

Reductive Elimination of Ether from T-Shaped, Monomeric Arylpalladium Alkoxides**

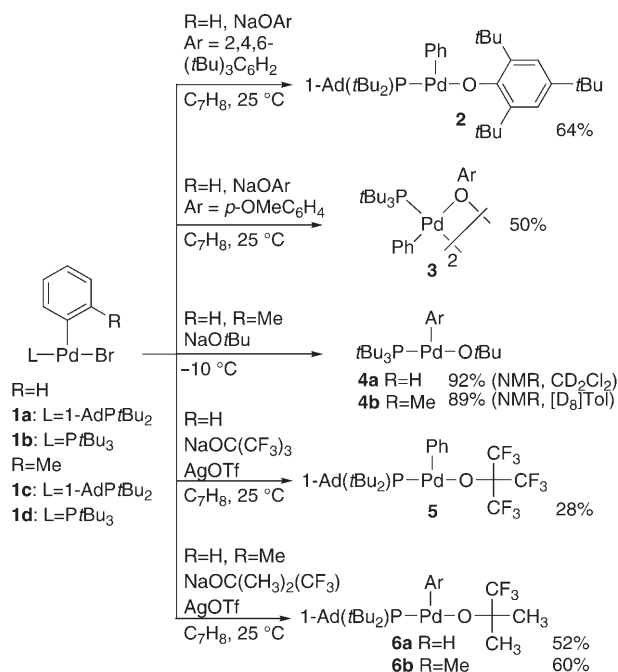
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Reductive elimination of ethers from organopalladium alkoxides is the C–O bond-forming step of the palladium-catalyzed etherification of aryl halides.^[1] At this time, examples of the reductive eliminations of ethers from isolated organopalladium alkoxide complexes are limited. Only reductive eliminations of alkyl aryl ethers from complexes generated in situ, reductive elimination of an oxygen heterocycle from a single oxapalladacycle,^[2] reductive eliminations from arylpalladium alkoxides containing activating groups on the aryl ring,^[3,4] and reductive eliminations of biaryl ethers in low yield from isolated complexes^[5,6] are documented. Most importantly, the most active catalysts for the palladium-catalyzed etherification of aryl halides contain sterically hindered monophosphines,^[1,6–15] and no reductive eliminations from arylpalladium alkoxides containing hindered monophosphines have been described.

We report reductive eliminations from isolated and structurally characterized examples of such arylpalladium alkoxides. We show that reductive eliminations occur from the observed species containing one aryl, one alkoxide, and one phosphine ligand. The structures of the reactive complexes match those of proposed intermediates in the catalytic etherifications,^[1] and the rate of their eliminations of ethers can be compared to those from related amido complexes.^[16]

The synthesis of arylpalladium alkoxide complexes ligated by PrBu_3 or 1- AdPrBu_2 (1- Ad = 1-adamantyl) is summarized in Scheme 1. Reaction of the hindered sodium 2,4,6-tri-*tert*-butylphenoxide with [(1- AdPrBu_2)Pd(Ph)(Br)] (**1a**) formed phenoxide complex **2** in 64% yield. This complex was crystallized from pentane and was characterized by standard spectroscopic methods and X-ray diffraction (see below).

Reaction of [(PrBu_3)Pd(Ph)(Br)] (**1b**)^[17,18] with NaOAr (Ar = C_6H_4 -4-OMe) formed the dimeric phenoxide complex [(PrBu_3)Pd(Ph)(OAr)]₂ (**3**) in 50% yield. The connectivity of this complex in the solid state was determined by X-ray diffraction, and this dinuclear structure appeared to be preserved in solution, at least at low temperatures. Solutions



Scheme 1.

of [(PrBu_3)Pd(*o*-tol)(OAr)]₂ and [(PrBu_3)Pd(Ph)(OAr)]₂ (6.25 mM) alone generated singlet ³¹P NMR resonances at –60 °C. A mixture of the two compounds at –60 °C generated four resonances, one for each homodimer and two that most likely correspond to the inequivalent PrBu_3 ligands in the heterodimer [(PrBu_3)Pd(Ph)Pd(OAr)]₂[(PrBu_3)Pd(*o*-Tol)(PrBu_3)]₂.^[19]

Reaction of [(PrBu_3)Pd(Ar)(Br)] (Ar = Ph **1b**, Ar = *o*-tol **1d**)^[17,18] with NaOtBu at –10 °C generated [(PrBu_3)Pd(Ar)(OtBu)] (Ar = Ph **4a**, Ar = *o*-Tol **4b**) in 92% and 89% yields, as determined by NMR spectroscopy with an internal standard. We could not isolate these complexes because they reacted at 0–25 °C (see below). Thus, **4a** and **4b** were characterized by low-temperature ¹H and ¹³C NMR spectroscopy (see Supporting Information).

