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Chemoselectivity in the Reductive Elimination from High Oxidation State Palladium Complexes – Scrambling Mechanism Uncovered

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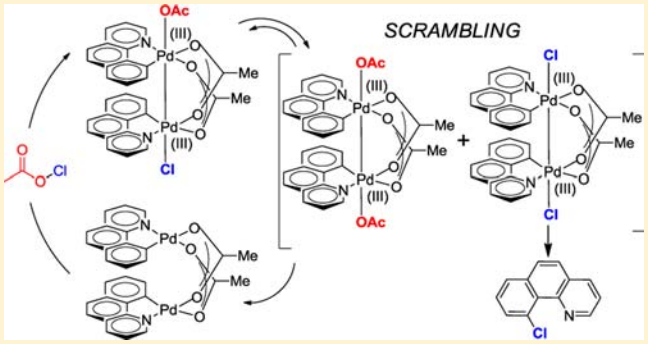
Supporting Information



ABSTRACT: With the objective to increase understanding of the factors that control selectivities in high oxidation state palladium chemistry, we examined the chemoselectivity in the reductive elimination of a dinuclear Pd(III) complex bearing different apical ligands. Experimental, computational, and spectroscopic studies were applied to understand the product selectivity derived from the mixed Cl/OAc dinuclear Pd(III) complex. Analogous species were previously implicated in oxidative C−H functionalizations. The observed experimental chemoselectivity for ArCl was found to be inconsistent with the direct reductive elimination of the mixed Cl/OAc containing Pd(III) dimer. The latter complex is therefore not the key intermediate that ultimately determines the product selectivity. Our spectroscopic and computational studies of the stoichiometric reactivity suggest that the mixed dinuclear Pd(III) complex scrambles readily to give the two Pd(III) homodimers [AcO−Pd(III)−Pd(III)−OAc and Cl−Pd(III)−Pd(III)−Cl], of which the dichlorinated Pd(III) dimer ultimately gives ArCl upon reductive elimination.

INTRODUCTION

The reductive elimination from high oxidation state palladium species constitutes a key step in C−H functionalization processes.[1] These high-valent palladium intermediates bear multiple sites that could potentially undergo reductive elimination.[1−3] Considering the Pd(IV) complex **4** (Figure 1), for example, three different products could in principle arise from reductive eliminations (i.e., $ArCF_3$, ArOAc, and ArOH). A key challenge in the development of selective C−H functionalization processes lies therefore in the fundamental understanding of the factors that control reductive elimination to eventually steer processes in the desired fashion.[3] An additional challenge is posed by the fact that multiple intermediates could potentially be reactive in catalytic C−H functionalization processes. In this context, not only Pd(IV),[4,5] but also dinuclear Pd(III) complexes[6] were implicated as intermediates in oxidative C−H functionalizations for substrates resembling the 2-phenyl-pyridine framework (i.e., complexes **1**−**5**; see Figure 1).

It is not clear, however, whether these intermediates are the key species from which direct reductive elimination to the products subsequently takes place. Instead, they might be intermediates en route toward alternative reactive species, and the latter might then control the reaction outcome (i.e., product selectivity).[7] Canty, Ritter, Sanford, et al. showed very recently, for example, that dinuclear Pd(III) and mononuclear Pd(IV) pathways can be connected in oxidative trifluoromethylation reactions.[8]

This article describes our efforts to investigate the likeliness of direct reductive elimination from a mixed dinuclear Pd(III)−Pd(III) complex in oxidative chlorination reactions. We studied a number of mechanisms for reductive elimination and identified that scrambling to the corresponding homo dimers occurs readily prior to reductive elimination.

We decided to investigate the chemoselectivity of the mixed dinuclear Pd(III) complex **6** (see Scheme 1), the reason being that (i) strong support was recently obtained by Ritter et al. for the intermediacy of the analogous dinuclear complex **2** (shown in Figure 1) in the oxidative chlorination of ArH with *N*-chlorosuccinimide.[9] (ii) Previous computational analyses by Canty, Yates, and co-workers concluded that **6** is a true Pd(III)−Pd(III) complex, rather than Pd(IV)−Pd(II).[10] The NBO population and charge analyses of **6** showed values nearly identical to those calculated for dichlorinated Pd(III)-dimer **1** (Figure 1).[10] The latter complex **1** in turn was previously suggested to give rise to reductive elimination, in which the dinuclear Pd−Pd core stays intact.[6c,11] As part of our ongoing studies to understand the chemistry derived from dinuclear Pd(I) complexes,[12] we have recently demonstrated the usefulness of combining experimental and computational chemoselectivity studies to gain indirect mechanistic information on key catalytic species.[13] We therefore envisaged that the study of the chemoselectivity in the reductive elimination of the unsymmetrical dimer **6** may give valuable information on

