# **ORGANOMETALLICS**

### Syntheses and Thermolysis of Arylpalladium Hydroxide Complexes: Implications for C(sp<sup>2</sup>)–OH Bond-Forming Reductive Elimination To Generate Phenol Derivatives

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**Supporting Information** 

**ABSTRACT:** The decomposition of arylpalladium hydroxide complexes gave the corresponding phenolic products, which may form through a  $C(sp^2)$ -OH bond-forming reductive elimination either by treatment of arylpalladium halide complexes with cesium hydroxide or by heating arylpalladium hydroxide complexes. Treatment of a *p*-nitrophenylpalladium iodide complex possessing a 'BuXPhos ligand with cesium hydroxide formed a mixture of *p*-nitrophenol and 4,4'-di-*p*-nitrobiphenyl. The reaction of a D'BPP-ligated *p*-nitrophenylpalladium iodide complex with cesium hydroxide gave a mixture of *p*-nitrophenylpalladium hydroxide complex, cesium *p*-nitrophenoxide, and D'BPP-bridged dinuclear



Pd(0) complex. Gradual decomposition of *p*-nitrophenylpalladium hydroxide complex to cesium *p*-nitrophenoxide and a D'BPP-bridged dinuclear Pd(0) complex suggested that the  $C(sp^2)$ -OH bond-forming reductive elimination took place. While an isolated *p*-tolylpalladium hydroxide complex gave no phenolic product upon heating, thermolysis of an isolated trifluoromethyl-substituted arylpalladium hydroxide complex enabled us to observe *p*-trifluoromethylphenol directly. Although an ester-substituted hydroxide complex did not form free *p*-methoxycarbonylphenol, its invisibility enabled us to handle the kinetic equation to estimate the rate constant  $k_1$  for reductive elimination. Polar solvents such as THF and DMF accelerated the reductive elimination with a large negative entropy of activation. Comparison of these results with those in the literature suggested direct  $C(sp^2)$ -OH bond-forming reductive elimination with a concerted three-centered pathway. DFT calculations also predicted the hydrogen bond between the hydroxo ligand and the solvent molecule to stabilize the transition state.

#### INTRODUCTION

Carbon-heteroatom bond-forming reductive elimination reactions for C-P, C-S, C-N, and C-O are some of the most important organometallic elementary reactions, studied as a part of mechanistic investigations on transition-metal-catalyzed reactions.<sup>1</sup> It was indicated that the relative rate for these reductive elimination reactions could be described as C-P > $C-S > C-N > C-O^2$  Despite the slow rate of C-O bondforming reductive elimination reactions, these processes have been carefully investigated because they may possibly be an elementary reaction for designing difficult catalytic reactions such as anti-Markovnikov hydration of alkene<sup>3</sup> and direct terminal oxidation of alkane.<sup>3'a,4</sup> Previous examples of directly observed C-O bond-forming reductive elimination reactions could be classified into several groups by the central metals and their oxidation states, such as Pd(II),<sup>5</sup> Ni(III),<sup>6</sup> Pd(IV),<sup>7</sup> and Pt(IV).8 Detailed mechanistic studies generally suggested that C-O bond-forming reductive elimination proceeded via a concerted three-centered pathway induced by an oxidation of the metal center,<sup>6</sup> a dissociation of other ligand(s),<sup>5,7a-c</sup> or a stepwise pathway containing dissociation of anionic oxygen ligand from the metal center followed by its S<sub>N</sub>2-type attack at the alkyl ligand.<sup>8a-d</sup> Some of these studies on C-O bondforming reductive elimination using Pt(IV) complexes contained  $C(sp^3)$ –OH bond-forming reductive elimination from alkylmetal hydroxide complexes to produce aliphatic alcohols.<sup>8c-f</sup> High-valent Pd(IV) complexes are also known to undergo  $C(sp^2)$ –OH bond-forming reductive elimination.<sup>7d</sup>

On the other hand, catalytic syntheses of phenol derivatives from the corresponding aryl halide and hydroxide anion have been reported by use of a palladium complex and a bulky monophosphine ligand.<sup>9</sup> The catalytic cycles of these reactions were considered to include  $C(sp^2)$ –OH bond-forming reductive elimination as a product-forming step. However, there has been no information about this process because arylpalladium hydroxide intermediates possessing the bulky monophosphine ligand were too unstable to be observed. Here we report syntheses and thermolyses of arylpalladium hydroxide complexes bearing a monophosphine or diphosphine ligand to implicate  $C(sp^2)$ –OH bond-forming reductive elimination reactions.

