Bimetallic Reductive Elimination from Dinuclear Pd(III) Complexes

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Abstract: In 2009, we reported C–halogen reductive elimination reactions from dinuclear Pd(III) complexes and implicated dinuclear intermediates in Pd(OAc)₂-catalyzed C–H oxidation chemistry. Herein, we report results of a thorough experimental and theoretical investigation of the mechanism of reductive elimination from such dinuclear Pd(III) complexes, which establish the role of each metal during reductive elimination. Our results implicate reductive elimination from a complex in which the dinuclear core is intact and suggest that reducton synergy between the two metals is responsible for the facile reductive elimination reactions observed.

Introduction

Metal-metal redox cooperation during catalysis can potentially lower activation barriers of chemical transformations and thus allow access to reaction pathways that are difficult to access with mononuclear catalysts.¹ Redox chemistry of multinuclear complexes has been intensely studied, in part due to potential advantages in catalysis; however, metal-metal cooperation during redox chemistry has been difficult to establish. Mononuclear Pd(IV) complexes have been suggested as intermediates in palladium-catalyzed C–H oxidation reactions since 1971.² In 2009, we proposed dinuclear Pd(III) intermediates in catalysis as an alternative to Pd(II)/Pd(IV) redox cycles.³ In a preliminary study of C–Cl reductive elimination from the dinuclear Pd(III) complex 1 (eq 1), we were unable to establish whether reductive elimination proceeded with simultaneous, co-operative redox participation of both metals or via one-centered redox chemistry. Herein, we report a detailed investigation of the mechanism of C–Cl reductive elimination from 1 and present a tool for evaluating redox-metal synergy during redox transformations of multinuclear complexes. Our results implicate synergistic redox chemistry of both metals during reductive elimination, which leads to an energetic advantage as compared to related mononuclear reductive elimination reactions. This analysis is the first detailed evaluation of reductive elimination from Pd(III) and, more importantly, gives insight into evaluating and understanding metal-metal redox synergy in general.

Redox catalysis in synthesis is often accomplished by homogeneous, mononuclear catalysts.⁴ Oxidative addition and reductive elimination, two of the fundamental redox transformations of organometallic chemistry, have been well studied for mononuclear complexes. Oxidative additions are reactions in which the oxidation state and coordination number of a transition metal center increase by two upon addition of a small molecule.⁵ Oxidative addition can proceed via concerted,⁶ S₈2-like,⁷ and radical⁸ mechanisms. Reductive elimination—formally the reverse of oxidative addition—describes a transformation in which the oxidation state and coordination number of a metal are

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reduced by 2, with concurrent formation of a small molecule. Like oxidative addition, reductive elimination can proceed via various mechanisms. In a catalytic cycle, the mechanisms of oxidative addition and reductive elimination need not be the microscopic reverse of one another.

Redox chemistry in biology often occurs at multinuclear sites. For example, biologically relevant redox catalysis, such as the reduction of dinitrogen by nitrogenase, is frequently accomplished by multinuclear active sites. While redox catalysis involving more than one metal is frequently encountered, it is difficult to ascertain the specific role of each individual metal center during a redox transformation.

The mechanisms of redox transformations at multinuclear complexes are less understood than the corresponding reactions of mononuclear complexes. Stoichiometric oxidative addition to and reductive elimination from dinuclear complexes have been observed, and dinuclear intermediates have been proposed as intermediates in catalysis.\(^{3,15}\) The potential of utilizing metal-redox synergy to accomplish challenging transformations has long been recognized, and while proposals of mechanisms involving metal-metal cooperation have been posited, identification of the intimate role of each metal center during redox transformations at dinuclear complexes is difficult to establish experimentally. Understanding how metal-metal redox synergy can be used in catalysis requires insight into the role of each metal during redox chemistry.

During our efforts to utilize metal-metal redox synergy in catalysis, we found it useful to employ a two-tiered nomenclature scheme in which organometallic redox transformations are classified by both the nucleality of the complex undergoing the redox transformation and the metallicity of the transformation. Nucleality is a descriptor of structure and refers to the number of metal centers present in the complex undergoing the redox transformation. Metallicity is a descriptor of the mechanism of a redox transformation and refers to the number of metal centers that undergo redox chemistry coupled to substrate oxidation or reduction. The presence of multiple metal centers (nucleality) in a redox transformation does not necessitate redox participation (metallicity) of all metal centers.

- **Nucleality** — descriptor of structure; the number of metal centers in a complex that undergoes a redox transformation.
- **Metallicity** — descriptor of mechanism; the number of metal centers that participate in redox chemistry during a redox transformation.

One can, in principle, determine the nucleality of a redox transformation using the tools of reaction kinetics. For example, fragmentation of a dinuclear complex into two identical mononuclear complexes prior to reductive elimination can afford a half-order rate law with respect to the dinuclear transition metal complex. While redox transformations that take place at mononuclear complexes are by definition mononucleal, redox transformations at dinuclear complexes can be either mononuclear or bimetallic, depending on whether one or both metals change.
their oxidation state in the redox transformation. Differentiating between mono- and bimetallic mechanisms is experimentally challenging.

Mono- and bimetallic transformations are kinetically indistinguishable, because the transition states do not differ in chemical composition but only in specific roles of the metal center in the dinuclear core. Further, the identity of the transition metal fragment produced by a redox transformation is not sufficient to assign the metallicity of a given reaction. For example, the oxidative addition of MeI to dinuclear Au(I) complex 4 affords dinuclear Au(II) complex 6 illustrates the difficulty in assigning the metallicity of a redox transformation. If oxidative addition proceeds initially at a single Au site to afford the Au(I)/Au(III) mixed-valence species 5, before competitive isomerization to complex 6, the oxidative addition to 5 is monometallic (eq 2). Alternatively, if oxidative addition proceeds with Au–Au bond formation concurrent with Au–C bond formation to form 6 via 7 (eq 3), the redox transformation is bimetallic.

