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Preparation and C−X Reductive Elimination Reactivity of Monoaryl Pd^{IV}−X Complexes in Water (X = OH, OH$_2$, Cl, Br)

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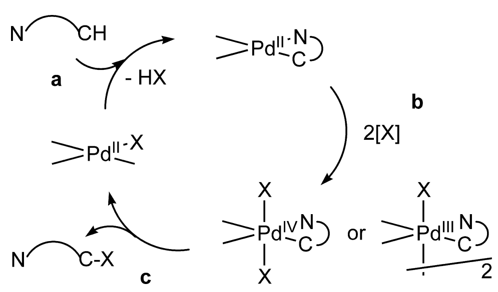
Abstract: Monohydrocarbyl palladium(IV) complexes bearing OH, OH$_2$, Br, and Cl ligands at the metal and supported by facially chelating 1-hydroxy-1,1-bis(2-pyridyl)methoxide were readily prepared in water at 0 °C. These complexes reductively eliminate Ar−X (X = OH, Br, Cl) in water at room temperature in high yield, and the corresponding first-order rate constants k_{OH}, k_{Cl}, and k_{Br} are on the same order of magnitude.

High-valent organopalladium complexes were introduced into organometallic chemistry about 30 years ago[1] and have recently received much attention as intermediates in a variety of Pd-catalyzed oxidative functionalization reactions.[2−7] Hydrocarbyls of Pd^{IV} and/or Pd^{III} have been proposed as key intermediates in oxidative Pd-catalyzed ligand-directed C−H functionalization (Scheme 1),[6−9] olefin difunctionalization,[3,4] heterocyclization,[10] and others.[7] Many of these processes exploit the remarkable ability of high-valent palladium hydrocarbyls to undergo facile C−Y bond reductive elimination (e.g., see Scheme 1, step **c**; Y = C, N, O, halogen, etc.). Synthesis and C−Y bond elimination reactivity studies of a number of model tri- and dihydrocarbyl Pd^{IV} complexes have been reported.[7,11−13] At the same time, Pd^{IV} monohydrocarbyls remain elusive, and their reactivity is poorly known. In particular, it is unknown whether Pd^{IV} monohydrocarbyls can be generated in water,[13] a solvent of choice for "green" chemistry. Few Pd^{IV} monohydrocarbyls have been isolated to date[14−17] (Scheme 2). C−F and C−Cl bond reductive elimination reactivity in organic solvents has been reported for some of these complexes.

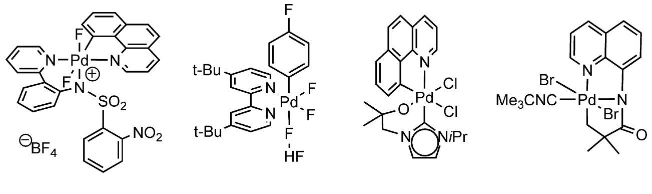
We disclose here a simple protocol for the preparation in aqueous solution of a number of cationic and neutral zwitterionic monoaryl palladium(IV) complexes supported by 1-hydroxy-1,1-bis(2-pyridyl)methoxide (L)[18] (Scheme 3) with various ligands X = OH, OH$_2$, Cl, Br, or OC(OH)(2-pyridyl)(2-phenylene) at the metal. We also report some results from studies of their reactivity, including C−O, C−Cl, and C−Br bond-forming reactions. These results may be important for development of Pd^{II}/Pd^{IV}-mediated C−H functionalization chemistry in aqueous media.

We first targeted the more stabilized[19] cationic monohydrocarbyl Pd^{IV} complexes **3** and **4** having two facially chelating 1-hydroxymethoxide ligands: L derived from di-2-pyridyl ketone (dpk) and L′ derived from 2-aroylpyridine (aroyl = benzoyl or 3-methylbenzoyl) (Scheme 3). Both L and L′ were expected to provide better support for a M^{IV} center than analogous sulfonate ligands L″ (Scheme 3) used in our previous works,[19] which feature the poorer O-donor sulfonate group. Complexes **3** and **4** were prepared using 2 mM aqueous solutions of ionic Pd^{II}−2-aroylpyridine adducts **1**(OAc) and **2**(OAc), respectively, and 2 equiv of hydrogen peroxide as an oxidant (Scheme 3, step **a**). In both cases, a dark-yellow color typical of **3** and **4** developed. Both reactions were quantitative, according to NMR spectroscopy. The oxidation was faster for the methyl-substituted analogue **2**(OAc),[20] where the transformation was complete in 30 min at room temperature. The cations **3** and **4** are stable in neutral aqueous solutions for an indefinitely long time and were characterized by means of ^{1}H and ^{13}C NMR spectroscopy, selective nuclear Overhauser effect (NOE) experiments, and electrospray ionization mass spectrometry (ESI-MS). Complex **3**(OAc) was also characterized by X-ray diffraction (XRD) (Figure 1a).