Received: November 16, 2011 Published: February 1, 2012

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Synthesis of a Bulky Monodentate Phosphine Ligated Arylpalladium Halide Complex To React with Hydroxide. Complexation of <sup>t</sup>BuXPhos, which was reported to be a good ligand for phenol synthesis,<sup>9a</sup> with CpPd(allyl)<sup>10</sup> in the presence of *p*-iodonitrobenzene afforded the three-coordinate palladium complex (<sup>t</sup>BuXPhos)Pd(C<sub>6</sub>H<sub>4</sub>-*p*-NO<sub>2</sub>)I (1) in 78% yield (Scheme 1). The <sup>1</sup>H, <sup>13</sup>C, and <sup>31</sup>P NMR spectra of **1** were

Scheme 1. Synthesis of *p*-Nitrophenylpalladium Iodide Complex 1 Bearing a <sup>t</sup>BuXPhos Ligand



consistent with the expected structures. The whole structure was confirmed by X-ray crystallography (Figure S15, Supporting Information). A three-coordinate structure was found in the solid state of 1 to have a relatively short contact between the central palladium and 1-position of the triisopropylphenyl ring (Pd1---C21 = 2.566(5) Å), as the related monophosphine-ligated arylpalladium fluoride or bromide complexes had a similar structure.<sup>11</sup> Then, we attempted to generate an arylpalladium hydroxide complex by the treatment of 1 with cesium hydroxide hydrate (Scheme 2).

Scheme 2. Attempted Synthesis of Arylpalladium Hydroxide Complex from Arylpalladium Iodide 1 with  $CsOH^a$ 



<sup>a</sup>Yields were estimated from the <sup>1</sup>H NMR spectrum.

Instead of detecting any arylpalladium hydroxide complex, however, *p*-nitrophenol **2-NO**<sub>2</sub> and biaryl **3-NO**<sub>2</sub> were observed after quenching with proton. The Pd counterpart may form metallic Pd(0) in the absence or presence of an additional amount of <sup>1</sup>BuXPhos, because a large amount of black precipitate was observed. Beller et al. reported a similar observation for generation of phenol from arylpalladium bromide possessing a P–N bidentate ligand and tetrabutylammonium hydroxide via a rapid reductive elimination.<sup>9c</sup> The formation of biaryl could be explained by the C–C bondforming reductive elimination from the diarylpalladium complex, which may be generated by intermolecular aryl exchange reaction of **1**.<sup>12</sup>

Syntheses of Bulky Bidentate Phosphine-Ligated Arylpalladium Halide Complexes. To synthesize isolable arylpalladium hydroxide, which can undergo  $C(sp^2)$ –OH bond-forming reductive elimination, the bulky bidentate ligand D<sup>t</sup>BPP (1,3-bis(di-*tert*-butylphosphino)propane) was used as a supporting ligand. A series of arylpalladium halide complexes bearing D'BPP were synthesized from various palladium precursors (Scheme 3). From the iodide-bridged dinuclear





complex  $[(o-tol)_3PPd(C_6H_4-p-NO_2)I]_2$ , replacement of  $(o-tol)_3P$  with D<sup>t</sup>BPP gave  $(D^tBPP)Pd(C_6H_4-p-NO_2)I$  (4-NO<sub>2</sub>) in 67% yield. A ligand exchange reaction of (tmeda)Pd(p-tol)Iwith D<sup>t</sup>BPP gave the corresponding  $(D^tBPP)Pd(p-tol)I$ complex (4-Me) in 54% yield. Mixing of D<sup>t</sup>BPP, aryl halide, and CpPd(allyl)<sup>10</sup> afforded  $(D^tBPP)Pd(C_6H_4-p-CF_3)Br$  (4-CF<sub>3</sub>) and  $(D^tBPP)Pd(C_6H_4-p-CO_2Me)I$  (4-CO<sub>2</sub>Me) in 89% and 86% yields, respectively.

Three of the four complexes were structurally characterized by X-ray analysis (Figures S16–S18, Supporting Information). A THF molecule was cocrystallized with **4-Me** to cause disorder of the whole molecule. All complexes showed a typical square-planar four-coordinate structure with a cis-chelate of the D<sup>t</sup>BPP ligand having a wide bite angle of around 98°.

Reactions of Bidentate Phosphine-Ligated Arylpalladium Halide Complexes with CsOH. Reaction of 4-NO<sub>2</sub> with an excess amount of solid cesium hydroxide in THF- $d_8$ was monitored by <sup>1</sup>H NMR spectroscopy (Scheme 4). Leaving the reaction mixture at room temperature for 3 h led to a complete consumption of 4-NO<sub>2</sub> and formation of cesium pnitrophenoxide 7-NO<sub>2</sub> and dinuclear palladium(0) complex 8. The <sup>1</sup>H NMR spectrum measured 1.5 h before the complete consumption of 4-NO<sub>2</sub> showed the formation of the thermally unstable arylpalladium hydroxide complex 5-NO2, characterized by NMR spectroscopy as a mixture of  $7-NO_2$  and 8 (see the Supporting Information). On comparison of the <sup>1</sup>H NMR spectrum of the mixture with those of the isolated  $4-NO_{2}$  7-NO<sub>2</sub>, and 8, characteristic signals for the *p*-nitrophenyl moiety and two distinct tBu groups were observed for 5-NO2. Gradual decomposition of 5-NO<sub>2</sub> to 7-NO<sub>2</sub> and 8 supported the notion that the  $C(sp^2)$ -OH bond-forming reductive elimination Scheme 4. Generation of Arylpalladium Hydroxide Complex 5-NO<sub>2</sub> and Subsequent Reactions



occurred from 5-NO<sub>2</sub>. The product 8 was independently synthesized and fully characterized, as illustrated in Scheme 5.<sup>13</sup>





