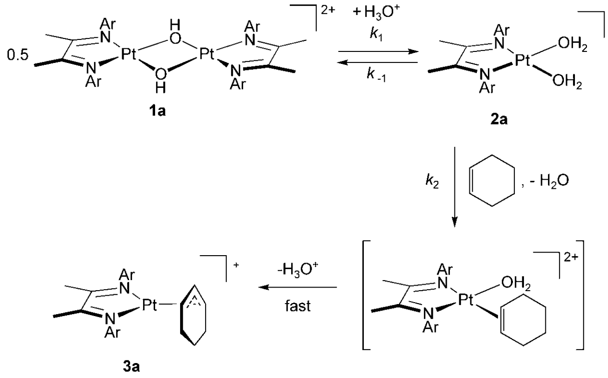
DOI: 10.1002/ange.200804455

C–H Bond Activation by [{(Diimine)Pd(μ-OH)}$_2$]$^{2+}$ Dimers: Mechanism-Guided Catalytic Improvement**

John E. Bercaw, Nilay Hazari, Jay A. Labinger,* and Paul F. Oblad*

Practical methods for the selective functionalization of C–H bonds could have a significant environmental and economic impact, in areas ranging from fuels and commodity chemicals to pharmaceuticals.[1] Although there are now many transition-metal complexes that can activate C–H bonds, most of these compounds are unstable or inactive in the presence of water or potential functionalized products, such as alcohols. As water is usually a by-product of oxidative functionalization (especially when using O_2) and alcohols are often desirable products, this incompatibility represents a large barrier to the development of catalysts for the transformation of C–H bonds. To address this problem, several groups have reported C–H bond activation reactions using metal alkoxide and hydroxy complexes which occur even in the presence of free alcohols and, in some cases, water.[2]

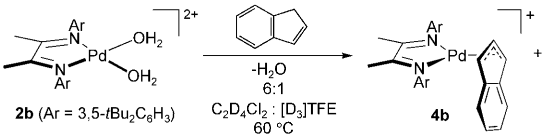
We recently reported that the air- and water-tolerant dimeric hydroxy-bridged dimers [{(diimine)M(OH)}$_2$]$^{2+}$ (M = Pt (**1a**), Pd (**1b**)), can effect not only stoichiometric activation of a variety of C–H bonds (subject to the requirement that a multidentate ligand can be produced), but also the catalytic conversion of cyclohexene into benzene, using dioxygen as the terminal oxidant, when the metal is Pd.[3] The proposed mechanism for C–H bond activation of cyclohexene by Pt involves initial acid-mediated conversion of dimeric [{(diimine)Pt(OH)}$_2$]$^{2+}$ (**1a**) into monomeric [(diimine)Pt(OH$_2$)$_2$]$^{2+}$ (**2a**), subsequent displacement of water by cyclohexene at a comparable rate, and then fast conversion of the cyclohexene adduct into an η^3-cyclohexenyl species **3a**, with concomitant loss of H_3O^+ (Scheme 1). In dichloroethane (or a dichloroethane/trifluoroethanol mixture) the dimeric complex **1a** reacts extremely slowly (or not at all) with C–H bonds in the absence of acid, and kinetic data in the presence of acid are consistent with consecutive (pseudo) first-order reactions, with the first step being first order in HBF_4 and the second step being first order in cyclohexene. Surprisingly, the second step is also first order in HBF_4. We expected that the palladium analogue would follow a similar pathway for C–H bond activation, but results presented herein indicate significant differences between the mechanisms of reactions involving **1b** and **1a**.



Scheme 1. Proposed mechanism for C–H bond activation of cyclohexene by **1a**. Ar = 3,5-$tBu_2C_6H_3$.

Whereas compound **2a**, the proposed active species for C–H activation starting with dimeric **1a**, has not been isolated, and only characterized using ^{1}H NMR spectroscopy,[3] we have previously isolated monomeric [(diimine)Pd(OH$_2$)$_2$]$^{2+}$ (**2b**).[4] Although stoichiometric reactions of **2b** with cyclohexene do not yield clean products (presumably because the η^3-cyclohexenyl complex rapidly undergoes further reaction[5]), stoichiometric reactions with indene were shown to cleanly yield the η^3-indenyl species **4b** [Eq. (1)].[3] This reaction was used for detailed mechanistic studies.[6]