Scheme 1

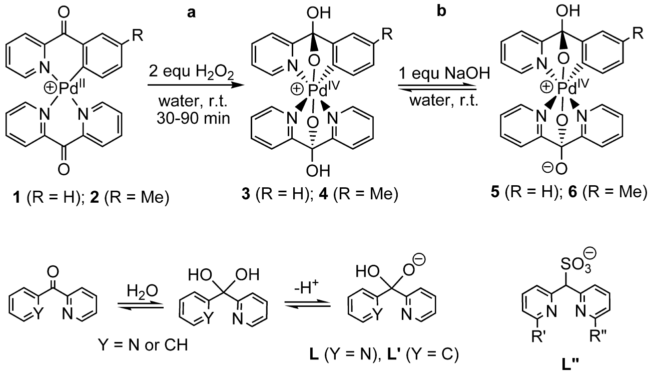


Scheme 2



The use of acetate as the counterion imparted relatively high solubility in water to these and similar Pd(IV) complexes, but their isolation and purification were greatly facilitated by precipitation of cations **3** and **4** in the form of the corresponding less soluble tetrafluoroborate or trifluoroacetate salts **3**(Z) and **4**(Z) (Z = BF$_4$, CF$_3$COO). These BF$_4$ and CF$_3$COO salts are stable in the solid state and could be characterized by elemental analysis. In contrast, the acetates decompose readily in the solid phase and in aprotic polar solvents such as dimethyl sulfoxide. This reactivity may be

Scheme 3



10.1021/ja107185w

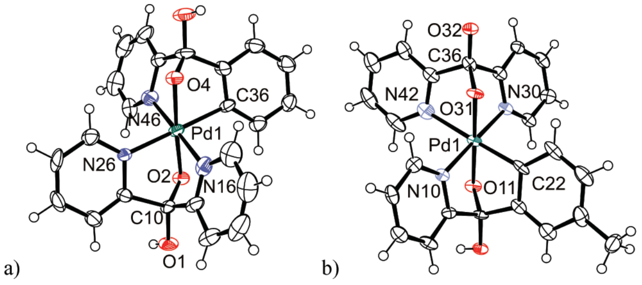


Figure 1. ORTEP drawings (50% probability ellipsoids) of (a) cation **3** in **3**(OAc)·MeOH and (b) complex **6**.

attributed in part to the presence in these salts of the relatively basic acetate counterion and acidic hydroxo groups of the ligands L and L′ (e.g., cation **3** has $pK_{a1} = 8.15 \pm 0.02$).

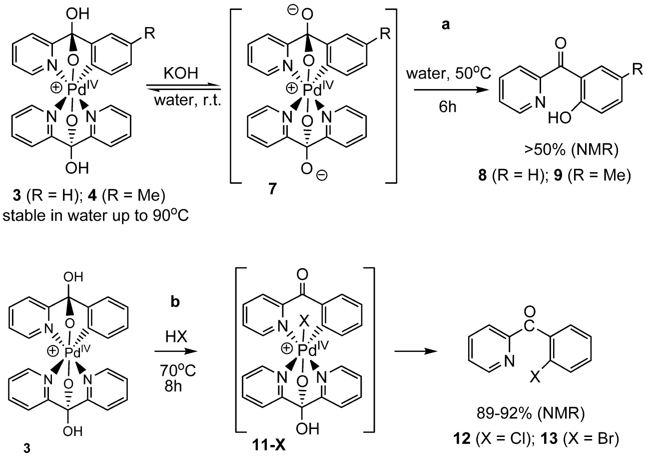
Reactions of **3** and **4** with 1 equiv of NaOH in water led to the formation of yellow precipitates of the poorly water-soluble neutral zwitterionic monoaryl Pd^{IV} complexes **5** and **6**, respectively (Scheme 3, step **b**), and full characterization of these complexes, including single-crystal XRD (Figure 1b), was performed.