Formation of phenoxide 7-NO<sub>2</sub> may come from a deprotonation of the reductively eliminated phenol 2-NO<sub>2</sub> by cesium hydroxide. The resulting D<sup>t</sup>BPP-ligated palladium(0) complex 6 may dimerize to form 8 in moderate yield. The addition of trifluoroacetic acid to the reaction mixture liberated *p*nitrophenol 2-NO<sub>2</sub> in high yield. Thus, it was difficult to isolate arylpalladium hydroxide complex 5-NO<sub>2</sub> probably due to the rapid  $C(sp^2)$ -OH bond-forming reductive elimination.

Treatment of the arylpalladium halide complexes 4-Me, 4- $CF_3$ , and 4- $CO_2Me$  with cesium hydroxide in THF enabled us to isolate the corresponding arylpalladium hydroxide complexes 5-Me, 5- $CF_3$ , and 5- $CO_2Me$  (Scheme 6). In the case of 5- $CF_3$ 





and **5-CO<sub>2</sub>Me**, addition of a catalytic amount of 18-crown-6 was effective for improvement of the yield. These complexes were fully characterized by NMR and IR spectroscopy and elemental analysis. Isolated arylpalladium hydroxide complexes showed two doublet <sup>31</sup>P signals accompanied by <sup>2</sup> $J_{PP}$  cis coupling, indicating an unsymmetrically coordinating bisphosphine moiety. The existence of the hydroxo ligand was confirmed by a treatment of their solutions with D<sub>2</sub>O to lead to

a disappearance of hydroxide proton in their <sup>1</sup>H NMR spectra and by an observation of a  $\nu_{OH}$  vibration (3422 cm<sup>-1</sup> for 5-Me, 3422 cm<sup>-1</sup> for 5-CF<sub>3</sub>, 3410 cm<sup>-1</sup> for 5-CO<sub>2</sub>Me) in their IR spectra.

Structures of isolated arylpalladium hydroxide complexes 5 were unambiguously characterized by X-ray crystallography (Figures 1–3). Hydrogen atoms of hydroxo ligands were



**Figure 1.** ORTEP drawing of **5-Me** (50% thermal ellipsoids). Hydrogen atoms, except the hydroxide proton, and one of the two independent molecules are omitted for clarity; R1 = 0.0386, GOF = 1.121. Selected bond distances (Å) and angles (deg)s: Pd1–C1, 2.046(3), 2.045(3); Pd1–O1, 2.046(2), 2.038(2); Pd1–P1, 2.2853(12), 2.2870(12); Pd1–P2, 2.4215(13), 2.4005(12); C1--O1, 2.707, 2.703; P1–Pd1–P2, 98.10(4), 98.10(4); C1–Pd1–O1, 82.82(12), 82.89(12); P1–Pd1–C1, 92.53(10), 93.34(10); P2–Pd1–O1, 86.58(8), 85.59(8).

placed by peaks in the differential Fourier maps. Each complex has no intermolecular hydrogen bond through the hydroxo ligand, probably due to the steric bulkiness of the D'BPP ligand. The hydroxo ligand is coplanar with the square plane of the central palladium atom. Bite angles of the D'BPP ligand were similar to those of the arylpalladium halide precursors 4. The C1–Pd1–O1 angles of 82–83° were slightly larger than the C–Pd–X (X = halogen) angles of arylpalladium halide precursors 4.

Thermolysis of Bidentate Phosphine-Ligated Arylpalladium Hydroxide Complexes. To observe the  $C(sp^2)$ -OH bond-forming reductive elimination, thermolysis of the arylpalladium hydroxide was examined. Heating 5-Me induced decomposition of the complex; however, no phenolic product was obtained. Instead, the reaction afforded the biaryl product 3-Me (36%; 18% of the *p*-tolyl group is included), the dinuclear complex 8 (92%), and a significant amount, at least five kinds, of unidentified compounds containing a *p*-tolyl group (Scheme 7).