Kinetics were monitored by ^{1}H NMR spectroscopy under the conditions shown in Equation (1), with varying indene concentration, and the results show that the reaction is first order in Pd and indene.[7] The effect of adding acid to the reaction described in Equation (1) was also tested by varying the BF_3 concentration (which reacts with cosolvent trifluoroethanol (TFE) to generate H^+). The data are consistent with a two-term rate law, in which one component is zero order in BF_3 and the other component is first order in BF_3.[7] Chemically, these data could be explained by parallel steps for the displacement of coordinated water by indene, one acid-assisted and the other not. The acid dependence is analogous to that for the reaction of **2a** with cyclohexene,[3] and suggests that general acid catalysis assists in the displacement of



(1)

---

[*] J. E. Bercaw, N. Hazari, J. A. Labinger, P. F. Oblad
Arnold and Mabel Beckman Laboratories of Chemical Synthesis, California Institute of Technology
Pasadena, CA 91125 (USA)
E-mail: bercaw@caltech.edu
jal@caltech.edu

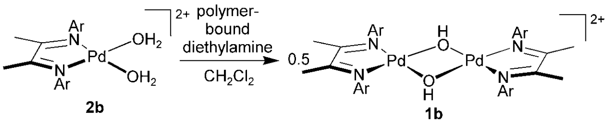
[**] This work was supported by BP through the MC^2 program, and Caltech through a Switzer fellowship to P.F.O. We thank Larry Henling and Michael Day for assistance with crystallography.

Supporting information for this article (Experimental details, kinetics analyses, and X-ray information for **1b** and **2b**) is available on the WWW under http://dx.doi.org/10.1002/anie.200804455.

coordinated water by indene, as a result of weakening the Pd–OH_2 or Pt–OH_2 bond; a similar effect has been reported in related systems.[8] Thus, under acidic conditions, both **2a** and **2b** effect C–H activation by the same pathway: rate-limiting coordination of substrate followed by rapid C–H activation.

The reaction of **2b** with indene is not inhibited by water, indicating that substitution of coordinated water by indene is associative. On the other hand, addition of greater than 50 equivalents of water causes an increase in the rate.[7] Analysis of the ^{1}H NMR spectrum (in the absence of indene) reveals that, as the quantity of free water is increased, resonances corresponding to the hydroxy-bridged dimer **1b** are detected along with those of **2b**. Thus, at high concentrations, it appears that water is a sufficiently strong base to deprotonate **2b** and establish an equilibrium between **1b** and **2b**. When such a solution is treated with indene, the resonances for **1b** disappear significantly faster than those for **2b**, as resonance peaks corresponding to the indenyl species **4b** emerge. These results imply that there is a direct pathway for C–H activation with **1b** that does not involve **2b** as an intermediate, in contrast to the platinum analogue **1a**.

Addition of stronger bases, such as 2,6-lutidine, triethylamine, or 1,8-bis(dimethylamino)naphthalene, to solutions of **2b** results in rapid and complete deprotonation to **1b**.[7] When these deprotonation reactions were attempted on a preparative scale, the protonated amine could not be cleanly separated from the product. However, the use of a solid-supported base, polystyrene-bound diethylamine, allowed the isolation of pure **1b** in 85% yield [Eq. (2)],[7] representing a significant improvement on the previous method.[3,4]



(2)

A solution of **1b** in CH_2Cl_2 reacted with indene to form **4b** even at room temperature, albeit very slowly ($t_{1/2} \approx 3$ days). Addition of a small amount of TFE or MeOH (typically a 6:1 ratio of CH_2Cl_2 to the alcohol) results in a dramatic increase in rate ($t_{1/2} \approx 5$ min). A smaller increase in rate is obtained by adding THF, pentafluoropyridine, or even water ($t_{1/2} \approx 1$ day), but those reactions give lower yields and more impurities. In contrast, **1a**, **2a**, and **2b** all require elevated temperatures to react with indene at an appreciable rate.

The kinetics for the reaction of **1b** with varying concentrations of indene and TFE (or MeOH, when it was used as additive) were determined using both ^{1}H NMR and UV/Vis spectroscopy. The results reveal half-order dependence on Pd concentration (Figure 1) and first-order dependence on both indene and TFE (or MeOH) concentrations.[7] These findings are consistent with the mechanism shown in Scheme 2, consisting of an equilibrium involving the fast, solvent-assisted separation of **1b** into two monocationic monomers[9] (which explains both the half-order Pd-concentration dependence and the substantial increase in rate when TFE or MeOH is added), followed by the rate-determining displacement of coordinated solvent by indene, and finally by fast C–H activation. The rate-determining step, indicated by the detected first-order indene-concentration dependence and also the absence of a detectable π-bound indene intermediate, also explains why the reaction is faster for **1b** than for dications **2a** and **2b**, as water is probably more tightly bound to the dicationic center in the latter, thus slowing displacement, whereas TFE or methanol bound to the monocationic monomer generated from **1b** would be more readily displaced.[10]