Both **5** and **6** dissolve in the presence of 1 equiv of aqueous alkali metal hydroxide to form clear solutions that can eliminate phenols **8** and **9**, respectively (Scheme 4, step **a**). In particular, the phenolate derived from **8** was formed in 53% yield[21] after 6 h at 50 °C; the reaction rate followed first-order kinetics with an observed first-order rate constant $k = (2.04 \pm 0.02) \times 10^{-4}\ s^{-1}$ at 50 °C. The observed rate constant was virtually independent of the excess amount of base present in the solution, suggesting the involvement of the same predominant anionic species such as **7** (Scheme 4, step **a**) in the C−O bond elimination step.

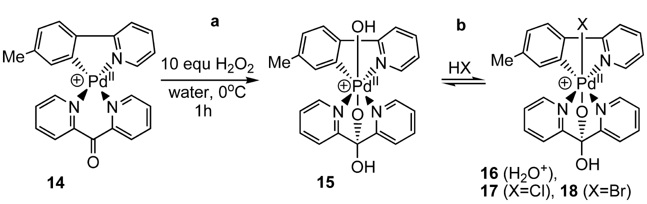
Though **3**($OOCCF_3$) is stable in neutral aqueous solutions up to ~90 °C, in neat acetic acid it formed phenol **8** and the corresponding arylacetate **10** in an ~1:2 ratio. The combined NMR yield of **8** and **10** was 94% after 4 h at 50 °C. The reaction exhibited clean first-order kinetics over the temperature range 20−70 °C with the following activation parameters: $\Delta H^{\ddagger} = 23.4 \pm 0.2$ kcal/mol and $\Delta S^{\ddagger} = -6 \pm 6$ cal $mol^{-1}\ K^{-1}$.

The reductive elimination of C−Y bonds (Y = Cl, Br) was also efficient in aqueous solutions of **3**($OOCCF_3$) containing 20 equiv of HCl or HBr at 70 °C. The corresponding aryl halides **12** and **13** were produced in 89−92% yield after 8 h (Scheme 4, **b**). Formation of **12** and **13** presumably proceeds via the intermediacy of corresponding Pd^{IV}−X complexes such as **11-X** in Scheme 4, step **b**, which were detected in the reaction mixtures using ^1H NMR spectroscopy and ESI-MS.

Scheme 4



Scheme 5



The reactivity pattern that was observed for complexes **3** and **4** helped us design and accomplish the synthesis of the more reactive monoaryl Pd^{IV} complexes **15**−**18** possessing only one facially chelating ligand L. The monoaryl hydroxo Pd^{IV} complex **15**(OAc) could be generated quantitatively from palladacycle **14**(OAc) in aqueous solutions at 0 °C using 10 equiv of H_2O_2 (Scheme 5, step **a**). The complex was characterized in the same solvent by means of ^1H and ^{13}C NMR spectroscopy, NOE experiments, and ESI-MS. An attempt to isolate **15** from these solutions as a trifluoroacetate salt in the presence of excess CF_3COOH led instead to the poorly soluble dicationic monoaryl Pd^{IV} *aqua* complex **16** (Scheme 5, step **b**; X = H_2O^+) which was fully characterized by means of NMR spectroscopy, ESI-MS, elemental analysis, and single-crystal XRD (Figure 2a).

Similar low solubilities in cold water were observed for the dichloride **16**$(Cl)_2$ and dibromide **16**$(Br)_2$ derived from the same monoaryl Pd^{IV} *aqua* dication **16**, which were isolated upon addition of excess HCl or HBr to aqueous **15**(OAc) at 0 °C. The aqua ligand in **16** can be readily substituted with the halide anions. In particular, upon careful drying under vacuum, the aqua complexes **16**$(Cl)_2$ and **16**$(Br)_2$ were cleanly converted into the monoaryl chloro and bromo Pd^{IV} derivatives **17**(Cl) and **18**(Br), respectively (Scheme 5). The latter two compounds were characterized by ^1H NMR spectroscopy, NOE studies, ESI-MS, and, in the case of **18**(Br),[22] elemental analysis. Importantly, all three substances **16**$(Z)_2$ (Z = $OOCCF_3$, Cl, Br) exhibited identical ^1H NMR and ESI-MS spectra in water that are distinct from those of **17**(Cl) and **18**(Br). Independent syntheses of the monoaryl chloro and bromo Pd^{IV} complexes **17** and **18** could be accomplished by reacting **14**(OAc) with *N*-chloro- and *N*-bromosuccinimide, respectively, in water at 0 °C.