Considering that the *p*-nitrophenylpalladium hydroxide **5**-**NO**<sub>2</sub> underwent rapid phenoxide formation and that heating **5**-**Me** did not give any phenolic product, one can expect that the  $C(sp^2)$ -OH bond-forming reductive elimination follows the tendency for other  $C(sp^2)$ -heteroatom bond-forming reductive eliminations, where the electron-poor aromatic ring



**Figure 2.** ORTEP drawing of **5-CF**<sub>3</sub> (50% thermal ellipsoids). Hydrogen atoms, except hydroxide proton, are omitted for clarity; R1 = 0.0271, GOF = 1.128. Selected bond distances (Å) and angles (deg): Pd1–C1, 2.044(2); Pd1–O1, 2.0698(16); Pd1–P1, 2.2927(7); Pd1–P2, 2.3998(8); C1--O1, 2.716; P1–Pd1–P2, 97.98(2); C1–Pd1–O1, 82.63(8); P1–Pd1–C1, 93.23(6); P2–Pd1–O1, 86.09(5).



Figure 3. ORTEP drawing of  $5 \cdot CO_2Me$  (50% thermal ellipsoids). Hydrogen atoms, except hydroxide proton, and the cocrystallized ether molecule are omitted for clarity; R1 = 0.0407, GOF = 1.087. Selected bond distances (Å) and angles (deg): Pd1–C1, 2.049(4); Pd1–O1, 2.042(3); Pd1–P1, 2.2782(16); Pd1–P2, 2.3911(17); C1--O1, 2.691; P1–Pd1–P2, 98.92(4); C1–Pd1–O1, 82.28(14); P1–Pd1– C1, 95.09(11); P2–Pd1–O1, 83.64(9).

accelerates the reaction.<sup>1,2</sup> Therefore, thermolysis of arylpalladium hydroxide bearing a moderately electron-poor aromatic ring was next examined to observe the  $C(sp^2)$ –OH bondforming reductive elimination.

Reaction of the arylpalladium hydroxide complex  $5\text{-}CF_3$  in THF- $d_8$  at 90 °C for 15 min gave a mixture of four species: namely, *p*-trifluoromethylphenol  $2\text{-}CF_3$ , dimeric palladium(0) complex **8**, arylpalladium aryloxide complex  $9\text{-}CF_3$ , and water (Scheme 8). A prolonged reaction time (60 min) allowed the









<sup>*a*</sup>Estimated from <sup>31</sup>P NMR spectrum. <sup>*b*</sup>Not detected.

consumption of all 5-CF<sub>3</sub> and conversion of 2-CF<sub>3</sub> to 9-CF<sub>3</sub>, indicating that 9-CF<sub>3</sub> may form by a condensation reaction between 5-CF<sub>3</sub> and 2-CF<sub>3</sub>. Observation of a gradual increase of the signal for water in <sup>1</sup>H NMR spectra also supported the condensation reaction. This is the first example for direct observation of the C(sp<sup>2</sup>)-OH bond-forming reductive elimination from Pd(II) species. The side product 9-CF<sub>3</sub> was independently synthesized and fully characterized (Scheme 9

### Scheme 9. Independent Synthesis of Arylpalladium Aryloxide Complex 9-CF<sub>3</sub>



and Figure 4). Thus, thermolysis of **5-CF**<sub>3</sub> in THF- $d_8$  contains two reactions, the C(sp<sup>2</sup>)-OH bond-forming reductive elimination and subsequent condensation.

On the other hand, thermolysis of  $5-CO_2Me$  in THF gave 8 and arylpalladium aryloxide complex  $9-CO_2Me$  with no appearance of the phenolic intermediate  $2-CO_2Me$  over the course of the reaction in the NMR probe (Scheme 10). The side product  $9-CO_2Me$  was independently synthesized and fully characterized (Scheme 11 and Figure 5). It was confirmed that  $5-CO_2Me$  could react with  $2-CO_2Me$  rapidly in THF at room temperature. Thus, similarly to the case of  $5-CF_3$ , heating



Figure 4. ORTEP drawing of  $9\text{-}CF_3$  (50% thermal ellipsoids). Hydrogen atoms and a minor part of the disordered fluorine atoms are omitted for clarity; R1 = 0.0333, GOF = 1.052. Selected bond distances (Å) and angles (deg): Pd1–C1, 2.040(4); Pd1–O1, 2.076(3); Pd1–P1, 2.2798(10); Pd1–P2, 2.4060(10); C1--O1, 2.795; P1–Pd1–P2, 99.15(3); C1–Pd1–O1, 85.54(16); P1–Pd1–C1, 93.60(13); P2–Pd1–O1, 82.05(9).

## Scheme 10. Thermal Decomposition of $5-CO_2Me$ (A = $CO_2Me$ )



Scheme 11. Independent Synthesis of 9-CO<sub>2</sub>Me



arylpalladium hydroxide complex **5-CO<sub>2</sub>Me** may induce the  $C(sp^2)$ -OH bond-forming reductive elimination, although the reaction could not be directly observed due to rapid condensation of the phenolic product with starting **5-CO<sub>2</sub>Me**. However, the invisibility of **2-CO<sub>2</sub>Me** enabled us to perform a kinetic analysis as follows.