Monometallic Pathway

\[ \text{Ph} \begin{array}{c} \text{Pd} \text{Au} \text{Ph} \end{array} \begin{array}{c} \text{Ph} \text{P} \text{Ph} \text{P} \text{Ph} \end{array} \text{CH}_3 \]

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Bimetallic Pathway

\[ \text{Ph} \begin{array}{c} \text{Pd} \text{Au} \text{Ph} \end{array} \begin{array}{c} \text{Ph} \text{P} \text{Ph} \text{P} \text{Ph} \end{array} \text{CH}_3 \]

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\[ \begin{array}{c} \text{Au} \text{P} \text{Ph} \text{P} \text{Ph} \text{P} \text{Ph} \end{array} \text{CH}_3 \]

Development of catalysis concepts that rely on metal-metal synergy during redox transformations requires fundamental understanding of the role of each metal involved in the redox transformation. Potentially, metal-metal cooperation during catalysis could allow development of reactions that are difficult to accomplish with monometallic systems. We have sought to evaluate the potential advantage of utilizing two metals during redox chemistry in desirable but currently challenging transformations. Transition-metal-mediated halogenation reactions are difficult, and only a few methods are available.1,2 If oxidative addition proceeds initially at a single Au site to afford the Au(I)/Au(III) mixed-valence species 5, before competitive isomerization to complex 6, the oxidative addition to 5 is monometallic (eq 2). Alternatively, if oxidative addition proceeds with Au–Au bond formation concurrent with Au–C bond formation to form 6 via 7 (eq 3), the redox transformation is bimetallic.

\[ \text{Ph} \begin{array}{c} \text{Pd} \text{Au} \text{Ph} \end{array} \begin{array}{c} \text{Ph} \text{P} \text{Ph} \text{P} \text{Ph} \end{array} \text{CH}_3 \]

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Results

Two fundamental questions are addressed in this manuscript. First, does C–Cl reductive elimination from 1 proceed from a mono- or dinuclear complex? Second, do both metals participate in the redox chemistry of reductive elimination? The redox activity of each metal is difficult to evaluate experimentally; no experimental observable can be directly correlated with reaction metallicity. We have thus pursued a computational investigation of reaction metallicity. The computational model used to assay metallicity was benchmarked by comparing the computed mechanism with three experimental observables: (1) the ground-state structure of 1, (2) the activation parameters for C–Cl reductive elimination from 1, and (3) the ability of computed charge distributions to correlate with experimentally obtained ρ-values from Hammett analysis.

Synthesis and Structure of Pd(III) Dichloride 1. Dinuclear Pd(III) complex 1 was chosen as a suitable substrate to investigate reductive elimination from dinuclear Pd complexes for two reasons. First, Pd(OAc)₂ is frequently used as a catalyst in directed C–H oxidations. Second, the bridging acetate ligands hold the two palladium centers in proximity, and therefore allow for metal-metal interaction. Treatment of complex 9, derived from cyclometalation of benzo[a]quinoline (8) with Pd(OAc)₂, with PhCl₂ resulted in the formation of dinuclear Pd(III) dichloride 1 in 92% yield (Figure 1).

By 1H NMR spectroscopy, complex 1 is diamagnetic, consistent with a Pd–Pd single bond. At −50 °C, the 1H NMR spectrum displays eight nonequivalent aromatic resonances and a single resonance for the bridging acetate ligand at 2.69 ppm. In the solid state, the Pd–Pd distance in 1 is 2.5672(5) Å, 0.27 Å shorter than the corresponding distance in 9, consistent with the formation of a Pd–Pd bond upon oxidation.24 The Pd–O bonds are nonequivalent; the Pd–O bond trans to the carbon ligand is 2.133(3) Å, and the Pd–O bond trans to the nitrogen ligand...
is 2.042(3) Å, consistent with the stronger structural trans effect of the aryl ligand as compared to the substituted pyridine ligand.25

Potential ligand fluxionality, in which the apical and bridging ligands might exchange with one another, was probed by variable-temperature NMR spectroscopy of dinuclear Pd(III) tetraacetate 10-d₈, in which the bridging acetate ligands were perdeuterated. At −60 °C, the ¹H NMR spectrum of 10-d₈ displayed a single ¹H NMR resonance at 1.48 ppm (apical acetate). Upon warming of the sample to 23 °C, the integration of the signal at 1.48 ppm (apical acetate) decreased with concurrent development of a new resonance at 2.71 ppm (bridging acetate). Acetate scrambling was determined to be fast relative to reductive elimination; warming a sample of 10-d₈ to 23 °C afforded a 1:1 mixture of 12 and 12-d₃ (Scheme 1).26

C–Cl Reductive Elimination from 1. Upon warming of complex 1 to 23 °C, 10-chlorobenzo[h]quinoline (2) was isolated in 94% yield based on 1 (eq 1). Monitoring the thermolysis of 1 by ¹H NMR spectroscopy established that both decomposition of 1 and formation of 2 obey first-order rate laws. The activation parameters of C–Cl reductive elimination were determined to be ΔH° = 17.2 ± 2.7 kcal·mol⁻¹, ΔS° = −11.2 ± 9.4 cal·K⁻¹, and ΔG°₂₉₈ = 20.5 ± 0.1 kcal·mol⁻¹ by monitoring the evolution of 2 as a function of temperature (between 5 and 35 °C). The rate of reductive elimination was unaffected by exogenous chloride (up to 17.1 mM in n-ButNCI; 1.17 equiv with respect to 1) and acetate (up to 11.8 mM in n-ButNOAc; 0.81 equiv with respect to 1).