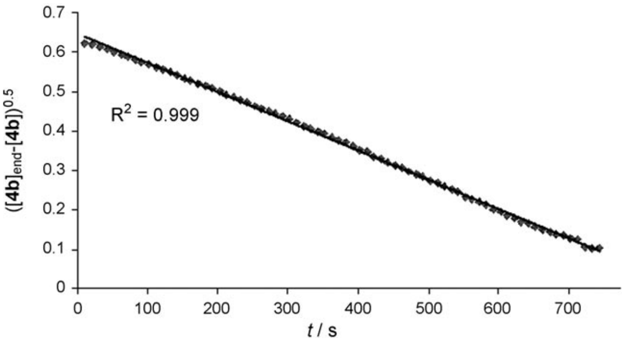
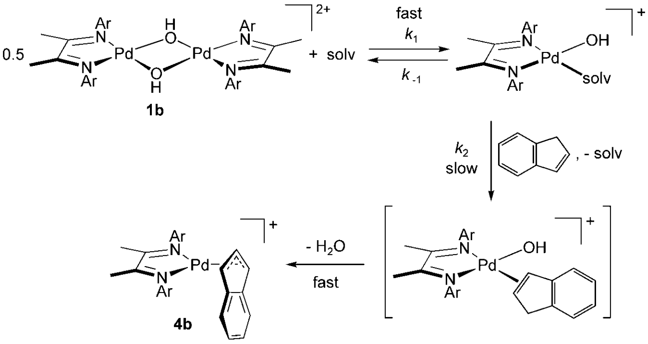


Figure 1. Graph of $([\mathbf{4b}]_{end}-[\mathbf{4b}])^{0.5}$ against time during the reaction of **1b** with 40 equivalents of indene in CH_2Cl_2/TFE (5.5:1 mixture, 675 equivalents of TFE). $[\mathbf{4b}]_{end}$ = final concentration of product **4b**.[7]

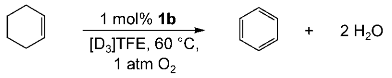


Scheme 2. Proposed mechanism for palladium-catalyzed C–H bond activation of indene by **1b**. Ar = 3,5-$tBu_2C_6H_3$, solv = MeOH or TFE.

The kinetic isotope effect (KIE) for the conversion of 1,1,3-trideuteroindene[11] into the deuterated indenyl complex [D_2]-**4b** was determined by comparing rate constants for parallel reactions, which reveals a value of $k_H/k_D = 1.6(1)$. This value is slightly larger than expected for rate-determining π coordination of indene ($k_H/k_D \approx 1$) but significantly lower than would be expected for rate-determining C–H activation ($k_H/k_D \approx 3.5$–6). Previously, we have tentatively postulated that KIE values of around 2 (detected for similar C–H activation reactions with other {Pt(diimine)} systems) indicate that neither coordination of the substrate nor C–H activation is completely rate-determining, and the measured KIE reflects both steps.[12] That possibility cannot be discounted in this case, although it is clear that C–H activation is not entirely rate determining.

At this stage, the exact reasons for the differences in reactivity between **1a** and **1b** are unclear. The proposed mechanism implies that the hydroxy bridges are more readily broken by solvent for **1b** than for **1a**, although **1b** seems to be less basic than **1a** ($K_{eq} \approx 1000\,\text{M}^{-1}$ for the reaction of **1b** with HBF_4 (3.62 equiv) at room temperature to form **2b**, whereas the corresponding reaction with **1a** results in complete conversion into **2a**).[7] Conversely, the reaction between acid and **1a** takes almost 3 days to go to completion, whereas the corresponding reaction with **1b** equilibrates in 10 minutes, suggesting that the kinetic barrier to breaking apart **1a** is considerably greater than that for **1b**. After **1a** and **1b** have been protonated, the reactivities of the resulting Pt and Pd complexes **2a** and **2b** are more similar: the two complexes activate C–H bonds by the same pathway and at comparable rates.

These conclusions—that the hydroxy-bridged dimer **1b** is the most reactive species in the Pd system, considerably more reactive than either **2a** or **2b** towards C–H bond activation, and that there is an important solvent-assisted component in the rate law—suggest a way to substantially improve the catalytic conversion of cyclohexene into benzene [Eq. (3)]. Our previous studies involved **2b** (or mixtures of **1b** and **2b**) in the noncoordinating solvent dichloroethane. In a typical experiment, after 24 h under 1 atm of O_2 with 5 mol% of **2b** as the catalyst, 8% of the cyclohexene had been converted into benzene; furthermore, there was an initiation period before any reaction occurred, and competing disproportionation of cyclohexene to benzene and cyclohexane was a major side reaction.[3] In contrast, under the same conditions but using only 1 mol% of pure **1b** as the catalyst and TFE as solvent, conversion was 25% after 24 h, with no induction period or competing isomerization.[7]



(3)

Such optimization of catalytic reactions by means of mechanistic understanding is a major goal of fundamental research in homogeneous catalysis, which we hope to continue to exploit in our further studies aimed at utilizing **1b** and related species for catalytic C–H activation.