Kinetic Studies on the  $C(sp^2)$ -OH Bond-Forming Reductive Elimination from 5-CO<sub>2</sub>Me. Based in Scheme 10, the following eqs 1-4 could be derived.

$$-\frac{d[\mathbf{5}]}{dt} = k_1[\mathbf{5}] + k_2[\mathbf{5}][\mathbf{2}]$$
(1)

$$-\frac{d[2]}{dt} = k_1[\mathbf{5}] - k_2[\mathbf{5}][\mathbf{2}]$$
(2)



Figure 5. ORTEP drawing of  $9-CO_2Me$  (50% thermal ellipsoids). Hydrogen atoms and the cocrystallized hexane molecule are omitted for clarity; R1 = 0.0748, GOF = 1.172) Selected bond distances (Å) and angles (deg): Pd1–C1, 2.037(6); Pd1–O1, 2.086(4); Pd1–P1, 2.2901(15); Pd1–P2, 2.4280(16); C1--O1, 2.796; P1–Pd1–P2, 98.21(5); C1–Pd1–O1, 85.4(2); P1–Pd1–C1, 90.60(16); P2–Pd1–O1, 85.12(12).

$$1 + 2$$

$$-\frac{d[\mathbf{5}]}{dt} = 2k_1[\mathbf{5}] - \frac{d[\mathbf{2}]}{dt}$$
(3)

$$k_{\rm obs} = 2k_{\rm l} \tag{4}$$

Taking advantage of the invisibility of 2-CO<sub>2</sub>Me during the reaction, a steady-state approximation for d[2]/dt = 0 was applied to eq 3. Under this condition, consumption of 5-CO<sub>2</sub>Me obeys a first-order rate equation with the rate constant  $k_{obs} = 2k_1$  (eq 4). The rate constants in C<sub>6</sub>D<sub>6</sub>, THF-d<sub>8</sub>, and DMF-d<sub>7</sub> at 60 °C were estimated by monitoring the consumption of starting complex 5-CO<sub>2</sub>Me in the <sup>1</sup>H NMR spectra with the use of 1,3,5-trimethoxybenzene as an internal standard. CD<sub>3</sub>CN could not be used, because a significant amount of unknown compounds having two doublets in the aromatic region was observed to interfere with the kinetic analysis. The consumption of 5-CO<sub>2</sub>Me obeyed first-order kinetics over 3 half-lives in all three cases. The obtained first-order rate constants  $k_1$  are summarized in Table 1. Solvent

Table 1. First-Order Rate Constants of  $k_1$  (60 °C) with Various Solvents and Their Relative Values for Reductive Elimination of Phenol 2-CO<sub>2</sub>Me from 5-CO<sub>2</sub>Me

$k_1 (s^{-1})$	$k_{ m rel}$
$(2.16 \pm 0.07) \times 10^4$	1
$(4.73 \pm 0.23) \times 10^4$	2.19
$(1.68 \pm 0.09) \times 10^3$	7.78
	$k_1 (s^{-1})$ (2.16 ± 0.07) × 10 <sup>4</sup> (4.73 ± 0.23) × 10 <sup>4</sup> (1.68 ± 0.09) × 10 <sup>3</sup>

effects on the reaction rate showed that more polar solvents accelerated the reductive elimination. Addition of the D<sup>t</sup>BPP ligand (3 equiv) to the C<sub>6</sub>D<sub>6</sub> solution of **5-CO<sub>2</sub>Me** did not change the reaction rate  $(2.08 \times 10^4 \text{ s}^{-1})$ , indicating there may be no associative pathway via a five-coordinate complex. On the other hand, treatment of **5-CO<sub>2</sub>Me** with CsOH·H<sub>2</sub>O at 60 °C for 3.5 h induced a formation of cesium *p*-methoxycarbonyl-phenoxide (**7-CO<sub>2</sub>Me**) in 66% yield after full conversion;

however, the rate constant in the presence of additional CsOH could not be estimated, due to the moderate yield of 7-**CO**<sub>2</sub>**Me**, reflecting the formation of a significant amount of unidentified byproducts and overlapping the signals of 7-**CO**<sub>2</sub>**Me** with the byproducts. Variable-temperature experiments ( $C_6D_6$ , 50–75 °C; THF- $d_8$ , 35–60 °C) afforded activation parameters of C(sp<sup>2</sup>)–OH bond-forming reductive elimination step via an Eyring plot (Figure 6, Table 2).



Figure 6. Eyring plot for reductive elimination of  $5\text{-}\mathrm{CO_2Me}$  in  $\mathrm{C_6D_6}$  or THF- $d_8$ .