Reductive elimination of 2 from 1 is accompanied by the formation of a mixture of Pd-containing products (3). Treatment of the crude reaction mixture after reductive elimination with excess pyridine provided a mixture of 2 and five palladium-containing species, identified as Pd(II) complexes 13, 14, 15, 16, and 17 on the basis of comparison of the ¹H NMR spectrum of the mixture with the ¹H NMR spectra of authentic samples (Scheme 2). By ¹H NMR, the combined yield of complexes 13–17 was determined to be 99%. The observed products of reaction with pyridine establish that the oxidation state of Pd in 3 is +II. The exact structure of the Pd(II) complex immediately after reductive elimination is unknown. (See the Supporting Information for further discussion of the identity of the Pd-containing byproducts of reductive elimination.)

Effect of 7-Substitution of the Benzo[h]quinolinyl Ligand on the Rate of C–Cl Reductive Elimination. Dinuclear Pd(III) dichloride complexes 18a–e with 7-substituted benzo[h]quinolinyl ligands were prepared by cyclometalation of 7-substituted benzo[h]quinolines with Pd(OAc)₂ followed by oxidation with PhICl₂. Dinuclear Pd(III) complexes with NO₂ (18f) and CN (18g) substituents were not sufficiently soluble to be used in kinetics experiments. Thermolysis of 18a–e at 29 °C afforded 7-substituted-10-chlorobenzo[h]quinolines 19a–e in 84–95% yield. Reaction yields did not correlate with the ω-values of the substituents. In all cases, C–Cl bond formation was observed exclusively; C–O reductive elimination to afford 7-substituted 10-acetoxbenzo[h]quinolines was not detected. The rate of C–Cl bond formation was measured by monitoring the formation of 19a–e by ¹H NMR spectroscopy. The Hammett plots generated from these data (Figure 2) shows that C–Cl reductive elimination from dinuclear Pd(III) complexes is accelerated by electron-withdrawing 7-substituents on the benzo[h]quinolinyl ligand (ρ = 1.46).

Effect of Bridging Carboxylate Ligand on the Rate of C–Cl Reductive Elimination. Benzate-bridged dinuclear Pd(III) complexes 20a–e were prepared by treatment of 9 with 4-substituted benzoic acids at reduced pressure followed by oxidation with PhICl₂. Decomposition of 20a–e at 29 °C afforded compound 2 in 91–96% yield, with no C–O reductive elimination.

(26) Exchange of carboxylate ligands can proceed intermolecularly (see Supporting Information). For simplicity, here we depict only those complexes arising from intramolecular exchange; intermolecular exchange does not change our conclusions based on these experiments because exchange, whether intra- or intermolecular, is fast relative to reductive elimination.

elimination observed in any case. The Hammett plot\(^{27}\) (Figure 3) generated from these data shows that reductive elimination is accelerated by electron-withdrawing substituents on the bridging carboxylate ligands (\(\rho = +0.71\)). For complexes 20f (R = Me) and 20g (R = OMe), bearing electron-donating substituents, \(\log(k_x/k_H)\) was not linearly correlated with the substituent \(\sigma\)-values.

**Competitive Reductive Elimination of Substituted Benzoate Ligands.** Because the electronic properties of chloride cannot be altered, the electronic demand of the apical ligand during reductive elimination from 1 cannot be investigated. Dinuclear Pd(III) tetrabenzoates were selected as substrates to probe the electronic demand of the apical ligand during reductive elimination because the electronic properties of benzoate ligands can be modified (Scheme 3).\(^{26}\) In the following experiments, the 2-phenylpyridyl ligand was used in lieu of the benzo[h]quinolinyl ligand because 2-(pyridin-2-yl)phenyl benzoate is more stable toward hydrolysis than benzo[h]quinolin-10-yl benzoate, which simplified product isolation and analysis. Further, pyridine is added to the dinuclear Pd(III) complexes prior to thermolysis because we have previously observed that, in the absence of pyridine, the products of C–O reductive elimination can react with the palladium-containing byproducts of reductive elimination.\(^{26}\)

Oxidation of Pd(II) benzoate 21 with \(p\)-nitrobenzoyl peroxide (24) afforded Pd(III) complex 22, which, after subsequent warming to 23 °C in the presence of 20.0 equiv of pyridine, afforded a 4:1 mixture of 26 and 27, as determined by both \(^1\)H NMR spectroscopy and isolated yields of 26 and 27 (Scheme 3a). Oxidation of \(p\)-nitrobenzoate-bridged complex 23 with benzoyl peroxide (25) also afforded a 4:1 mixture of 26 and 27 (Scheme 3b), which confirmed that carboxylate exchange is fast relative to C–O reductive elimination.

Intramolecular carboxylate exchange in tetrabenzoate dipalladium(III) complex 22 could generate an equilibrium mixture of three isomers (Scheme 4).\(^{26}\) Reductive elimination from isomer 28 can afford either 26 or 27, while reductive elimination from 22 or 29 can afford only 26 or 27, respectively. Without knowledge of all four product-forming rate constants, the ratio of 26 and 27 cannot be deconvoluted to provide \(k_2/k_{27}\), the relative rate of benzoate over \(4\)-nitrobenzoate reductive elimination.\(^{28}\)

Oxidation of 23 with unsymmetrical peroxide 30 at \(-50^\circ\text{C}\), followed by treatment with pyridine at 23 °C, afforded a 2:1 mixture of 26 and 27 (Scheme 5).\(^{26}\) Intramolecular carboxylate exchange in dinuclear Pd(III) complex 31, which features three \(4\)-nitrobenzoate ligands and one benzoate ligand, could generate either one of two isomers (31 or 32). Reductive elimination from 32 can afford only 27 (\(k_3\)), while reductive elimination from 31 can afford both 26 (\(k_1\)) and 27 (\(k_2\)). The observed 2:1 ratio of 26 and 27 shows that \(k_1 > k_2 + k_3\cdot K_{eq}\) and that benzoate undergoes reductive elimination faster than \(4\)-nitrobenzoate.