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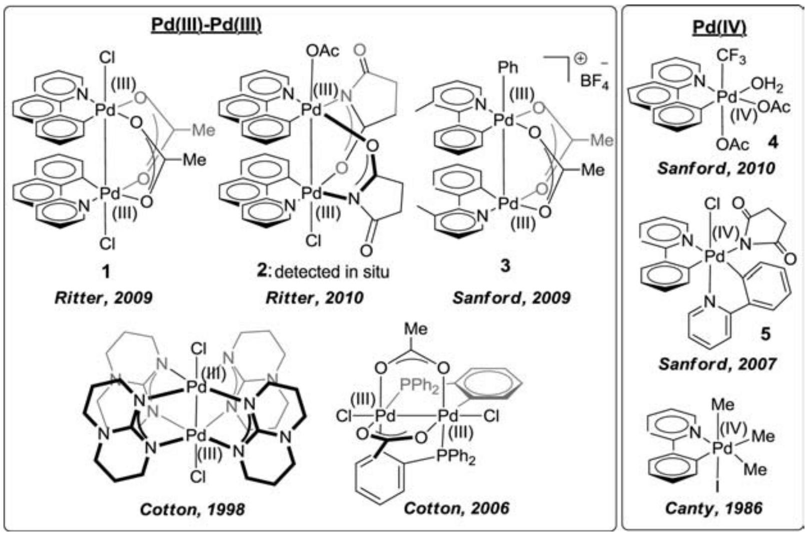
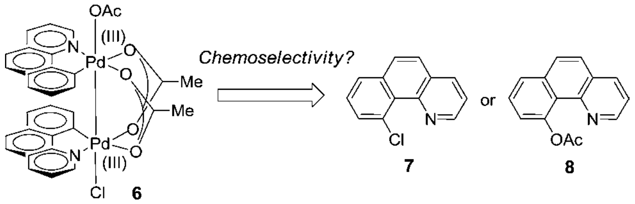


Figure 1. Selected examples of Pd(III)−Pd(III) and Pd(IV) complexes.

Scheme 1. Planned Chemoselectivity Investigation



whether the direct reductive elimination from this species to the product is in fact likely.

■ RESULTS AND DISCUSSION

Investigation of the Likeliness of Direct Reductive Elimination from Pd(III) Dimer 6. We initially calculated[14,23] the transition states (TSs) for direct reductive elimination of ArCl **7** and ArOAc **8** from the dinuclear complex **6** using Density Functional Theory.[15] Figure 2 illustrates the transition state geometries. For the reductive elimination of ArOAc, a bridging five-membered TS geometry (as opposed to three-membered) was found to be favored, consistent with recent findings by Sanford and co-workers.[16] The computationally predicted selectivity for ArCl versus ArOAc formation ($\Delta\Delta G^{\ddagger}$) was calculated with a variety of functionals, and the results are summarized in Table 1. All methods predict a significant preference for C−OAc over C−Cl bond formation (by $\Delta\Delta G^{\ddagger}$ = 8−12 kcal/mol). The reductive elimination to a substrate bound complex is endergonic in both cases.[17] However, the product complex resulting from C−OAc transfer is more stable than that arising from Ar−Cl elimination (by $\Delta\Delta G_{\mathrm{rxn}}$ = 14.8 kcal/mol[20]). The calculations therefore suggest that the direct reductive elimination of ArOAc **8** from dinuclear complex **6** is both kinetically and thermodynamically[18] favored over ArCl elimination.

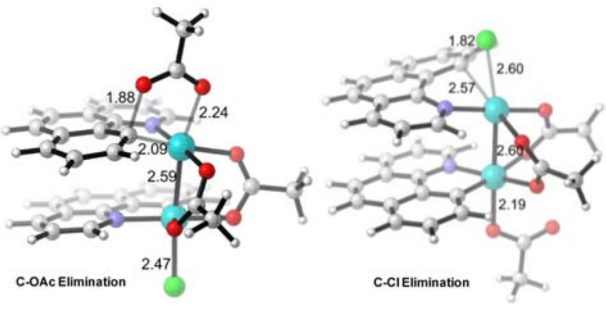


Figure 2. TSs for the reductive elimination of ArOAc (left) and ArCl (right) from **6**.[19] C−OAc transfer is favored by $\Delta\Delta G^{\ddagger}$ = 8−12 kcal/mol (see Table 1).

We performed the analogous calculations also for succinimide-derived dimer **2** (see Figure 1) that was previously suggested to be involved in catalysis.[9] Once again, we find that reductive elimination of ArOAc is predicted to be favored over ArCl (by $\Delta\Delta G^{\ddagger}$ = 8.4 kcal/mol[20] in DCM[21]). The chemoselectivity of reductive elimination therefore seems independent of the bridging ligands [acetate (in **6**) versus succinimide (in **2**)].

In contrast to these predictions, in the catalytic oxidative C−H functionalization of benzo[*h*]quinoline with *N*-chlorosuccinimide, the chlorinated product was isolated as the nearly exclusive product, along with only trace amounts of ArOAc.[9,22] This inconsistency of experimental product selectivity and computational predictions suggests that direct reductive elimination from the Pd(III)-dimer does not occur under catalytic conditions, and instead transformation to a different intermediate takes place prior to reductive elimination.

To get deeper insights, we decided to perform stoichiometric experiments on the reductive elimination of dimer **6**. Ritter and co-workers previously prepared the succinimide complex **2** (Figure 1) in situ via reaction of Pd(II) dimer **17** with acetyl hypochlorite, and subsequently studied the reductive elimination in the presence of pyridine to mimic catalytic conditions, which, as indicated by the authors,[24] could have changed the mechanism.[25] Our aim was to study the product selectivity arising from "direct" reductive elimination of **6** in the absence of additives.

