate the relative energies of the three isomers in 4, to study the effect of the halide *trans* influence $\text{Br}^- > \text{Cl}^- > \text{F}^-$. Table IV reports the relative energies of isomers. Complex (a), with the strongly *trans*-directing alkyl ligand *trans* to X, is always more stable than complex (b) with alkyl *trans* to PMe_3 . The stabilization decreases as the *trans* influence of X increases. Stabilization of complex (c), analogous to **2-cis-Cl**, shows a similar trend.

FIG. 4. Three different coordinatively unsaturated complex isomers (X=F,Cl and Br).

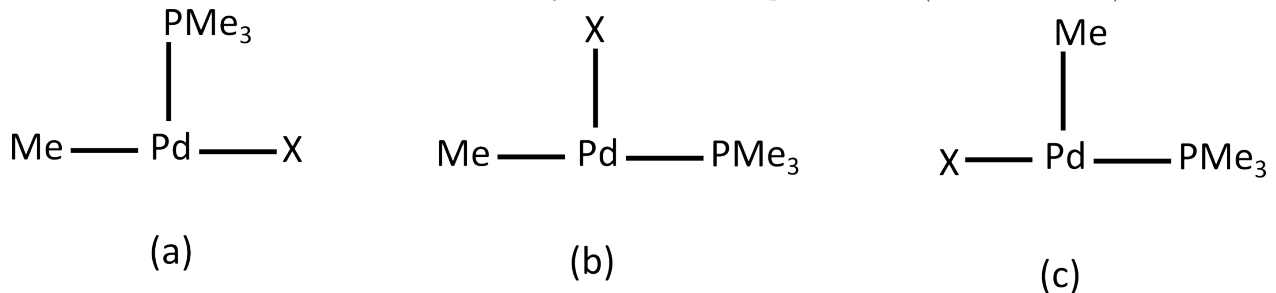


TABLE IV. Relative Gibbs energies (kcal/mol) of isomers of 4 with different halides (X=F,Cl and Br). Electronegativities of halides are in parenthesis.

X=	trans-me-Pd-X (a)	cis-Me-Pd-X (b)	cis-me-Pd-X (c)
F (4.0)	0.0	22.8	-2.6
Cl (3.0)	0.0	18.0	-0.5
Br (2.8)	0.0	15.0	-0.3

V. CALCULATED TURNOVER FREQUENCIES (TOF)

We use the Eyring equation to calculate the TOF of individual reaction steps in the catalytic cycle. The following tables report calculated TOFs of all reaction pathway discussed in the main article. The TOF is calculated as

$$TOF = \frac{K_b T}{h} e^{-\Delta G^\ddagger / RT} \quad (1)$$

Here $T=298.15$ K, h is Plank's constant, and k_B is Boltzman's constant. ΔG^\ddagger is obtained from the theoretical calculations using the energetic span approximation. While the absolute TOF are likely unreliable, due to their exponential dependence on errors in the calculation, relative TOF of different pathways give insights into selectivity.

TABLE V. Oxidative Addition (Figure 3- main article): Neutral Intermediates before transition states

Reactant-Complex	Transition state	ΔG^\ddagger (kcal mol ⁻¹)	TOF(s ⁻¹)
1-Cl	TS12-Cl-I	15.7	19.0
1-CNa	TS12-CNa-I	18.9	8.6×10^{-2}
1-CNb	TS12-CNb-SN2	16.4	4.9

TABLE VI. Anionic pathways of Oxidative Addition (Figure 4- main article): Barriers relative to [PMe₃-Pd-Cl]⁻ and 2-chloropropane nitrile.

Reactant-Complex	Transition state	ΔG^\ddagger (kcal mol ⁻¹)	TOF(s ⁻¹)
1-H+Cl	TS12-Cl+Cl-I	34.0	7.2×10^{-13}
1-CNa+Cl	TS12-CNa+Cl-I	25.7	8.8×10^{-7}
1-CNb+Cl	TS12-CNb+Cl-SN2	13.0	1.8×10^3

TABLE VII. Anionic pathways of Oxidative Addition (Figure 4- main article): Barriers relative to complexations.

Reactant-Complex	Transition state	ΔG^\ddagger (kcal mol ⁻¹)	TOF(s ⁻¹)
1-H+Cl	TS12-Cl-I	31.4	5.8×10^{-13}
1-CNa+Cl	TS12-CNa-I	19.6	2.6×10^{-2}
1-CNb+Cl	TS12-CNb-SN2	6.4	1.2×10^8

TABLE VIII. β -hydride Elimination pathways (Figures 5 and 6- main article)

Reactant-Complex	Transition state	ΔG^\ddagger (kcal mol ⁻¹)	TOF(s ⁻¹)
2-cis-beta	TS23-cis-beta	4.5	3.1×10^9
2H-cis-beta	TS23H-cis-beta	2.2	1.5×10^{11}
2H-trans-beta	TS23H-trans-beta	14.6	1.2×10^2

TABLE IX. β -hydride Elimination (Figure 9- main article) pathways

Reactant-Complex	Transition state	ΔG^\ddagger (kcal mol ⁻¹)	TOF(s ⁻¹)
5-cis-beta	TS56-cis-beta	15.0	62.0
5-trans-beta	TS56-trans-beta	10.7	8.8×10^4

TABLE X. Reductive Eliminations pathways (Figure 10- main article)

Reactant-Complex	Transition state	ΔG^\ddagger (kcal mol ⁻¹)	TOF(s ⁻¹)
5-cis-CN	TS56-cis-CN	14.3	2.0×10^2
5-cis-alpha	TS56-cis-alpha	13.0	1.8×10^3
5-cis-Ph	TS56-cis-Ph	9.6	5.6×10^5

VI. COUNTERPOISE ENERGIES OF COMPLEXES

Table XI reports calculated basis set superposition errors for the complexation energies in Figures 3,4 and 7 of the main article.

TABLE XI. Counterpoise Energies (E_{BSSE}) in Hartrees

Complex	E_{BSSE}	Complex	E_{BSSE}	Complex	E_{BSSE}
1-Cl	0.0021746938	1-H+Cl	0.0043466	4A-FB	0.006531316
1-CNa	0.0027528665	1-CNa+Cl	0.0038327	4-FB-Ph	0.004961846
1-CNb	0.0026439000	1-CNb+Cl	0.0037209	4A-OB	0.003628719
1-N	0.0021539119	4-F	0.00285279	4-OB-Ph	0.002182558

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