(28) Attempts to accomplish Hammett analysis using esp-bridged complex 37, anticipated to prevent carboxylate exchange, were unsuccessful because, unlike C–Cl reductive elimination from 35, C–O reductive elimination does not proceed from esp-bridged complex 37.
Reactive Elimination in the Presence of Exogenous AcOH. We have proposed that reactive elimination from dinuclear Pd(III) complexes similar in structure to 1 is the product-forming step of a variety of Pd-catalyzed C–H functionalizations. During catalysis, substrate is present in large excess relative to Pd, and thus we investigated C–Cl reactive elimination in the presence of exogenous benzo[h]quinoline (8). By 1H NMR and UV−vis spectroscopy, no interaction between complex 1 and 8 was observed between −50 and 23 °C. We have observed a reproducible acceleration of C–Cl bond formation in the presence of exogenous benzo[h]quinoline (8) at 23 °C.16 We now report a re-examination of the observed rate enhancement for the formation of 2 from 1 upon addition of 8, which indicates that the observed acceleration is due to acid generated by palladation of added 8, not N-coordination of 8 to 1, as we previously proposed.16

Examination of the thermolysis of 1 in the presence of exogenous benzo[h]quinoline (8) revealed that the concentration of 8 decreased during the evolution of 2. (For quantitative kinetic data regarding the rate of reactive elimination from 1 as a function of initial benzo[h]quinoline concentration, see the Supporting Information.) Cyclometalation of 8 (for example, 8−9 shown in Figure 1) by the Pd(II)-containing byproducts of reactive elimination (3) generates an equivalent of acid, as a result of C–H bond cleavage during metalation. We therefore examined the potential effect of acid on the rate of reactive elimination from 1 by monitoring the formation of 2 as a function of AcOH concentration ([AcOH]). AcOH was selected because potential exchange of the conjugate base, acetate, with the acid ligands of 1 is a degenerate process. The rate of formation of 2 was monitored at AcOH concentrations up to 1.16 M in CD2Cl2 by 1H NMR spectroscopy. The rate of formation of 2 is accelerated in the presence of AcOH (Figure 4). The plot of first-order rate constant vs [AcOH] has a nonzero intercept, reflective of the background rate of C–Cl reactive elimination in the absence of AcOH, and shows that at least two pathways are available for C–Cl reactive elimination: one pathway independent of and one pathway linearly dependent on the concentration of AcOH.

Computational Studies. a. Structure of 1. Description of the halogen−metal−metal−halogen tetrad present in 1 was antici-

\begin{align*}
&\text{Scheme 5. Oxidation of 23 with Unsymmetrical Peroxide 30} \\
&\text{Affords a 2:1 Mixture of 26 and 27, which Establishes the Kinetic Preference for Reductive Elimination of More Electron-Rich Benzoate Ligands}
\end{align*}

\begin{align*}
&\text{Reductive Elimination from Dinuclear Pd(III) Complexes}
\end{align*}

Figure 4. First-order rate constant of C—Cl reactive elimination as a function of [AcOH].

Figure 5. Calculated gas-phase stationary points in the mechanism of C–Cl reductive elimination from A. Energies are solvent-corrected electronic energies at 0 K (E0K); ΔH° and AG° (transition state B) for the reductive elimination are at 298 K.

Table 1. Comparison of Experimental and Computational Activation Parameters for Reductive Elimination from 1

<table>
<thead>
<tr>
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<th>ΔH° (kcal·mol⁻¹)</th>
<th>ΔS° (cal·K⁻¹)</th>
<th>ΔG°'0K (kcal·mol⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>experiment</td>
<td>17.2 ± 2.7</td>
<td>-11.2 ± 9.4</td>
<td>20.5 ± 0.1</td>
</tr>
<tr>
<td>computation</td>
<td>18.9</td>
<td>-7.5</td>
<td>21.2</td>
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structure A (Figure 5). This agrees well with the experimentally determined activation parameters (ΔG°'0K = 20.5 ± 0.1 kcal·mol⁻¹ and ΔH° = 17.2 ± 2.7 kcal·mol⁻¹, Table 1).

Unlike in structure A, the Pd nuclei in B are non-equivalent because C–Cl bond formation proceeds at Pd₂ while ionization of Cl⁻ proceeds at Pd₁. The Pd–Pd distance is longer in B (2.65 Å) than in A (2.62 Å) by 0.03 Å. The bond lengths between Pd₁ and the carbon (Cₜ) and chlorine (Clₜ) ligands that participate in reductive elimination are longer by 0.20 and 0.12 Å in the transition state, respectively. The Pd–O bond trans to Cₜ is 0.16 Å longer in B than it is in A.