Table 2. Activation Parameters  $\Delta H^{\ddagger}$  and  $\Delta S^{\ddagger}$  for Reductive Elimination of Phenol 2-CO<sub>2</sub>Me from 5-CO<sub>2</sub>Me

solvent	$\Delta H^{\ddagger}$ (kcal/mol)	$\Delta S^{\ddagger} \; (cal/(mol \; K))$
C <sub>6</sub> D <sub>6</sub>	$18.5 \pm 0.8$	$-19.9 \pm 2.5$
$THF-d_8$	$18.6 \pm 0.9$	$-18.0 \pm 3.0$

Mechanistic Considerations on the  $C(sp^2)$ -OH Bond-Forming Reductive Elimination from 5-CO<sub>2</sub>Me. Six possible reaction pathways for  $C(sp^2)$ -OH bond-forming reductive elimination are illustrated in Scheme 12. Path A

Scheme 12. Six Possible Pathways for  $C(sp^2)$ -OH Bond-Forming Reductive Elimination from 5-CO<sub>2</sub>Me (A =  $CO_2Me$ )



involves a partial dissociation of the D<sup>t</sup>BPP ligand and subsequent reductive elimination from the three-coordinate complex. Direct reductive elimination from four-coordinate species is shown as path B. Path C contains a formation of a separated ion pair by a reversible dissociation of the hydroxide ligand and subsequent outer-sphere ipso attack of hydroxide. A C-F bond-forming reductive elimination from the Pd(IV) complex (Scheme 13) was reported to involve a dissociation of

Scheme 13. C–F Bond-Forming Reductive Elimination from Pd(IV) Species via Dissociation of Chelate Ligand<sup>*a*</sup>



chelate ligand with a positive entropy of activation  $(12.4 \pm 1.3 \text{ cal/(mol K)})$ .<sup>14</sup> Our observation of a negative entropy of activation could argue against path A having a similar dissociative pathway. On the other hand, ionic path C may also be excluded by the observed negatively large entropy of activation by comparison to the literature as follows. (1) Reductive elimination of iodomethane from a Pt(IV) complex having a diphosphine ligand was induced by the dissociation of iodide followed by an outer-sphere attack of I<sup>-</sup> at the Pt-bound methyl group in an S<sub>N</sub>2 fashion (Scheme 14a).<sup>15</sup> The reported

#### Scheme 14. Reported Mechanisms for Reductive Elimination Involving Dissociation of the Anionic Ligand and Its Attack from the Outer Sphere

(a) dissociation, then reductive elimination
 via associative TS (∠S<sup>‡</sup> = −2.9±0.2 cal/mol•K)

$$\begin{pmatrix} \mathsf{P} \\ \mathsf{P} \\ \mathsf{P} \\ \mathsf{H} \\ \mathsf{H}$$

(b) dissociation, then C-O bond-forming reductive elimination via associative TS (C<sub>6</sub>D<sub>6</sub> and THF-d<sub>8</sub> showed no difference in rate)

$$( \begin{array}{c} Me \\ P \\ P \\ I \\ OAr \end{array} \begin{array}{c} Me \\ P \\ OAr \end{array} \left( \begin{array}{c} P \\ P \\ P \\ OAr \end{array} \right) \begin{array}{c} Me \\ P \\ OAr \end{array} \left( \begin{array}{c} P \\ P \\ P \\ OAr \end{array} \right) \begin{array}{c} Me \\ P \\ OAr \end{array} \left( \begin{array}{c} P \\ P \\ OAr \end{array} \right) \left( \begin{array}{c} P \\ P \\ OAr \end{array} \right) \left( \begin{array}{c} P \\ P \\ OAr \end{array} \right) \left( \begin{array}{c} P \\ P \\ OAr \end{array} \right) \left( \begin{array}{c} P \\ P \\ OAr \end{array} \right) \left( \begin{array}{c} P \\ OAr \end{array} \right) \left( \begin{array}{c}$$

near-zero entropy value  $(-2.9 \pm 0.2 \text{ cal/(mol K)})$  was explained by a cancellation of positive entropy for dissociation of I<sup>-</sup> and negative entropy for association of I<sup>-</sup> to construct a C–I bond. (2) The reported CH<sub>3</sub>–OAr bond-forming reductive elimination from a Pt(IV) complex was also shown to have the same mechanism, where C<sub>6</sub>D<sub>6</sub> and THF-*d*<sub>8</sub> afforded similar reaction rates (Scheme 14b).<sup>8b</sup> The obtained data in the present study showed a large negative entropy of activation and the acceleration of the reaction by the use of more polar solvents (THF-*d*<sub>8</sub>, *k*<sub>rel</sub> = 2.19; DMF-*d*<sub>7</sub>, *k*<sub>rel</sub> = 7.78), indicating dissociative path C may be unlikely. Path D involves ligand exchange to form the dimeric Pd(II) species **10** with a bridging D'BPP ligand. However, first-order kinetics for the consumption of **5-CO<sub>2</sub>Me** and the trans regiochemistry of the phosphine ligand, not appropriate for reductive elimination, would argue against this mechanism. The remaining two mechanisms are induced by a homolytic cleavage of the Pd–Ar (path E) or Pd–OH bond (path F). However, previously calculated bond dissociation energies (BDE) of Pd–C (39 kcal/mol)<sup>16</sup> and Pd–OH (45 kcal/mol)<sup>17</sup> bond are larger than the experimentally obtained  $\Delta H^{\ddagger}$  values for C(sp<sup>2</sup>)–OH bond-forming reductive elimination (18–19 kcal/mol) in this study. Thus, path B is the most probable mechanism for C(sp<sup>2</sup>)–OH bond-forming reductive elimination.