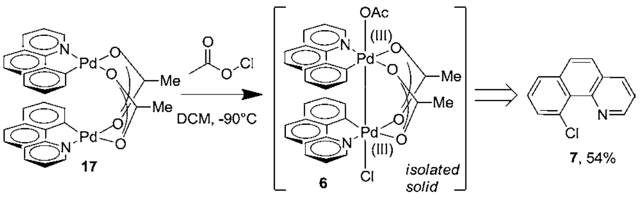
We reacted an excess of acetyl hypochlorite (1.5 equiv) with cyclopalladated Pd(II) dimer **17** in DCM at −90 °C under inert atmosphere for 10 min (Scheme 2). Cold hexane was subsequently added to precipitate **6** from the mixture, and various washings were subsequently undertaken (at −90 °C). ^{1}H NMR analysis (at −90 °C) of the solid indicated the

Table 1. Computational Methods Applied To Calculate the Activation Free Energy $\Delta G^{\ddagger}$ and $\Delta\Delta G^{\ddagger}$ Preference for C−OAc Transfer from 6[23] [a]

entry	method	$\Delta G^{\ddagger}_{\mathrm{C-OAc}}$	$\Delta\Delta G^{\ddagger\, c}$
1	SMD$_{(\mathrm{DCM})}$ ^{b} PBE0/6-31G(d)^{d}	19.0	10.3
2	M06L/6-31G(d)$_{(\mathrm{gas\ phase})}$ ^{b}	14.0	11.6
3	COSMO-RS$_{(\mathrm{DCM})}$ ^{b} M06L/6-311++G(d,p)^{e}	16.4	11.0
4	COSMO-RS$_{(\mathrm{DCM})}$ ^{b} PBE0-D3/6-311++G(d,p)^{e}	17.6	11.0
5	COSMO-RS$_{(\mathrm{DCM})}$ ^{b} B3PW91-D3/6-311++G(d,p)^{e}	17.8	12.1
6	CPCM$_{(\mathrm{DCM})}$ ^{b} M06L/6-311++G(d,p)^{e}	16.3	10.6
7	CPCM$_{(\mathrm{DCM})}$ ^{b} PBE0-D3/6-311++G(d,p)^{e}	17.9	9.1
8	CPCM$_{(\mathrm{DCM})}$ ^{b} B3PW91-D3/6-311++G(d,p)^{e}	18.2	10.4
9	CPCM$_{(\mathrm{DCM})}$ ^{b} PBE0/6-311++G(d,p)^{e}	18.6	10.6
10	CPCM$_{(\mathrm{DCM})}$ ^{b} B3PW91/6-311++G(d,p)^{e}	19.2	8.2

[a] Energies in kcal/mol (at 298 K). [b] ECP for Pd is SDD. [c] $\Delta\Delta G^{\ddagger} = \Delta G^{\ddagger}_{\mathrm{C-Cl}} - \Delta G^{\ddagger}_{\mathrm{C-OAc}}$. [d] Structure optimized with solvent continuum model SMD (DCM). [e] B3LYP/6-31G(d) (with LANL2DZ for Pd) geometry.

Scheme 2. Preparation of 6 and Test of Its Reactivity[a]



[a] ArOAc 8 was formed in 4% yield.

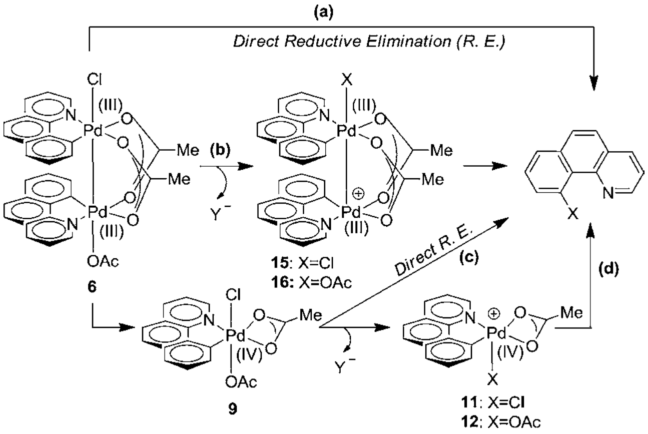
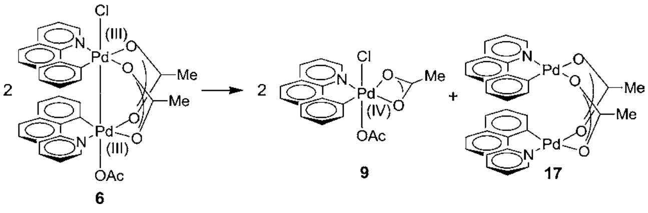


Figure 3. Potential pathways for reductive elimination.

Scheme 3. Disproportionation of 6



presence of the dimer 6 along with residual DCM and hexane (see the Supporting Information for ^{1}H NMR spectrum versus the internal standard dioxane). The aromatic region as well as the signals at 2.70 ppm (6H for bridging acetate ligands) and 1.48 ppm (3H for apical acetate) are in agreement with the data previously reported for 1, 2 (Figure 1), and the diacetate analogue of 1.[6a−c] A resonance at 7.84 ppm (1H, dd) was also present, which is more downfield than any of the signals characteristic of the dichlorinated Pd(III) or diacetate Pd(III) dimer analogues, supporting the presence of Pd(III) dimer 6.[26] The solid was then dissolved in DCM at −90 °C, and the mixture was subsequently allowed to warm to room temperature. After 2 h reaction time, we examined the mixture with ^{1}H NMR spectroscopy versus an internal standard, (i) directly after the reaction (i.e., after solvent removal) and (ii) after performing a workup in the presence of pyridine (to potentially release trapped material from the Pd-side products formed after reductive elimination), followed by purification with column chromatography. In both cases, essentially the same product yields have been determined. ArCl 7 was obtained as the predominant product in 54% yield along with a small amount of ArOAc 8 (4%).[27]

The formation of ArCl 7 contrasts the computational predictions and therefore suggests that direct reductive elimination from a mixed Cl/OAc Pd(III) dimer does not take place, neither under catalytic nor under stoichiometric conditions, as ArCl was isolated in these cases.

