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Bimetallic Palladium Catalysis: Direct Observation of Pd(III)−Pd(III) Intermediates

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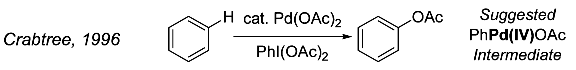
Pd(II)/Pd(IV) redox cycles have been proposed for a variety of palladium-catalyzed transformations since 1971.[1,2] In 2009, bimetallic Pd(III) intermediates were put forth as a mechanistic alternative to the frequently invoked Pd(II)/Pd(IV) redox cycles.[3] Our account disclosed previously unrecognized reactions from organometallic Pd(III) complexes but did not provide evidence for the generality of bimetallic Pd(III) intermediates in catalysis. Here we report the first direct observation of bimetallic Pd(III) complexes in C−H acetoxylation reactions. The Pd(III) intermediates were obtained by oxidation of Pd(II) catalysts with $PhI(OAc)_2$, one of the most common oxidants for oxidative palladium catalysis. Our results demonstrate that bimetallic Pd(III) complexes should be considered as relevant reaction intermediates in a class of Pd-catalyzed reactions previously suggested to proceed via Pd(II)/Pd(IV) redox cycles.[2]

Pd-catalyzed aromatic C−H acetoxylation was first reported in 1966.[4] In acetic acid, oxidants such as $K_2Cr_2O_7$, $Pb(OAc)_4$, and N_2O_2 oxidize benzene to phenyl acetate under Pd catalysis.[5] Stock proposed a Pd(II)/Pd(IV) mechanism for this class of reactions in 1981.[6] Crabtree reported the first $Pd(OAc)_2$-catalyzed acetoxylation of arenes with the terminal oxidant $PhI(OAc)_2$ (eq 1):[7]



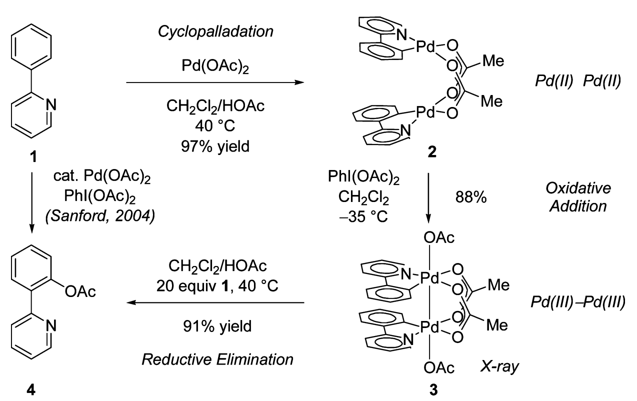
(1)

Since 2004, Sanford[8] and Yu[9] have pioneered practical, directed C−H acetoxylation reactions that also employ $Pd(OAc)_2$ as the catalyst. Reductive elimination from well-defined Pd(IV) complexes, shown for C−C bond formation by Canty[10] and for C−O bond formation by Sanford,[11] has been observed. However, the relevance of Pd(IV) complexes to Pd-catalyzed acetoxylation has not been established.

While several bimetallic complexes of Pt(III) have been reported,[12] only a few organometallic Pd(III) complexes have been described: five paddlewheel complexes by Cotton and Lahuerta[13] and five carboxylate-bridged bimetallic complexes by us.[3] We have shown that reductive elimination from bimetallic Pd(III) complexes can form carbon−heteroatom bonds and implicated bimetallic palladium complexes in catalysis through kinetic analysis. However, when oxidants such as NCS were employed, the proposed bimetallic Pd(III) complexes were not observed during catalysis. To evaluate the potential generality of bimetallic Pd(III) complexes as intermediates in catalysis, we studied the oxidation of Pd(II) catalysts with $PhI(OAc)_2$, one of the most common oxidants for Pd-catalyzed C−H bond functionalizations.[2]

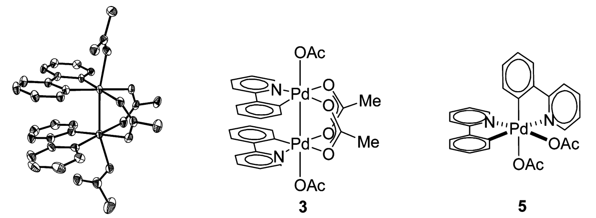
Cyclopalladation (first reported by Cope in 1965[14]) of 2-phenylpyridine (**1**) with $Pd(OAc)_2$ afforded the bimetallic Pd(II) complex **2**, in which the two palladium nuclei are held in proximity by bridging acetate ligands (Scheme 1). When bimetallic Pd(II) complex **2** was treated with $PhI(OAc)_2$ at −35 °C, the thermally sensitive bimetallic Pd(III) complex **3** was observed and could be isolated in 88% yield. Complex **3** is stable in solution and in the solid state below −10 °C and was characterized crystallographically (Figure 1).