The higher reactivity of complexes **15**−**18** in C−X reductive elimination in comparison with **3**−**6** is illustrated in Scheme 6. The C−O bond reductive elimination reaction of cation **15** leading to virtually quantitative formation of aryloxide **17** (see the X-ray structure in Figure 2b) occurred even at room temperature in water. The reaction followed first-order kinetics with rate constant $k_{OH} = (2.52 \pm 0.03) \times 10^{-5}\ s^{-1}$ at 22 °C (Scheme 6, step **a**). Interestingly, addition of 5 equiv of pyridine did not inhibit the reaction.[23] The corresponding phenol, 2-(2-hydroxy-4-methylphenyl)pyridine, could be isolated in pure form upon treatment of aqueous solutions of **19**(OAc) with excess CF_3COOH. C−O reductive elimination of arylacetates from some Pd^{IV} *diaryl* dicarboxylate complexes was studied previously, and a conclusion was made that five-coordinate

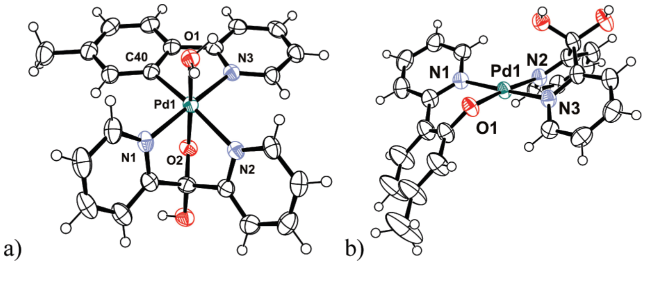
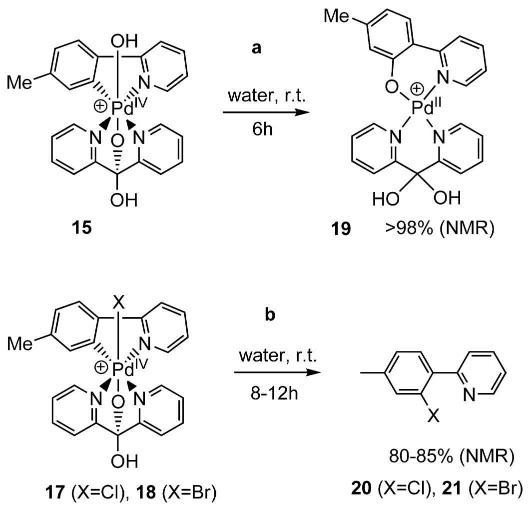


Figure 2. ORTEP drawings (50% probability ellipsoids) of (a) dication **16** in **16**$(OOCCF_3)_2$·H_2O and (b) Pd^{II} aryloxide cation **19** in **19**(OAc).

Scheme 6

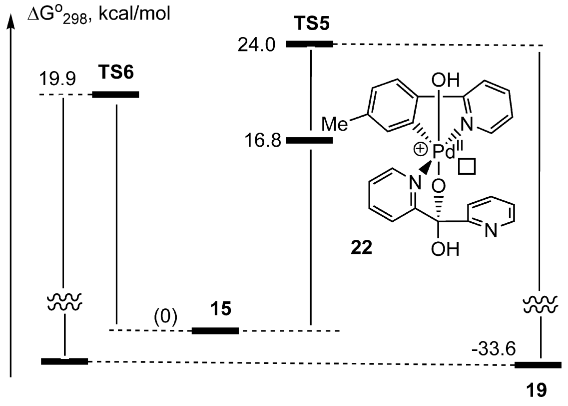


Pd^{IV} intermediates are most likely involved in the reaction.[24] While a more detailed study of the C$-$X elimination reactions reported here is required in order to explore their mechanisms, some comment can be made now. The absence of inhibition of step **a** in Scheme 6 by pyridine is consistent with C$-$O reductive elimination directly from the starting six-coordinate Pd^{IV} complex **15.** This reaction path involving the "six-coordinate" transition state **TS6** was studied by us computationally using density functional theory (Scheme 7; all data shown are for the gas-phase reactions; the same trend was seen when aqueous solutions were modeled[20]). In **TS6**, the pyridyl nitrogen atom trans to the aryl carbon is only partially dissociated, with a Pd$-$N distance of 2.518 Å (vs 2.239 Å in **15**). Another reaction pathway via five-coordinate Pd^{IV} intermediate **22** and transition state **TS5** was also analyzed. According to these results, the latter pathway is less competitive than the direct mechanism via **TS6**.