Received: September 10, 2008

Keywords: C–H activation · homogeneous catalysis · kinetics · oxidation · palladium

---

[1] a) R. H. Crabtree, *J. Chem. Soc. Dalton Trans.* **2001**, 2437; b) J. A. Labinger, J. E. Bercaw, *Nature* **2002**, *417*, 507; c) U. Fekl, K. I. Goldberg, *Adv. Inorg. Chem.* **2003**, *54*, 259.

[2] a) W. J. I. Tenn, K. J. H. Young, G. Bhalla, J. Oxgaard, W. A. Goddard, R. A. Periana, *J. Am. Chem. Soc.* **2005**, *127*, 14172; b) Y. Feng, M. Lail, K. A. Barakat, T. R. Cundari, T. B. Gunnoe, J. L. Petersen, *J. Am. Chem. Soc.* **2005**, *127*, 14174; c) S. K. Hanson, D. M. Heinekey, K. I. Goldberg, *Organometallics* **2008**, *27*, 1454.

[3] T. J. Williams, A. J. M. Caffyn, N. Hazari, P. F. Oblad, J. A. Labinger, J. E. Bercaw, *J. Am. Chem. Soc.* **2008**, *130*, 2418.

[4] L. J. Ackerman, J. P. Sadighi, D. M. Kurtz, J. A. Labinger, J. E. Bercaw, *Organometallics* **2003**, *22*, 3884.

[5] Previous studies have shown that **2b** is able to catalytically convert cyclohexene into benzene under an atmosphere of O_2.[3] We believe that, in stoichiometric reactions, an η^3-cyclohexenyl species is initially formed, but is unstable and decomposes to give palladium(0) and organic by-products, such as 1,3-cyclohexadiene.

[6] To exclude the possibility that the difference in behavior is due to changing the organic substrate rather than the metal, some kinetic studies were carried out for the reaction of $[\{(\text{diimine})\text{Pt}(\mu\text{-OH})\}_2]^{2+}$ (**1a**) and indene in the presence of acid.[7] The mechanism of C–H activation appears to be completely the same as that for reactions between **1a** and cyclohexene.[3]

[7] Experimental details and more extensive discussion are provided in the Supporting Information.

[8] a) G. Annibale, P. Bergamini, V. Bertolasi, M. Bortoluzzi, M. Cattabriga, B. Pitteri, *Eur. J. Inorg. Chem.* **2007**, 5743; b) M. Bortoluzzi, G. Annibale, G. Paolucci, B. Pitteri, *Polyhedron* **2008**, *27*, 1497.

[9] Consistent with this proposal it has been demonstrated that reaction of **1a** with PEt_3 results in the formation of $[(\text{diimine})\text{Pt}(\text{OH})(\text{PEt}_3)]^+$. Similarly, reaction of **1b** with MeCN or DMSO results in the formation of new complexes which contain resonances in the ^{1}H NMR spectrum consistent with species of the type $[(\text{diimine})\text{Pd}(\text{OH})(\text{MeCN})]^+$ or $[(\text{diimine})\text{Pd}(\text{OH})(\text{dmso})]^+$, respectively; both of these Pd species activate indene to form **4b** (see the Supporting Information for more details). Furthermore, half-order dependence on Pd concentration has been detected in the $[(\text{neocuproine})\text{Pd}(\text{OAc})_2]$-catalyzed aerobic oxidation of alcohols, for which a hydroxy-bridged dimeric palladium complex was proposed to be the active species. See I. W. C. E. Arends, G. ten Brink, R. A. Sheldon, *J. Mol. Catal. A: Chem.* **2006**, *251*, 246.

[10] For a discussion on the effect of charge in C–H activation by dicationic platinum(II) complexes see: T. G. Driver, T. J. Williams, J. A. Labinger, J. E. Bercaw, *Organometallics* **2007**, *26*, 294.

[11] For the synthesis of 1,1,3-trideuteroindene, see M. Yasuda, C. Pak, H. Sakurai, *Bull. Chem. Soc. Jpn.* **1980**, *53*, 502.

[12] H. A. Zhong, J. A. Labinger, J. E. Bercaw, *J. Am. Chem. Soc.* **2002**, *124*, 1378.