Scheme 1. Discrete Bimetallic Pd(III) Intermediate in Acetoxylation



Bimetallic **3** is not the catalyst resting state and cannot be observed during catalysis. However, we observed the formation and reaction of **3** under pseudocatalytic conditions by sequential addition of reagents at controlled temperatures. We treated $Pd(OAc)_2$ with excess substrate **1** and observed the dimer **2** in the presence of 5 equiv of **1**.[15] Subsequent addition of 5 equiv of $PhI(OAc)_2$ at −10 °C afforded the Pd(III) dimer **3** in 66% yield.[16] When the purified intermediate **3** in the presence of 20 equiv of substrate **1** was warmed to 40 °C, bimetallic reductive elimination occurred, affording product **4** in 91% yield. Reductive elimination from **3** in the absence of **1** afforded product **4** in only 6% yield. Likewise, the $Pd(OAc)_2$-catalyzed reaction **1** → **4** with 100 mol % Pd did not afford **4** upon heating at 80 °C for 12 h. Both results suggest the consumption of product **4** by Pd after reductive elimination.[17]

After reductive elimination from **3** in the presence of **1**, the bimetallic Pd(II) complex **2** was observed by ^1H NMR spectroscopy.



X-ray structure of **3**,
Pd–Pd bond:
2.5548(5) Å

Pd(III)–Pd(III) **3**,
kinetically competent for catalysis

Pd(IV) ***5, not***
kinetically competent for catalysis

Figure 1. ORTEP diagram of Pd(III) **3** with ellipsoids drawn at the 50% probability level; kinetic competence of **3** and incompetence of **5**.

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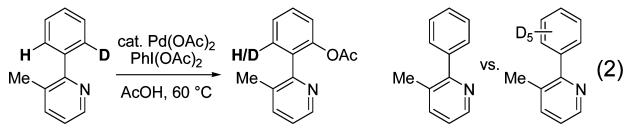
Reductive elimination by first-order kinetics in bimetallic Pd(III) complex was established by following product formation from a methylated analogue of **3** for accurate ^{1}H NMR integration. All of the reactions shown in Scheme 1 can be carried out in CH_2Cl_2, AcOH, or a mixture thereof. The isolation of **3**, however, required addition of CH_2Cl_2 because **3** was not stable at the freezing point of AcOH (17 °C) or above. Observation of both oxidation of **2** with $PhI(OAc)_2$ and reductive elimination from **3** to **4** is consistent with the participation of bimetallic Pd(III) intermediates in the Pd-catalyzed C−H functionalization of arenes with the oxidant $PhI(OAc)_2$.

Discrete monometallic Pd(IV) complexes such as **5** (Figure 1) have been considered as models for the high-valent palladium complexes from which C−O reductive elimination could occur during catalysis.[11b] We measured the initial rate of the reaction from **1** to **4** (shown on the left of Scheme 1) catalyzed by 8 mol % $Pd(OAc)_2$, 8 mol % monometallic Pd(IV) complex **5**, or 4 mol % bimetallic Pd(III) complex **3**. The initial rate of product formation with catalyst **5** was half as fast as the initial rate with $Pd(OAc)_2$ as the catalyst. Therefore, the Pd(IV) complex **5** is not kinetically competent for catalysis. The initial rate of product formation with bimetallic Pd(III) complex **3** is higher than the rate observed with $Pd(OAc)_2$, which demonstrates that **3** is kinetically competent for catalysis. The observation and kinetic competence of **3**, as well as the kinetic incompetence of **5**, cannot exclude the potential transient intermediacy of Pd(IV) complexes other than **5**. For example, our data cannot rule out the formation and relevance to catalysis of monoaryl Pd(IV) complexes.