Elimination of aryl halides **20** and **21** from halogeno Pd^{IV} complexes **17**(Cl) and **18**(Br), respectively, was also facile at room temperature (Scheme 6, step **b**). These products formed in 90$-$95% NMR yield after 12$-$38 h. The first-order rate constants for the C$-$X elimination step at 22 °C could be estimated from our kinetics modeling performed for these reactions as $k_{\mathrm{Br}} = (2.50 \pm 0.10) \times 10^{-5}\ \mathrm{s}^{-1}$ and $k_{\mathrm{Cl}} = (1.60 \pm 0.05) \times 10^{-5}\ \mathrm{s}^{-1}$. Surprisingly, both rate constants are on the same order of magnitude as k_{OH}. The aryl halides ArX could also be produced in 51$-$59% yield along with 31$-$37% ArOH by heating aqueous solutions of **15**(OAc) and 10 equiv of the corresponding HX at 70 °C.

Finally, the possibility of developing a mild Pd-catalyzed aromatic C$-$H hydroxylation utilizing H_2O_2 as the oxidant and facially chelating ligands for tuning reactivity of the metal was demonstrated. Though the oxidation of the dpk-supported complex **14** to give **15** can be fast enough (Scheme 5, step **a**), the C$-$O reductive elimination from **15** is slow (Scheme 6). Therefore, we used the sulfonate ligand L″ (Scheme 3, R′ = R″ = Me) to enhance the reactivity[19] of the expected high-valent metal intermediates. The reaction between 2-*p*-tolylpyridine and 8 equiv of 30% aqueous H_2O_2 was performed in AcOH solvent in the presence of 10% $Pd(OAc)_2$ and L″ or dpk at 35 °C. Formation of 2-(2-hydroxy-4-methylphenyl)pyridine as the only reaction product was observed after 7 h in yields of 61% (L″), 19% (no ligand), and 10% (dpk), respectively, according to ^{1}H NMR spectroscopy.

Scheme 7



In summary, we have developed a procedure for the preparation of monohydrocarbyl Pd^{IV} complexes from the corresponding monoaryl Pd^{II} precursors in water using H_2O_2 as an oxidant, and we have fully characterized a series of compounds with alkoxide, OH, OH_2, Cl, and Br ligands at the Pd^{IV} center. The C$-$Y (Y = O, Br, Cl) bond reductive elimination reactions from these species have also been documented. These include the first C$-$Br and C$-$O bond reductive eliminations from isolated monohydrocarbyl Pd^{IV} complexes. We also demonstrated the possibility of Pd-catalyzed C$-$H oxidative functionalization with H_2O_2 in the presence of a facially chelating bis(2-pyridyl)methanesulfonate ligand. A much greater variety of monohydrocarbyl Pd^{IV} complexes may be accessible using the approach described here. Studies of its substrate scope, the C$-$X reductive elimination reactivity of complexes of this class, and applications in catalysis involving C$-$H bond breaking and C$-$Y bond making in aqueous media are currently underway in our lab.

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Supporting Information Available: Experimental details; CIF files for **3**(OAc), **5**, **6**, **16**($OOCCF_3$)$_2$, and **19**(OAc); and computational details. This material is available free of charge via the Internet at http://pubs.acs.org.

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(20) See the Supporting Information for details.
(21) Another product of this reaction was the cyclopalladated 2-benzoylpyridine complex supported by 2-picolinate, which was formed in 33% yield.
(22) Solid **17**(Cl) was too unstable for such characterization.
(23) The first-order rate constant $k_{\mathrm{OH,py}}$ measured in the presence of 5 equiv of pyridine was $(4.02 \pm 0.04) \times 10^{-5}\ \mathrm{s}^{-1}$ at 22 °C.
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