Consideration of Alternative Pathways: Is Direct Elimination from Pd(IV) Likely? We next undertook computational studies to investigate which species is likely to form from 6 prior to reductive elimination. Figure 3 gives an overview of possible reaction pathways and intermediates. In principle, the dinuclear complex 6 could disproportionate to the Pd(IV) complex 9 and a cyclopalladated (Bzq)Pd(II)OAc monomer.[8] The latter should subsequently dimerize to the more stable Pd(II) complex 17 (see Scheme 3).[28]

The dispersion corrected[29] DFT functionals PBE0-D3,[30a] B3PW91-D3,[30b,c] and also the M06L[31] functional with two different solvation models (COSMO-RS[23] and CPCM to account for the reaction medium DCM) with the basis set 6-311++G(d,p) were applied in the calculations (Table 2).[15] The need for dispersion for the accurate treatment of dimeric complexes was demonstrated previously.[32] Moreover, COSMO-RS[23] was suggested to better account for dispersion in solution.[33] All methods predict that the disproportionation of 6 is endergonic (by ΔG_{rxn} = 3−17 kcal/mol). Consistently for each method applied, this energetic penalty is lower, however, than the activation free barrier for the direct reductive elimination of ArOAc from the Pd(III) dimer 6 ($\Delta G^{\ddagger}$ = 16−18 kcal/mol; see Table 1), and might hence be mechanistically viable. We therefore investigated next whether the reductive elimination from the thereby generated Pd(IV) complex 9 is consistent with the observed reactivity.

Table 2. Computational Methods Applied To Calculate the Reaction Free Energy ($\Delta G_{\rm rxn}$) for Disproportionation of 6 to 9 and 17 (See Scheme 3)[a]

entry	method	$\Delta G_{\rm rxn}$[c]
1	COSMO-RS$_{\rm (DCM)}$ M06L/6-311++G(d,p)[b]	9.7
2	COSMO-RS$_{\rm (DCM)}$ PBE0-D3/6-311++G(d,p)[b]	3.1
3	COSMO-RS$_{\rm (DCM)}$ B3PW91-D3/6-311++G(d,p)[b]	14.1
4	CPCM$_{\rm (DCM)}$ M06L/6-311++G(d,p)[b]	12.3
5	CPCM$_{\rm (DCM)}$ PBE0-D3/6-311++G(d,p)[b]	5.8
6	CPCM$_{\rm (DCM)}$ B3PW91-D3/6-311++G(d,p)[b]	16.8

[a] Energies in kcal/mol (at 298 K).[34] [b] B3LYP/6-31G(d) geometry. [c] $\Delta G_{\rm rxn}$ = [2·G(9) + G(17)] − [2·G(6)].[34]

The activation free energy barriers for C−OAc and C−Cl reductive elimination from Pd(IV) complex **9** were calculated. Table 3 summarizes the results. Once again, C−OAc bond formation is predicted to be favored (by $\Delta\Delta G^\ddagger$ = 1.3−3.2 kcal/mol, depending on the level of theory applied), which is inconsistent with the experimentally observed selectivity for ArCl. Moreover, adding the activation free energy barrier for reductive elimination to the energy required for disproportionation of **6** gives a total free energy barrier of $\Delta G^\ddagger$ > 20 kcal/mol for elimination of ArOAc via the Pd(IV) complex **9** (see Figure 4, Tables 2 and 3),[34] which would be higher than the analogous direct reductive elimination from Pd(III)-dimer **6** ($\Delta G^\ddagger \leq$ 19 kcal/mol; see Table 1). Thus, on the basis of the calculated activation free energy barriers as well as predicted selectivity, the experimentally observed formation of ArCl is inconsistent with the direct reductive elimination from the Pd(IV) complex **9**.[35,36]

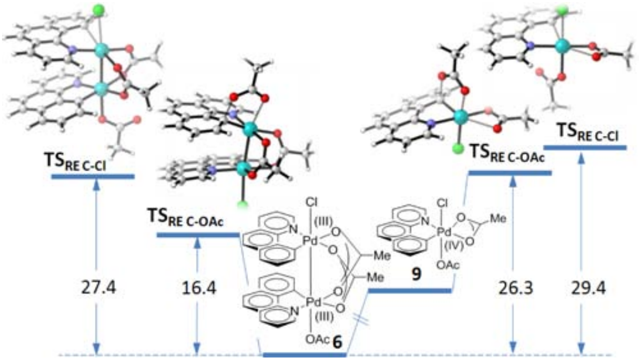
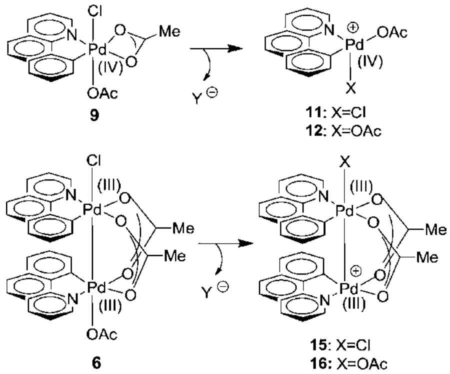


Figure 4. Direct reductive elimination of **6** (left) versus disproportionation of **6**, followed by reductive elimination of **9** (right) at COSMO-RS (DCM) M06L/6-311++G(d,p)//B3LYP/6-31G(d). Free energies in kcal/mol.[34] See Tables 2 and 3 for other methods.

Is Dissociation of Acetate from a Pd(IV) or Dinuclear Pd(III) Complex Followed by Elimination from the Corresponding Cation Likely?