Structure C has been located as a local energy minimum in the gas phase; C is not an energy minimum when a CH₂Cl₂ solvent model is applied but is depicted in Figure 5 to better illustrate the path of reductive elimination. In C, the C–Cl bond is 1.76 Å long, indicating that bond formation is nearly complete (for comparison, the C–Cl bond in E is 1.75 Å). Ionization of Cl₁ from C affords ion pair D, which is 6.8 kcal·mol⁻¹ higher in energy than A. Experimentally, the structure of the Pd(II) complex immediately following reductive elimination has not been determined. Computationally, the ion pair D evolves to Pd(II) structure E. Several other Pd(II) complexes could form by ligand rearrangement, and structure E was only chosen as a stationary point in Figure 5 to illustrate that, as observed by experiment, reductive elimination from a dinuclear Pd(III) complex to form a Pd(II) complex, such as E, is energetically favorable.

c. Comparison of Computed Transition State with Hammett Analyses. We have computed natural charge distributions of structure A and transition state B (Figure 6) from natural population analyses.° The difference in computed charge distribution in the transition state B and structure A was compared with the experimentally determined ρ-values from the Hammett analyses. The relative charge distributions in A and B are in qualitative agreement with the experimentally determined ρ-values. For example, the increased anionic charge in the transition state of the Cₜ atom bound to Pd₁ (0.05 for A; −0.04 for B) is consistent with the positive ρ-value (+1.46) that was experimentally determined for benzo[h]quinolinyl ligand substitution.

Discussion

In the following discussion we will first analyze experimental and computational evidence consistent with reductive elimination proceeding from a dinuclear palladium complex. Subsequently, we will evaluate the redox participation of both metals during reductive elimination (metallicity). Because metallicity cannot be probed experimentally, we have pursued a computational description of metallicity.

Nuclearity of Pd Complex during Redox Transformation. C–Cl bond formation from complex 1 could proceed via reductive elimination from a mononuclear (after dissociation of 1) or a dinuclear complex (Figure 7).

Figure 6. Partial charge distribution in structure A and transition state B (numbers in parentheses). Hammett analyses of benzo[h]quinolinyl, bridging carboxylate, and apical ligands are consistent with the computed charge distributions.

Figure 7. C–Cl reductive elimination could, in principle, proceed from mononuclear or dinuclear complexes.

Reductive elimination from a mononuclear complex following initial Pd–Pd bond cleavage could, in principle, afford observed...
Reductive Elimination from Dinuclear Pd(III) Complexes

Figure 8. Potential pathways via mononuclear Pd complexes. Path 1: Dissociation into two Pd(III) monomers followed by reductive elimination from mononuclear Pd(III). Path 2: Disproportionation to Pd(II) and Pd(IV) followed by reductive elimination from Pd(IV).

We have considered two processes by which the dinuclear core could fragment into mononuclear palladium complexes prior to reductive elimination: (1) homolytic Pd–Pd bond cleavage to afford two mononuclear Pd(III) complexes and (2) heterolytic Pd–Pd bond cleavage to afford one Pd(IV) complex and one Pd(II) complex (Figure 8). For each pathway, either Pd–Pd bond cleavage or subsequent reductive elimination from mononuclear Pd complexes could be rate determining.

Fast homolytic Pd–Pd bond cleavage to afford two identical Pd(III) monomers, followed by rate-determining reductive elimination, would proceed with a reaction order of 0.5 with respect to 1 and was excluded by the observed first-order rate law for decomposition of 1 and formation of 2.\(^\text{(18)}\)

Rate-determining homolytic Pd–Pd bond cleavage, followed by fast reductive elimination, was excluded by comparison of the activation parameters for C–Cl reductive elimination \(\Delta H^\ddagger = 17.2 \pm 2.7 \text{ kcal} \cdot \text{mol}^{-1}\), \(\Delta S^\ddagger = -11.2 \pm 9.4 \text{ cal} \cdot \text{K}^{-1}\), and \(\Delta G^\ddagger_{298} = 20.5 \pm 0.1 \text{ kcal} \cdot \text{mol}^{-1}\) with the calculated Pd–Pd bond strength. The Pd–Pd bond in A was calculated to be 35.3 kcal\text{mol}^{-1} by calculating the energy required to separate the palladium nuclei to 3.65 Å. Stretching of the Pd–Pd bond led to geometrical distortions of the bridging acetate ligands. Therefore, the Pd–Pd bond energy was also calculated for structure F, in which the bridging acetate ligands have been replaced by chelating propanedialato ligands \(33.2 \text{ kcal} \cdot \text{mol}^{-1}\) (eq 4). The computed value of 35.3 kcal\text{mol}^{-1} is likely an underestimate of the energy required to cleave the dinuclear core because cleavage requires breaking of the Pd–Pd bond in addition to two Pd–O bonds. The effect of solvent polarization (Poisson–Boltzmann model) in CH\(_2\)Cl\(_2\) was included while calculating the Pd–Pd bond strength in F to account for solvent stabilization of the complexes generated after bond cleavage.

Reductive elimination could potentially proceed by disproportionation of 1 into a Pd(II) and a Pd(IV) complex, with subsequent monometallic reductive elimination from a mononuclear Pd(IV) complex (Path 2, Figure 8). Such disproportionative metal–metal bond cleavage has been reported for dinuclear Pt(III) intermediates during the oxidation of Pt(II) to Pt(IV).\(^\text{(36)}\) As with homolytic Pd–Pd bond cleavage, either heterolytic cleavage or subsequent reductive elimination could be rate limiting.

Possible pre-equilibrium dimer cleavage, followed by rate-determining reductive elimination, was evaluated by a crossover experiment between acetate-bridged complex 1 and benzoate-bridged complex 20a (Scheme 6). Complex 33, the product of crossover between 1 and 20a, was not observed during C–Cl reductive elimination, precluding pre-equilibrium dimer cleavage. Addition of 1.0 equiv of benzo[\(h\)]quinoline (8), a potentially coordinating ligand, did not lead to observed exchange either.