The electronic character for the transition state in path B was estimated as follows. One can imagine that the concerted path B has a neutral or charged transition state with a strong interaction between carbon and oxygen atoms, as illustrated in Figure 7. A neutral TS such as that in Figure 7a is sometimes



Figure 7. Possible characters of the transition state for path B.

assumed for C-C bond-forming reductive elimination.<sup>1</sup> However, the present  $C(sp^2)$ -OH bond-forming reductive elimination may involve a charged TS because of the difference in electronegativity between carbon and oxygen atoms. Acceleration by more polar solvents also supports the existence of a charged TS. We can expect two types of structures for the charged TS. One has a three-centered structure with a positively charged oxygen atom (Figure 7b), and the other has an opened structure without a Pd-O bond (Figure 7c), where the palladium atom is cationic. The latter corresponds to a model for  $C(sp^2)$ -OR bond-forming reductive elimination suggested by Widenhoefer and Buchwald.<sup>5b,c</sup> Since both of them have a delocalized negative charge over the aromatic ring, solvent molecules may have interactions with these charged TSs. Considering the delocalization of negative charge, a basic solvent or aromatic solvent may interact with the positively charged hydroxo ligand on the palladium atom through hydrogen bonding or an OH--- $\pi$  interaction<sup>18</sup> because of their localized charge density. If we could imagine a strong interaction between the charged TS and solvents to provide a large negative entropy of activation, as discussed for C-Cbond-forming reductive elimination from a Pt(IV) complex (Figure 8a),<sup>19</sup> solvent ordering may occur with a three-centered structure due to the presence of a hydrogen donor hydroxide ligand (Figure 8b). Therefore, we have decided to examine DFT calculations to clarify the nature of the charged TS.

Theoretical Studies on the  $C(sp^2)$ –OH Bond-Forming Reductive Elimination from 5-CO<sub>2</sub>Me. The arylpalladium hydroxide 5-CO<sub>2</sub>Me or its solvates were optimized by B3LYP//LanL2DZ/6-31G\* with IEFPCM solvation model with C<sub>6</sub>H<sub>6</sub>, THF, or DMF solvent (Figure 9). The obtained ground-state structure of 5-CO<sub>2</sub>Me without solvent could reproduce the crystal structure, where the hydroxo ligand was coplanar with the square plane of palladium. Addition of one THF or DMF molecule to 5-CO<sub>2</sub>Me led to a formation of a hydrogen bond between the proton of the hydroxo ligand and the oxygen atom of the solvent molecule; however, addition of



**Figure 8.** Models for solvent ordering with polar TS to induce a large negative entropy of activation (s =solvent).



**Figure 9.** Calculated structures of ground, transition, and product states ( $Pd = (D^{t}BPP-Pd)$ ,  $A = CO_{2}Me$ ), their free energy changes, and activation parameters  $\Delta H^{\ddagger}$  and  $\Delta S^{\ddagger}$  for C–OH reductive elimination from **5-CO\_2Me** without solvent (black), with THF (blue), and with DMF (red) using the B3LYP method with the LanL2DZ/6-31G\* basis set and the solvation model of IEFPCM ( $C_6H_6$  (black), THF (blue), or DMF (red)).

a  $C_6H_6$  molecule did not give any stable structure with a OH- - -  $\pi$  interaction. All obtained transition states show a close contact between the hydroxo ligand and the palladium-bonded carbon

atom (~1.8 Å), supporting the three-centered TS. This C-O contact corresponds to a vibration possessing an imaginary frequency in each transition state. The Pd-O bond in the transition state (2.13-2.14 Å) was slightly elongated, compared to that ( $\sim 2.05$  Å) in the ground state. In the transition states, the hydroxo ligand was rotated along with the Pd-O bond, in comparison to the ground state, as suggested by changes in dihedral angles of  $C(sp^2)$ -Pd-O-H (<5° for ground states;  $>97^{\circ}$  for TSs). The structure of the product obtained without solvent had an interaction between the Pd(0) center of 6 and the phenolic proton of 2-CO<sub>2</sub>Me. In the presence of THF or DMF, the Pd(0) center of 6 interacted with the  $\alpha$ -proton of THF or the N-methyl proton of DMF, together with a hydrogen bond from the oxygen atom of the solvent molecule to the phenolic proton of 2-CO<sub>2</sub>Me. A diagram of the relative free energies without or with solvent showed that transition states were more stabilized by a hydrogen bond between the hydroxo ligand and the polar solvent molecule. Because the hydroxo ligand can easily interact with solvent molecules, absolute values of activation entropy were larger than those obtained from  $C(sp^2)$ -OR (R = CH<sub>2</sub>CMe<sub>3</sub>) bond-forming reductive elimination from an arylpalladium neopentoxide complex  $(-9.3 \pm 0.3 \text{ cal/(mol K)})^{.55}$  The smaller calculated  $\Delta H^{\ddagger}$  values with more polar solvents and the order of  $\Delta H^{\ddagger}$ values reflected the order of rate constant for each solvent. The reason for the discrepancy between experimental and calculated  $\Delta H^{\ddagger}$  values may come from the lack of a C<sub>6</sub>H<sub>6</sub> molecule affording a weak OH--- $\pi$  interaction in the calculation. Similarly, calculated  $\Delta S^{\ddagger}$  values did not match with experimental values probably because only one solvent molecule was considered, while large numbers of solvent molecules should be involved in the real solution.