As summarized in Figure 3, potential mechanistic alternatives are that the dinuclear complex **6** converts to a cationic derivative after chloride or acetate loss. Reductive elimination from **15** or **16** might then take place (pathway b; see Figure 3). Analogously, the Pd(IV) complex **9**, generated after disproportionation of **6**, might convert further to a cationic species **11** or **12** (pathway d, Figure 3).[7]

Scheme 4. Dissociation of Anion from 9 or 6



The accurate computational consideration of the dissociation of ions from neutral complexes is challenging. Previous considerations showed an adequate performance of standard DFT functionals together with conductor-like polarizable continuum models to calculate the solvation free energies of small ions.[37] We first calculated the dissociation free energies of chloride and acetate from Pd(IV) complex **9** and Pd(III)-dimer **6** (Scheme 4) using the PBE0 or B3PW91 functionals along with a solvation model for DCM (CPCM). The results are given in Table 4. The dissociation of acetate or chloride from the dinuclear Pd(III) complex **6** is calculated to be lower in energy than the analogous dissociations from Pd(IV) complex **9**. While the dissociation of acetate from Pd(III) dimer **6** is favored, chloride loss is favored from Pd(IV). Thus, reductive elimination from a Pd(IV) derived cationic complex can be excluded as mechanism, as it should ultimately give rise to ArOAc as product. For Pd(III) dimer **6**, the situation is less clear-cut. Interestingly, when a method is applied that accounts better for dispersion, such as for M06L, chloride dissociation is favored from **6** also (see Table 4). Considering the functionals without dispersion, the loss of acetate from **6** (requiring $\Delta G_{\rm diss}$

Table 3. Computational Methods Applied To Calculate $\Delta G^\ddagger$ and the $\Delta\Delta G^\ddagger$ Preference for C−OAc Transfer from 9[a]

entry	method	$\Delta G^\ddagger_{\rm C-OAc}$ (9)	$\Delta\Delta G^\ddagger$[c]
1	COSMO-RS$_{\rm (DCM)}$ M06L/6-311++G(d,p)[b,d]	16.6	3.1
2	COSMO-RS$_{\rm (DCM)}$ PBE0-D3/6-311++G(d,p)[b,d]	17.4	1.9
3	COSMO-RS$_{\rm (DCM)}$ B3PW91-D3/6-311++G(d,p)[b,d]	17.2	2.7
4	CPCM$_{\rm (DCM)}$ M06L/6-311++G(d,p)[b,d]	16.0	3.2
5	CPCM$_{\rm (DCM)}$ PBE0-D3/6-311++G(d,p)[b,d]	16.4	1.5
6	CPCM$_{\rm (DCM)}$ B3PW91-D3/6-311++G(d,p)[b,d]	16.4	2.3
7	CPCM$_{\rm (DCM)}$ PBE0/6-311++G(d,p)[b,d]	16.3	1.3
8	CPCM$_{\rm (DCM)}$ B3PW91/6-311++G(d,p)[b,d]	16.1	2.0

[a] Energies in kcal/mol (at 298 K).[34] [b] B3LYP/6-31G(d) geometry with LANL2DZ (Pd). [c] $\Delta\Delta G^\ddagger = \Delta G^\ddagger_{\rm C-Cl} - \Delta G^\ddagger_{\rm C-OAc}$. [d] SDD for Pd.

Table 4. Dissociation Free Energy (ΔG_{diss} in kcal/mol) of Chloride or Acetate from 9 or 6, See Scheme 4, Calculated at 298 K with CPCM(DCM) DFT[a]/6-311++G(d,p)//B3LYP[b]/6-31G(d)[34]

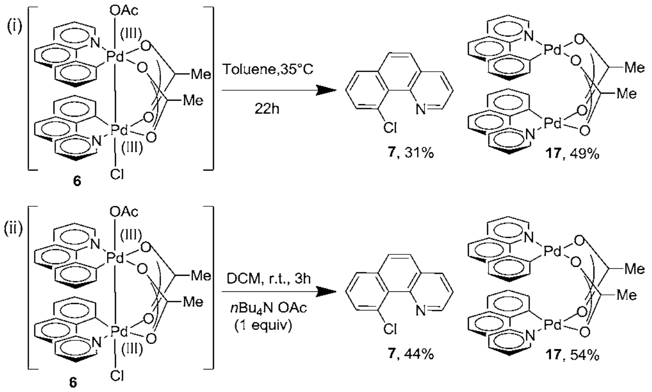
DFT	$9 \rightarrow 11 + AcO^-$	$9 \rightarrow 12 + Cl^-$	$6 \rightarrow 15 + AcO^-$	$6 \rightarrow 16 + Cl^-$
PBE0	33.5	30.5	12.9	15.6
B3PW91	30.1	27.2	9.6	12.8
M06L	37.9	29.8	22.6	20.6

[a] With SDD for Pd. [b] LANL2DZ for Pd.

= 12.9 kcal/mol at PBE0 and 9.6 kcal/mol at B3PW91) is lower in energy than the direct reductive elimination of ArOAc from Pd(III) dimer **6** ($\Delta G^\ddagger$ = 18.6 at PBE0 and 19.2 at B3PW91; see entries 9 and 10 in Table 1). However, the reductive elimination of ArCl from the Pd(III) cation **15** is calculated to require $\Delta G^\ddagger$ = 13.9 (at PBE0) and 14.4 (at B3PW91) kcal/mol, whereas ArOAc elimination from cation **16** is much lower ($\Delta G^\ddagger$ = 9.6 (at PBE0) and 9.7 (at B3PW91) kcal/mol). Presuming a reversible equilibrium of anion dissociation/association, ArOAc formation via a cationic Pd(III) dimer [$\Delta G^\ddagger_{total}$ = 25.2 (at PBE0) and 22.5 kcal/mol (at B3PW91)] would overall still be favored over ArCl [$\Delta G^\ddagger_{total}$ = 26.8 (at PBE0) and 24.0 kcal/mol (at B3PW91)]. This suggests that ion dissociation followed by reductive elimination of cationic intermediates is also unlikely.