To evaluate the possibility of rate-determining heterolytic Pd–Pd bond cleavage prior to C–Cl reductive elimination, the relative rates of reductive elimination from acetate-bridged complex 1 and esp-bridged complex 35 (eq 5) were measured at 35 °C \((\alpha,\alpha',\alpha''\prime\text{-tetramethyl-1,3-dibenzenedipropionate})\) (esp). Reductive elimination from esp-bridged Pd(III) complex 35 proceeds 16 times more slowly than that from acetate-bridged Pd(III) complex 1. However, the esp-bridged Pd(II) complex 34 dissociates at least 1500 times more slowly than acetate-bridged Pd(II) complex 9 (see Supporting Information). The relative rates of reductive elimination from 1 and 35 are therefore most consistent with reductive elimination proceeding from a dinuclear complex. In addition to the experimental data, we computed the barrier for heterolytic cleavage of the dinuclear core to generate a Pd(II) and a Pd(IV) complex to be at least 29.5 kcal\text{mol}^{-1} (see Supporting Information); the experimentally determined activation enthalpy for reductive elimination from 1 is \(H^\ddagger = 17.2 \pm 2.7 \text{ kcal} \cdot \text{mol}^{-1}\).

The combination of the observed first-order disappearance of 1 and formation of 2, the measured activation parameters which show that reductive elimination from 1 is more facile than homolytic Pd–Pd bond cleavage, and the lack of crossover between 1 and 20a are all consistent with reductive elimination from a dinuclear complex. Further, the computed reaction pathway agrees with experimental observations of ground-state structure, Arrhenius parameters for C–Cl reductive elimination,


The electron binding energy of a 4s electron is the energy function of reaction progress for pathways 3.

Energies were obtained from Natural Bond Orbital (NBO) analyses of a dinuclear complex, either monometallic or bimetallic redox of metal-metal cooperation during reductive elimination from proceeds provides no information about the role of each metal nuclearity of the complex from which reductive elimination and the electron is more effectively shielded from the nuclear electron binding energy decreases during reduction because the electron is less effectively shielded from the nuclear charge. Conversely, the electron binding energy increases during oxidation because the electron is less effectively shielded from the nuclear charge. When comparing the electron binding energies in metal centers with similar ligand sets, higher electron binding energies correlate with higher oxidation states. We suggest that the electron binding energies, which correlate with oxidation state, are suitable to ascertain the reducto participation of the metals.

We selected two hypothetical but well-defined limiting cases for monometallic reductive elimination (paths 3 and 5, Figure 9) and computed the pathways of reductive elimination for both. Subsequently, the electron binding energies of electrons in the 4s orbitals of both palladium centers, $Pd_a$ and $Pd_b$, have been calculated for each of the two pathways.

Hypothetical reductive elimination from $Pd_a$ with $Pd_b$ as a non-redox-active spectator ligand on $Pd_a$ would proceed through a dinuclear $Pd(I)/Pd(III)$ mixed-valence complex (Figure 10a, path 3). We investigated path 3 by computationally cleaving $A$ into two mononuclear $Pd(III)$ complexes ($G$). Computed intermediate $G$ serves as model for dinuclear compound $A$, in which potential metal-metal cooperation is eliminated. The electron binding energies were determined computationally to describe the redox chemistry of each $Pd$ center during hypothetical path 3 (Figure 10a). The cleavage from $A$ to $G$ is redox-neutral and does not significantly affect the computed electron binding energy of either $Pd_a$ or $Pd_b$. Monometallic reductive elimination from $Pd_a$ proceeds through transition state $H$ to afford structure $I$. Redox chemistry is occurring only at $Pd_a$ during the transformation of $G$ to $I$, and thus the electron binding energy of $Pd_a$ does not change. At the same time, the electron binding energy of $Pd_a$ decreases as $G$ is transformed to $I$, consistent with redox contribution at $Pd_a$. We selected the $Pd(II)$ complex $J$ as the end point, because complex $J$ has well-defined oxidation states on palladium. Further, the ligand sphere of palladium in $J$ is closely related to the ligand sphere of palladium in $A$, allowing for meaningful comparison of electron binding energies. Formal comproportionation of the mixed-valence structure $I$ to $J$ results in the electron binding energies of $Pd_a$ and $Pd_b$ converging. $Pd_a$ in structure $I$ is most accurately described as a $Pd(II)$ with a ligand-centered radical, and thus the electron binding energy of $Pd_a$ during comproportionation does not increase, as would be expected for oxidation of $Pd(I)$ to $Pd(II)$. The diagram in Figure 10a shows that only $Pd_a$.

Figure 8. Potential pathways from dinuclear Pd complexes. Path 3: Monometalic reductive elimination to form a $Pd(I)/Pd(III)$ mixed-valence complex and 2, followed by comproportionation to afford $Pd(II)$. Path 4: Computed low-energy pathway for reductive elimination (Figure 5). Path 5: Disproportionation to a $Pd(II)/Pd(IV)$ mixed-valence complex, followed by monometallic reductive elimination.

and Hammett $\rho$-values and also implicates dinuclear complexes in every step of reductive elimination.

**Metallicity of Reductive Elimination.** Knowledge of the nuclearity of the complex from which reductive elimination proceeds provides no information about the role of each metal center during reductive elimination. Depending on the extent of metal-metal cooperation during reductive elimination from a dinuclear complex, either monometallic or bimetallic redox pathways are possible (Figure 9).

