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

David C. Powers, Matthias A. L. Geibel, Johannes E. M. N. Klein, and Tobias Ritter

Department of Chemistry and Chemical Biology, Harvard University, 12 Oxford Street, Cambridge, MA

RECEIVED DATE: ritter@chemistry.harvard.edu

Pd(II)/Pd(IV) redox cycles have been proposed for a variety of palladium-catalyzed transformations since 1971. In 2009, bimetallic Pd(III) intermediates were put forth as a mechanistic alternative to the frequently invoked Pd(II)/Pd(IV) redox cycles. 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 are obtained by oxidation of Pd(II) catalysts with one of the most common oxidants for oxidative palladium catalysis—PhI(OAc)₂. 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.

Pd-catalyzed aromatic C–H acetoxylation was first reported in 1966. In acetic acid, oxidants such as K₂Cr₂O₇, Ph(OAc)₂, and N₂O₃ oxidize benzene to phenyl acetate under Pd catalysis. Stock proposed a Pd(II)/Pd(IV) mechanism for this class of reactions in 1981. Crabtree reported the first Pd(OAc)₂-catalyzed acetoxylation of arenes with the terminal oxidant PhI(OAc)₂ (eq 1). Since 2004, Sanford and Yu have pioneered practical, directed C–H acetoxylation reactions that also employ Pd(OAc)₂ as catalyst. Reductive elimination from well-defined Pd(IV) complexes, shown for C–C bond formation by Canty and for C–O bond formation by Sanford, has been observed. However, the relevance of Pd(IV) complexes to Pd-catalyzed acetoxylation has not been established. Crabtree, 1996

While several bimetallic complexes of Pd(III) have been reported, only few organometallic Pd(III) complexes have been described: five paddlewheel complexes by Cotton and Lahuerta, and five carboxylate-bridged bimetallic complexes by us. 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, 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.

Cyclopalladation, first reported by Cope in 1965, of 2-phenylpyridine (I) 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).

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 five equivalents of 1. Subsequent addition of five equivalents PhI(OAc)₂ at –10 °C afforded the Pd(III) dimer 3 in 66% yield. Upon warming the purified intermediate 3 in the presence of 20 equiv of substrate 1 to 40 °C, bimetallic reductive elimination occurred to afford 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.

After reductive elimination from 3 in the presence of 1, the bimetallic Pd(II) complex 2 was observed by ¹H NMR. Reductive elimination by first order kinetics in bimetallic Pd(III) complex was established by following product formation from a methylated analog of 3 for accurate ¹H NMR integration. All reactions shown in Scheme 1 can be carried out in CH₂Cl₂ or AcOH or a mixture thereof. The isolation of 3, however, required addition of CH₂Cl₂ because 3 was not stable at the freezing point of AcOH (17 °C) or above. Observation of both oxidation of 2 with Pd(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. We measured the initial rate of the reaction

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

crystallographic analysis and Sanofi implicated in the rate elimination; however, concentration showed a zero order kinetic dependence both
cannot exclude the potent formation w

bimetallic Pd(II)

Figure 1

Figure 2

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

REFERENCES

15. Cyclometallated Pd(II) complexes such as 2 are in equilibrium with mononuclear Pd(II) complexes bearing an additional ligand: Ryabov, A. D. Inorg. Chem. 1987, 26, 1252-1260.
16. Addition of 1 equiv Ph(OAc)₂ to 2 afforded 3 in 88% isolated yield. In the presence of excess 1 and Ph(OAc)₂, the thermally sensitive Pd(III) dimer 3 could not be isolated without reductive elimination to 4. The yield of 6% was determined by 1H NMR spectroscopy using an internal standard.
17. Acetoxylation of 1 with Ph(OAc)₂, with 100 mol% Ph(OAc)₂ proceeded in 0% yield. The yield of 4 increased when 50 mol% Ph(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 Supporting Information.
Phl(OAc)$_2$ is a common oxidant for Pd-catalyzed C–H bond functionalizations. Mechanistic hypotheses since the 1960’s have suggested a Pd(II)/Pd(IV) mechanism. Here we present evidence for the relevance of bimetallic Pd(III) complexes to catalysis. A bimetallic Pd(III) acetate was isolated and can afford product by bimetallic reductive elimination.