Given that the computational results for ion dissociation from the Pd(III) dimer **6** are not unambiguous, we decided to undertake experimental tests to support our studies. (i) We performed the reductive elimination of the putative Pd(III) dimer **6** (i.e., the solid that we isolated; synthesis shown in Scheme 2) in a nonpolar medium (toluene) that is expected to disfavor ion-dissociation from **6** (see Scheme 5). (ii) In a second experiment, we studied the reductive elimination of **6** in DCM (as we had done previously; see Scheme 2), but added one additional equivalent of *tetra*-butylammonium acetate to the mixture. In both cases, ArCl was isolated as the sole product (in 31% or 44% yield; see Scheme 5), reinforcing that ion-dissociation from the Pd(III) dimer **6**, followed by reductive elimination of the corresponding cationic dinuclear complex, is also not the favored pathway.

Scheme 5. Experiments To Test for Possible Ion Dissociation from 6, Performed (i) in Toluene and (ii) in the Presence of Excess Acetate[a]



[a] 2% of ArOAc **8** was also detected in experiment (ii).[27]

Consideration of Scrambling of Dinuclear Pd(III) Complexes. In previous mechanistic investigations on Pd(IV) and dinuclear Pd(III) complexes, facile exchanges of the acetate ligands have been noted.[6c,7a,38] Given that we calculated similar dissociation energies for chloride and acetate from the Pd(III) dimer **6** (see Table 4), we hypothesized that scrambling of the dinuclear Pd(III) complex **6** to the corresponding dichloro-Pd(III) dimer **1** and diacetate-Pd(III) dimer **18** might take place under our stoichiometric reaction conditions (see Scheme 6). Indeed, our calculations predict that the scrambling process is thermo-neutral (ΔG_{rxn} = −0.1 kcal/mol at CPCM (DCM) PBE0-D3/6-311++G(d,p)[39] and 0.6 kcal/mol at CPCM (DCM) M06L/6-31+G(d)[39] level of theory at 298 K), suggesting that the dinuclear Pd(III) complexes **1**, **6**, and **18** could exist in a reversible equilibrium.

We subsequently performed low-temperature ^{1}H NMR studies of **6** in DCM-D2. At −80 °C, clearly defined peaks can be observed, but the signals started to broaden at −40 °C. A relatively broad peak appeared at 6.75 ppm chemical shift, which is in the range of one of the characteristic signals (6.8 ppm) of the dichlorinated Pd(III) dimer **1**.[6a] (ArCl **7** was not observed at this temperature.) We also observed peaks at 6.69 ppm (*J* 8.0, 5.5 Hz) and 7.86 ppm (*J* 5.6, 1.1 Hz), which would match the signals of diacetate Pd(III) dimer **18** in chemical shift and coupling constants (see Figure 5). Most other signals of the Pd(III) dimers **1**, **6**, and **18** are very similar in chemical shift and do not allow unambiguous differentiation.

Independent syntheses of dichloro-Pd(III) dimer **1** and diacetate-Pd(III) dimer **18**, followed by a ^{1}H NMR study of a 1:1 mixture of dimers **1** and **18** in DCM-D2 at low temperature, show a spectrum similar to that of the putative Cl/OAc Pd(III) dimer **6** at −80 °C (see Figure 5), indicating that some scrambling to **6** had taken place. Overall, the analogous signals and behavior are observed in the ^{1}H NMR study of the 1:1 mixture of **1** and **18** as had been seen with **6**, supporting a reversible dynamic equilibrium of the dimers.

We additionally established that the species are fully reversible; that is, upon warming from −80 to −40 °C (as shown in Figure 5), we subsequently recooled the 1:1 mixture of **18** and **1** to −80 °C. This led to the identical ^{1}H NMR spectrum once again (see p S4 in the Supporting Information). Given the resemblance of spectra, and on the basis of the available computational and NMR data, we cannot exclude that the solid that we isolated from our attempted synthesis of **6** might also be a 1:1:1 mixture of the Pd(III) dimers **6**, **18**, and **1**.

It has previously been established that the diacetate Pd(III) dimer **18** is unique in its reactivity: it gives rise to ArOAc only in minor amounts (see Scheme 6).[6a−c] Instead, Pd(II) complex **17** is reformed in 67% yield (as we established separately) via an alternative, currently unknown pathway.[40] This would explain why barely any ArOAc was formed in the reaction of **6**. A lower energy pathway to form **17** seems to win over elimination of ArOAc, and this process is suggested to drive the equilibrium toward **1** and **18**. The dichlorinated Pd(III)-dimer **1** that is formed in the scrambling process gives ArCl **7** upon reductive elimination.[6a] In line with this proposal is the fact that the yield of ArCl was ~50%, consistent with the maximum theoretical amount of dichlorinated Pd(III) dimer **1** that can be formed in the scrambling process.