To probe the electronic contribution of each metal center during reductive elimination, the electron binding energies of the 4s core electrons of both $Pd_a$ and $Pd_b$ were calculated as a function of reaction progress for pathways 3 to 5 shown in Figure 9. The electron binding energy of a 4s electron is the energy required to remove an electron from the 4s orbital to infinite separation, without allowing any relaxation of the remaining electrons. For metal centers with similar ligand environments, electron binding energy is well correlated with formal oxidation state. The electron binding energy decreases during reduction of a metal center because the metal becomes more electron rich and the electron is more effectively shielded from the nuclear charge. Conversely, the electron binding energy increases during oxidation because the electron is less effectively shielded from the nuclear charge. When comparing the electron binding energies in metal centers with similar ligand sets, higher electron binding energies correlate with higher oxidation states. We suggest that the electron binding energies, which correlate with oxidation state, are suitable to ascertain the reducto participation of the metals.

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<table>
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<th>References</th>
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<tr>
<td>(37) The core and valence (available in the LACV3P+++(2f) basis set) natural atomic orbital energies of both $Pd_a$ and $Pd_b$ were obtained and plotted as a function of reaction progress. According to Janak’s theorem, the relative orbital energies are estimates of the relative vertical electron binding energies. The relative natural atomic orbital energies can be regarded as approximations of the vertical ionization potential or the negative of the electron affinity.</td>
</tr>
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<td>(38) Energies were obtained from Natural Bond Orbital (NBO) analyses of the M06 wavefunction using the NBO 5.0 module in Jaguar. The NBO analysis method is a popular mathematical treatment of wavefunctions to study bonding effects such as hybridization and covalency.</td>
</tr>
<tr>
<td>(40) Glendening, E. D.; Badenhoop, J. K.; Reed, A. E.; Carpenter, J. E.; Bohm, J. A.; Morales, C. M.; Weinhold, F. Jaguar; Theoretical Chemistry Institute, University of Wisconsin: Madison, 2001.</td>
</tr>
<tr>
<td>(42) The 4s orbital was selected because it is spherically symmetrical and more sensitive to perturbations in the electron density of the metal center than energetically lower lying s orbitals.</td>
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<td>(44) Similarly analysis of the carbon 1s orbitals of CH$_2$ bound to transition metals has been shown to correlate well with the electrophilicity or nucleophilicity of the methyl groups. Nielsen, R. J.; Goddard, W. A., III. J. Phys. Chem., manuscript in preparation.</td>
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<td>(45) In addition to calculating the electron binding energy from $A$, we have also computed the electron binding energies of both $Pd$ centers during C−Cl reductive elimination from cationic structure $M$, in which one of the apical chloride ligands is replaced by a pyridyl ligand. The results of these calculations are in the Supporting Information, and the conclusions drawn from this structure mirror those from complex $A$.</td>
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participates in redox chemistry during reductive elimination; hypothetical path 3 is therefore monometallic.

Alternatively, C–Cl bond formation could proceed by initial disproportionation of complex 1 to a mixed-valence Pd(II)/Pd(IV) complex prior to reductive elimination from Pd(IV), as shown in Figure 9, path 5. Previously, it was speculated that reductive elimination from dinuclear Pd(III) complexes may proceed via Pd(II)/Pd(IV) mixed-valence species. As shown in Figure 10b, the electron binding energy diagram computed for disproportionation from A to K shows increased electron binding energy of Pdα because Pdα is more oxidized in K than it is in A. Reductive elimination proceeds through transition state L, in which redox chemistry is occurring at Pdα. The electron binding energies of Pdα and Pdβ converge as reductive elimination affords two Pd(II) centers (J). During reductive elimination from Pdα, the electron binding energy of Pdβ is constant because Pdβ is not redox-active according to path 5. Hypothetical path 5 is therefore monometallic.

Both paths 3 and 5 were selected to illustrate and benchmark the electron binding energies in two limiting cases of monometallic reductive elimination. Path 4 is derived from the computed low-energy pathway shown in Figure 5. Both electron

Figure 10. (a) Plot of the 4s core electron binding energy of Pdα (solid) and Pdβ (dashed) as a function of reaction progress for monometallic reductive elimination via a Pd(I)/Pd(III) mixed-valence species (Figure 9, path 3). (b) Plot of electron binding energy of Pdα and Pdβ as a function of reaction progress for monometallic reductive elimination from a Pd(II)/Pd(IV) mixed-valence species (Figure 9, path 5). (c) Plot of electron binding energy of Pdα and Pdβ as a function of reaction progress for calculated bimetallic reductive elimination (Figure 5).
binding energies of Pd₄ and Pd₅ monotonically decrease while A is converted to C via transition state B. The electron binding energies continue to monotonically decrease until Pd(II) structure J. Neither metal center becomes oxidized beyond Pd(III) during the course of reductive elimination.

The calculated electron binding energies implicate simultaneous redox participation of both metals during reductive elimination. Monotonic reduction in electron binding energy at both metals is inconsistent with initial disproportionation to a Pd(II)/Pd(IV) complex prior to monometallic reductive elimination. A simultaneous change in the electron binding energies of both Pd₄ and Pd₅ is also inconsistent with initial monometallic reductive elimination to a Pd(I)/Pd(III) mixed-valence complex. Therefore, we conclude that reductive elimination from I is bimetallic.

**Kinetic Advantage of Bimetallic Reductive Elimination.** Based on the HOMO and LUMO calculated for structure A and transition state B (see Supporting Information), metal-metal bonding during reductive elimination is accomplished primarily by overlap of the palladium dₓ² orbitals. We have calculated the activation barrier for reductive elimination as a function of Pd–Pd distance. Computationally forced elongation of the Pd–Pd bond attenuates the overlap of the dₓ² orbitals and thus decreases electronic communication between the metals as compared to low-energy structure A (eq 6). By preventing electronic communication between the metals, bimetallic reductive elimination is forced to become increasingly monometallic.