The rotation of the hydroxo ligand to construct the TS can be explained as an orbital interaction (Figure 10). In the



Figure 10. HOMO and LUMO of 5-CO2Me and HOMO-9 of TSwo.

ground state of 5-CO2Me, where the hydroxo ligand was coplanar with the square plane of the palladium atom, the 2p orbital of the oxygen atom was found in the HOMO to interact with a d orbital of the central palladium. On the other hand, the LUMO has the character as a  $\pi^*$  orbital of the aromatic ring. In the transition state TS, the hydroxo ligand was orthogonal to the square plane of the palladium. An interaction between the 2p orbital of oxygen and the  $\pi^*$  orbital was found in HOMO-9 of the TS. On the basis of the above observations, it is indicated that the C(sp<sup>2</sup>)-OH bond-forming reductive elimination has the character of a nucleophilic attack of the hydroxo ligand at the aryl ligand. This is in agreement with the reactivity of 5, that an aryl ligand with an electron-withdrawing group accelerates reductive elimination (5-NO<sub>2</sub> > 5-CO<sub>2</sub>Me, 5-CF<sub>3</sub>  $\gg$  5-Me), which is also reported for other  $C(sp^2)$ -heteroatom bondforming reductive eliminations.<sup>2</sup>

#### CONCLUSION

The decomposition of arylpalladium hydroxide complexes gave the corresponding phenolic products, which may form through a  $C(sp^2)$ -OH bond-forming reductive elimination, either by treatment of arylpalladium halide complexes with cesium hydroxide or by heating arylpalladium hydroxide complexes. Treatment of nitrophenylpalladium iodide 1, possessing a <sup>t</sup>BuXPhos ligand with cesium hydroxide, formed a mixture of nitorophenol 2-NO<sub>2</sub> and 4,4'-dinitrobiphenyl 3. The reaction of D<sup>t</sup>BPP-ligated nitrophenylpalladium iodide 4-NO<sub>2</sub> with cesium hydroxide gave a mixture of arylpalladium hydroxide complex 5-NO<sub>2</sub>, cesium phenoxide 7-NO<sub>2</sub>, and dinuclear Pd(0)complex 8. Gradual decomposition of 5-NO2 to 7-NO2 and 8 suggested that the  $C(sp^2)$ -OH bond-forming reductive elimination took place from 5-NO2. Heating p-tolylpalladium hydroxide 5-Me gave no phenolic product. Thermolysis of the trifluoromethyl-substituted arylpalladium hydroxide 5-CF<sub>3</sub> enabled us to observe phenol 2-CF3 directly. In the case of ester-substituted hydroxide complex 5-CO<sub>2</sub>Me, no formation of phenol 2-CO<sub>2</sub>Me was observed. However, the invisibility of 2-CO<sub>2</sub>Me enabled us to establish the kinetic equation with a steady-state approximation to estimate the rate constant  $k_1$  for reductive elimination. The kinetic study showed that polar solvents such as THF and DMF accelerate the reductive elimination and there is a large negative entropy of activation. Comparison of these results with those in the literature suggested the direct pathway B and charged transition state to induce the solvent ordering for the  $C(sp^2)$ -OH bond-forming reductive elimination. DFT calculations also predicted the hydrogen bond between the hydroxo ligand and solvent molecule to stabilize the transition state. An analysis of molecular orbitals also suggested that the character of this process was nucleophilic attack of hydroxide ligand at the ipso carbon of the aryl ligand. Knowledge from this study on the acceleration of  $C(sp^2)$ -OH bond-forming reductive eliminations by polar solvents may inspire establishment of a new strategy for a challenging reaction containing the formation of carbon-hydroxide bonds.

#### ASSOCIATED CONTENT

#### **S** Supporting Information

Text, figures, tables, and CIF files giving details for all experimental, computational, and crystal structure studies. 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.

#### ACKNOWLEDGMENTS

This work was supported by the Funding Program for Next Generation World-Leading Researchers, Green Innovation from the JSPS and KAKENHI (No. 23105510) from MEXT of Japan. The computations were performed by the Research Center for Computational Science, Okazaki, Japan.

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