As another test of this mechanism, we mixed the independently prepared Pd(III) dimers **1** and **18** at −80 °C in DCM and subsequently allowed the mixture to warm to room temperature (Scheme 7). After 5 h reaction time, we

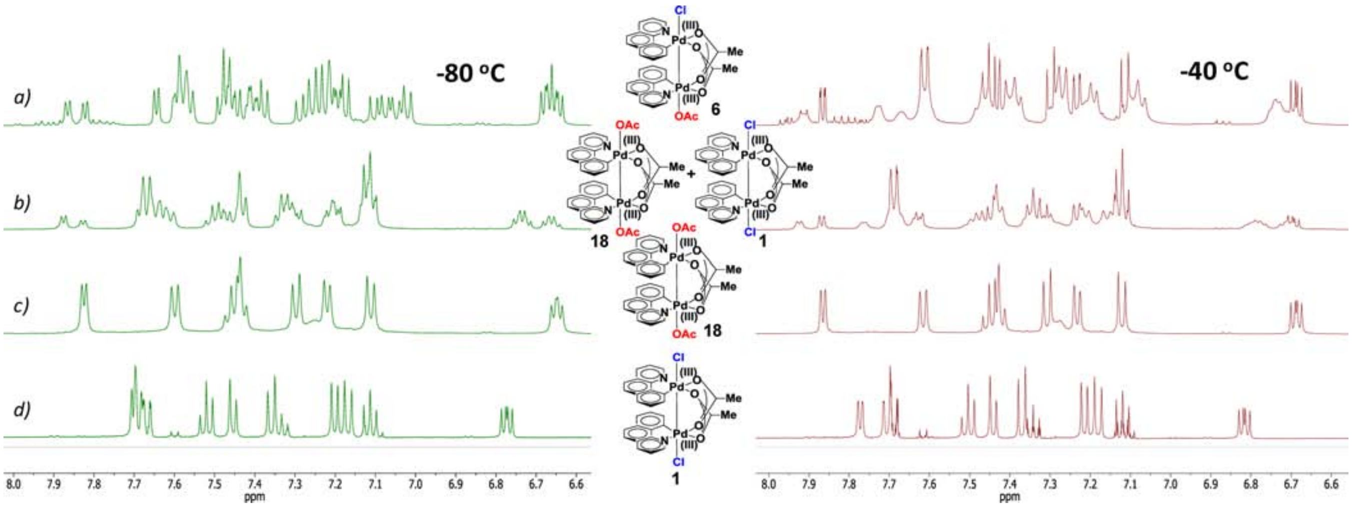
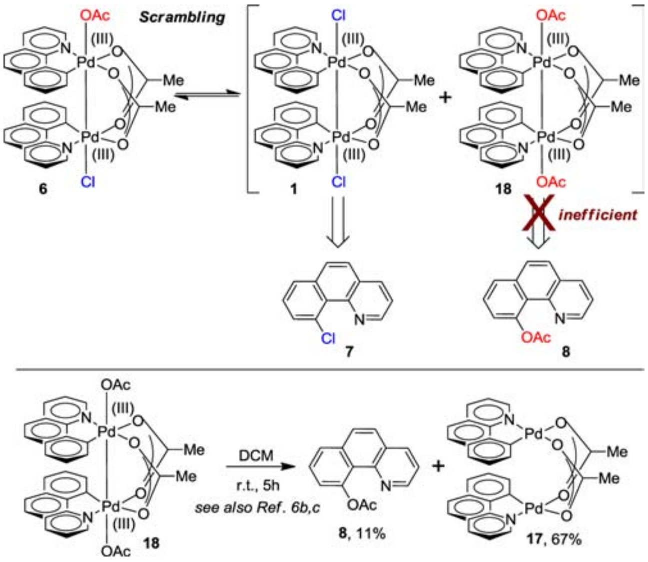
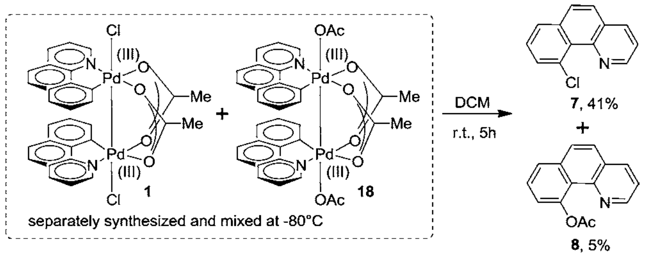


Figure 5. Low-temperature ^{1}H NMR study of (a) Cl/OAc−Pd(III) dimer **6**, (b) a 1:1 mixture of **18** and **1**, (c) **18**, and (d) **1** in DCM-D2 at −80 °C (left) and −40 °C (right).

Scheme 6. Proposed Scrambling of 6



Scheme 7. Mixing of Dimers 1 and 18 at Low Temperature, Followed by Reaction at Room Temperature in DCM[a]



[a] The yields are relative to the total amount of Pd(III) dimer.[41] Pd(II) dimer **17** was also formed in 30% yield.

observed exclusive formation of ArCl (41%), in agreement with the results observed with dimer **6**.