Kinetic analysis under conditions of catalysis, the isolation of both **2** and **3**, and the independent observation of all three fundamental reactions—bimetallic oxidative addition, bimetallic reductive elimination, and cyclometalation—are consistent with the proposed catalytic cycle shown in Figure 2. Measurement of the initial rate of acetoxylation as a function of $PhI(OAc)_2$ concentration showed a zeroth-order kinetic dependence with respect to oxidant, which precludes rate-determining oxidation. Observation of an intramolecular primary kinetic isotope effect of $k_H/k_D = 5.1$ and an intermolecular primary isotope effect of $k_H/k_D = 5.0$ is consistent with rate-determining cyclopalladation.[18] The isotope effects were determined by acetoxylation of substrate ***6-d*** and by competing acetoxylation between **6** and ***6-d*₅** (eq 2; see the Supporting Information):



(2)

6-d ***7 + 7-d*** *intramolecular* k_H/k_D = 5.1 **6** ***6-d*₅** *intermolecular* k_H/k_D = 5.0

Rate-determining cyclometalation precludes the kinetic implication of bimetallic Pd complexes during oxidation and reductive elimination; however, bimetallic palladium complexes were implicated in the rate-determining step of related C−H oxidations with weaker oxidants than $PhI(OAc)_2$, in which case cyclopalladation is not rate-determining.[3,19]

In conclusion, our report discloses the first evidence of bimetallic Pd(III) intermediates in Pd-catalyzed acetoxylation. On the basis of this evidence and our previous kinetic implication of a bimetallic Pd complex in the rate-determining step of C−H functionalization with NCS, we propose that bimetallic Pd(III) complexes are responsible for a large class of C−H oxidations previously proposed to proceed via Pd(II)/Pd(IV) redox cycles.

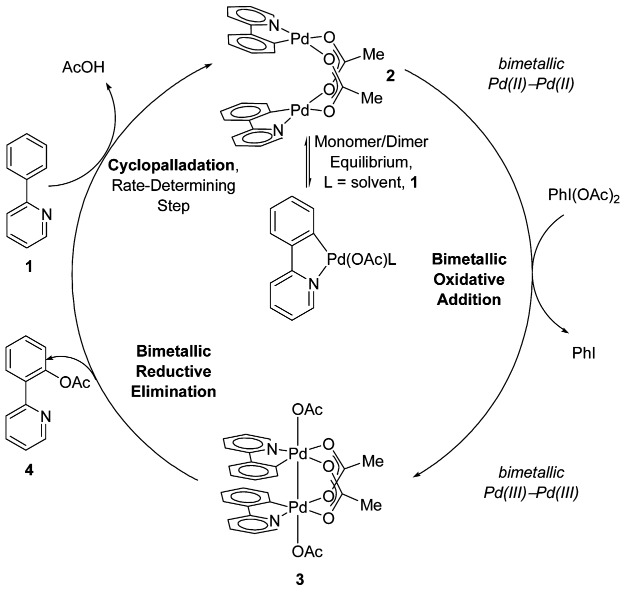


Figure 2. Proposed bimetallic Pd(II)/Pd(III) catalytic cycle.

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Supporting Information Available: Detailed experimental procedures, spectroscopic data for all new compounds, and crystallographic data for **3** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(15) Cyclometalated Pd(II) complexes such as **2** are in equilibrium with monometallic Pd(II) complexes bearing an additional ligand. See: Ryabov, A. D. *Inorg. Chem.* **1987**, *26*, 1252.
(16) Addition of 1 equiv of $PhI(OAc)_2$ to **2** afforded **3** in 88% isolated yield. In the presence of excess **1** and $PhI(OAc)_2$, the thermally sensitive Pd(III) dimer **3** could not be isolated without reductive elimination to **4**. The yield of 66% was determined by ^{1}H NMR spectroscopy using an internal standard.
(17) Acetoxylation of **1** with $PhI(OAc)_2$ using 100 mol % $Pd(OAc)_2$ proceeded in 0% yield. The yield of **4** increased when 50 mol % $Pd(OAc)_2$ was used. The yield of **4** from **3** in the absence of **1** could be increased from 6 to 82% by addition of 20 equiv of pyridine prior to reductive elimination. For details, see the Supporting Information.
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