![Reductive Elimination](Image)

### Table 2. Computed Reference Ground-State and Activation Energies of Reductive Elimination as a Function of Restricted Pd–Pd Distance

<table>
<thead>
<tr>
<th>Pd–Pd distance (Å)</th>
<th>ground-state energy (kcal·mol⁻¹)</th>
<th>activation energy (kcal·mol⁻¹) relative to A</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.62</td>
<td>0.0 (A)</td>
<td>17.1</td>
</tr>
<tr>
<td>2.95</td>
<td>6.2</td>
<td>21.8</td>
</tr>
<tr>
<td>3.30</td>
<td>20.5</td>
<td>33.3</td>
</tr>
<tr>
<td>3.65</td>
<td>35.3</td>
<td>46.0</td>
</tr>
</tbody>
</table>

* Energies are gas-phase electronic energies at 0 K (E₀,k). The activation barrier for electronic elimination when the Pd–Pd distance is fixed at 2.62 Å (the Pd–Pd distance in A) is 17.1 kcal·mol⁻¹. Computational elongation of the Pd–Pd distance to 2.95 Å (Table 2, entry 2) increased the activation barrier to 21.8 kcal·mol⁻¹. Further elongation to 3.30 and 3.65 Å led to activation barriers of 33.3 and 46.0 kcal·mol⁻¹, respectively (entries 3 and 4). Pd–Pd distances beyond 3.65 Å, which is greater than the sum of the two van der Waals radii of the palladium atoms, could not be accommodated while maintaining the bridging geometry of the acetate ligands. Comparison of the activation barriers for bimetallic reductive elimination (entry 1) and monometallic reductive elimination (entry 4) indicates that metal-metal cooperation during reductive elimination lowers the energy barrier by ∼30 kcal·mol⁻¹ as compared to monometallic reductive elimination, which approximately corresponds to the Pd–Pd bond dissociation energy in I.

Reductive Elimination in the Presence of AcOH. Previously, on the basis of the observation of C–C⁻⁴⁸ C–O⁻²⁴, C–Cl⁻⁴⁹ and C–F⁻⁵⁰ reductive elimination from isolated Pd(IV) complexes, Pd(II)/Pd(IV) redox cycles have been invoked as mechanistic rationales for Pd-catalyzed C–H oxidation reactions.⁵¹ We have proposed that reductive elimination from dinuclear Pd(III) complexes, similar to I, is the product-forming step in a variety of Pd-catalyzed C–H oxidation reactions on the basis of the observation of dinuclear complexes during chlorination³⁴ and acetoxylation³⁵ of 2-phenylpyridine derivatives.⁵²

During catalysis, C–H metalation by Pd(II) generates an equivalent of acid. We have found that the rate of reductive elimination is linearly correlated with [AcOH]. We propose that the observed C–Cl reductive elimination rate enhancement is due to protonation of one of the bridging acetic acid ligands of I to afford 36 (Figure 11). In the presence of acid, protonation of the acetate ligand would result in a pentacoordinate Pd center of a dinuclear complex, in which one Pd–O bond is cleaved. We suggest that reductive elimination from 36, in which one bridging acetic acid ligand is protonated, is faster than that from I. A dinuclear transition state for reductive elimination from cationic complex 36, similar in structure to the transition state for reductive elimination from I (B), has been located computationally. The barrier to reductive elimination from I was computed to be 21.8 kcal·mol⁻¹, whereas the barrier to reductive elimination from 36 was computed to be 20.1 kcal·mol⁻¹, consistent with the observed rate enhancement in the presence of AcOH.⁴⁵ Computed electron binding energies for both palladium atoms in A + H⁺ and in B + H⁺ indicate that, similar to reductive elimination from A, reductive elimination from a protonated dinuclear core is bimetallic as well. During Pd-catalyzed C–H functionalization, C–H metatation generates acid, and thus acid-catalyzed reductive elimination may be

![Figure 11](Image)

*rate = k[A] + k[A][AcOH]*

relevant during catalysis. On the basis of the presented data, we cannot distinguish between pre-equilibrium and rate-determining protonation in the acid-catalyzed pathway for reductive elimination from 1 ($k'$, Figure 11).

**Conclusions**

In this article we sought to address the following questions: Does the core of dinuclear Pd(III) complex 1 stay intact during reductive elimination? Do both metal centers participate in the redox transformation, and is there an energetic benefit to having two metals as opposed to a single metal? How closely related are previously proposed mononuclear Pd(IV) complexes to the dinuclear Pd(III) complexes reported here with respect to the mechanism of reductive elimination?

Experimental and theoretical analysis of C–Cl reductive elimination from complex 1 has implicated reductive elimination from a dinuclear core with synergistic, bimetallic redox participation of both metals during reductive elimination. The presence of the second metal in dinuclear complex 1 lowers the activation barrier of reductive elimination. If reductive elimination is artificially forced to proceed via a monometallic pathway by eliminating metal–metal communication, the barrier to reductive elimination is increased by $\sim$30 kcal·mol$^{-1}$.

Transition-metal-mediated C–heteroatom bond construction remains a synthetically challenging goal. We have shown that C–heteroatom bonds can be efficiently formed by bimetallic reductive elimination from dinuclear Pd(III) complexes. In this article we have provided a theoretical framework for bimetallic redox catalysis. Redox synergy between metal centers, as is seen for C–Cl reductive elimination here, also has the potential to lower the activation barriers for other redox processes. We anticipate that our findings may serve as a foundation for future reaction development.

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**Supporting Information Available:** Detailed experimental procedures and spectroscopic data for all new compounds; detailed computational methods and XYZ coordinates (PDF, CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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