■ CONCLUSIONS

We examined the chemoselectivity of the reductive elimination from the mixed Cl/OAc dinuclear Pd(III) complex **6** with a combination of experimental and computational studies. Analogous species were previously implicated in catalysis. The observed chemoselectivity for ArCl was found to be inconsistent with the direct reductive elimination of the mixed Cl/OAc containing Pd(III) dimer or Pd(IV) monomer [i.e., (Bzq)Pd(OAc)$_2$Cl], suggesting that these are not the intermediates that ultimately determine the product selectivity and instead convert to alternative intermediates prior to reductive elimination. Under stoichiometric reaction conditions, the selectivity for ArCl is consistent with initial scrambling of the mixed Cl/OAc Pd(III) dimer to the corresponding homodimers, followed by reductive elimination of a dichlorinated Pd(III) dimer. The reactivity of the diacetate Pd(III) dimer is special and gives rise to ArOAc only in trace amounts under these conditions (i.e., in the absence of coordinating additives),[6a−c] explaining the high product selectivity for ArCl. The results presented herein demonstrate the ease of intermolecular ligand exchanges in dinuclear Pd(III) complexes, and these are likely of relevance for species involving labile ions (e.g., Cl, Br, OAc). Whether such scrambling processes are also relevant to catalytic processes remains to be seen.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Details on experimental procedures, spectroscopic data, computational information, Cartesian coordinates of all calculated species, thermal data, and full ref 14. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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(17) The product complex ultimately following reductive elimination has the Pd−Pd bond still intact (structures shown on pages S22 and S28 in the Supporting Information). The reaction free energies are calculated with respect to these complexes, because the faith and nature of the Pd-species following reductive elimination are unknown. It is reasonable to assume that the fragmentations for the two product pathways are analogous and that the fragmentations will not be selectivity-determining. It was previously shown that the reductive elimination of ArCl from Pd(III) dimer is endergonic with respect to the substrate bound complex. A fragmentation pathway was also calculated and suggested; see ref 6c for information.

(18) We also exposed ArOAc **8** to typical chlorination conditions involving *N*-chlorosuccinimide and Pd(II) precatalyst **17**. ArOAc was fully recovered, supporting that once ArOAc is formed, it will not react further to ArCl. See the Supporting Information for details.

(19) The illustrated structures were optimized with M06L/6-31G(d) and SDD (for Pd) in the gas phase. See the Supporting Information for the coordinates of the structures optimized at the other levels of theory (from Table 1).

(20) The geometries were optimized with B3LYP/6-31G(d) and LANL2DZ (for Pd). CPCM (DCM) M06L/6-31+G(d) with SDD (for Pd) single point corrections were subsequently applied. See the Supporting Information for further information. $\Delta G_{\rm rxn}$(C−OAc) = 10.2 kcal/mol and $\Delta G_{\rm rxn}$(C−Cl) = 25.0 kcal/mol.

(21) The corresponding gas-phase selectivity is $\Delta\Delta G^{\ddagger}$ = 4.8 kcal/mol; calculated at M06L/6-31+G(d) (with SDD for Pd)//B3LYP/6-31G(d) and LANL2DZ (for Pd).

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(24) The possibility of substitution of the apical acetate ligand by pyridine was proposed in the Supporting Information (pp S10−S13 and S64) in ref 9.

(25) When we added pyridine to the putative Pd(III) dimer **6** in D2-DCM at −80 °C, ^{1}H NMR spectroscopic analysis revealed the disappearance of axial and bridging acetate ligands, suggesting that the Pd(III) dimer is not stable in the presence of such coordinating additives.

(26) On the basis of the ^{1}H NMR data, we cannot exclude the possibility of a 1:1:1 mixture of dichlorinated Pd(III) dimer **1**, diacetate Pd(III) dimer **18**, and mixed Cl/OAc Pd(III) dimer **6**.

(27) (a) The yield was based on the assumption that if 1 mol of dimer **6** generated 1 mol of **7**, then the yield would be 100%.

(28) At CPCM (DCM) M06L/6-311++G(d,p)//B3LYP/6-31G(d), the dimerization is favored by $\Delta G_{\rm rxn}$ = 16 kcal/mol.

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(34) The standard state was converted to 1 M in solution.

(35) The alternative homolytic dimer fragmentation of **6** to monomeric Pd(III)-radicals, followed by reductive elimination, is calculated to be disfavored also ($\Delta G^\ddagger$ > 40 kcal/mol; see the Supporting Information for details).

(36) A (Bzq)Pd(II)Cl complex could in principle also be formed upon disproportionation. However, such a Pd(II) complex would not give rise to ArCl, as we calculate an activation free energy barrier of $\Delta G^\ddagger$ > 50 kcal/mol for reductive elimination (at B3LYP/6-31G(d), LANL2DZ (for Pd)).

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(39) Geometry optimized at B3LYP/6-31G(d) with SDD (for Pd).

(40) The direct reductive elimination of ArOAc from diacetate Pd(III) dimer **18** is calculated to have a 1−2 kcal/mol higher barrier than reductive elimination of ArOAc from the mixed Cl/OAc Pd(III) dimer **6**. Reductive elimination from the dichloro Pd(III) dimer **1** is calculated be higher in energy than elimination of ArOAc from **18** or **6** (see Table S1 in the Supporting Information, p S8). The diacetate Pd(III) dimer **18** appears to undergo an alternative lower barrier transformation to reform Pd(II) dimer **17** instead of the direct reductive elimination of ArOAc. The precise mechanism is currently unknown, but this alternative pathway is expected to have a lower barrier than direct reductive elimination of ArOAc (see Table S1, p S8 in the Supporting Information). Consequently, the equilibrium will shift toward more dichloride Pd(III) dimer **1** (to a maximum amount of 50%), which will ultimately give ArCl upon elimination. In line with this is also the fact that Pd(II) dimer **17** was formed in the reaction of mixed Pd(III) dimer **6** (analogous to the product formed from diacetate Pd(III) dimer **18**).

(41) With respect to Pd(III) dimer **1**, that is, assuming that 100% reductive elimination from 1.0 equiv of **1** gives 1.0 equiv of ArCl **7**, then the yield of ArCl **7** is 82%. Similarly, relative to Pd(III) dimer **18**, the yield of ArOAc **8** is 9%.