To generate more stable alkoxide analogues of **4a** and **4b**, we treated **1** with fully and partially fluorinated versions of NaOtBu. Reaction of [(1- AdPrBu_2)Pd(Ar)(Br)] (Ar = Ph **1a**, Ar = *o*-tol **1c**)^[17,18] with the perfluoro *tert*-butoxide NaOC(CF₃)₃ or the trifluoro *tert*-butoxide NaOC(CH₃)₂CF₃, and subsequent AgOTf, generated [(1- AdPrBu_2)Pd(Ph)(OC(CF₃)₃)] (**5**) and [(1- AdPrBu_2)Pd(Ar)(OC(CH₃)₂CF₃)] (**6a,b**) cleanly, and these complexes were isolated in 28%, 52%, and 60% yields. Complexes **5** and **6a,b** were characterized by spectroscopic and microanalytical methods, and complexes **6a** and **6b** were characterized by X-ray crystallography.

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ORTEP diagrams of aryloxide **2** and trifluoro-*tert*-butoxide **6a** are shown in Figures 1 and 2. Both complexes are T-shaped monomers. An ORTEP drawing of **6b** is provided in the Supporting Information. Each complex contains an

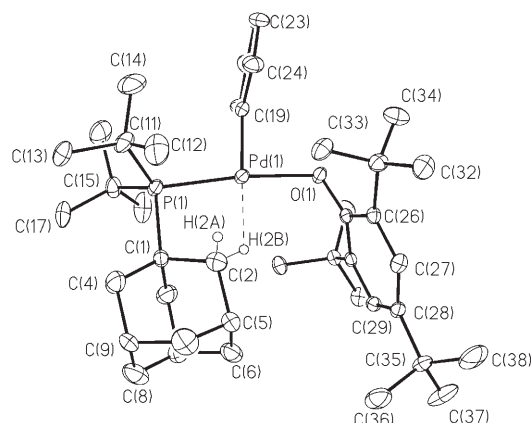


Figure 1. ORTEP diagram of $[(1\text{-AdPtBu}_2)\text{Pd}(\text{OC}_6\text{H}_2\text{-1,3,5-}t\text{Bu})(\text{Ph})]$ (**2**) with thermal ellipsoids set at 30% probability. Selected bond lengths [Å]: Pd(1)–C(19) 1.980(4), Pd(1)–O(1) 2.057(2), Pd(1)–P(1) 2.2795(11), Pd(1)–H(2B) 2.14.

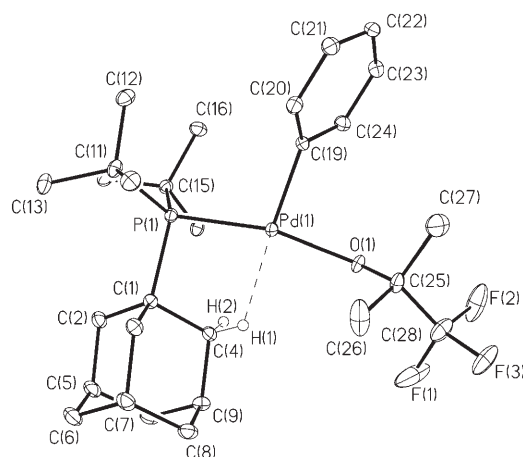
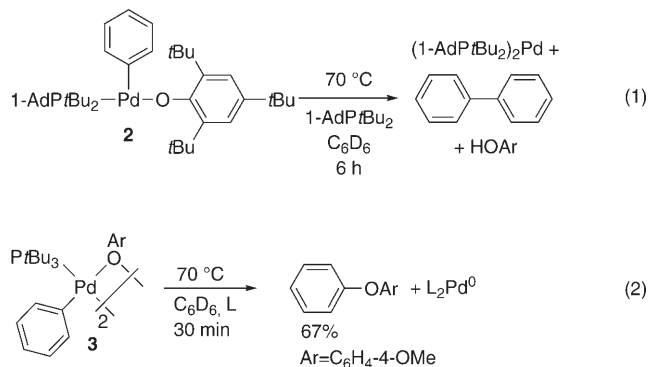


Figure 2. ORTEP diagram of $[(1\text{-AdPtBu}_2)\text{Pd}(\text{OC}(\text{CH}_3)_2\text{CF}_3)(\text{Ph})]$ (**6a**) with thermal ellipsoids set at 30% probability. Selected bond lengths [Å]: Pd(1)–C(19) 1.976(2), Pd(1)–O(1) 2.0193(17), Pd(1)–P(1) 2.2639(8), Pd(1)–H(1) 2.18.

adamantyl methylene hydrogen atom that is close (2.14, and 2.18(3) Å) to palladium. This hydrogen atom in **2** and **6a** was refined in an idealized position and is unlikely to deviate from this position significantly because of the rigidity of the adamantyl unit; the hydrogen atom in **6b** was located and refined. Both Pd⋯H distances are consistent with an agostic interaction^[20] that occupies a coordination site of these formally unsaturated species.^[21] If this C–H bond is included as a fourth ligand, the palladium complexes are square-planar; the sum of the angles about the palladium involving the heavy atoms are 360 and 357°, respectively. The Pd–O and the Pd–P distances in **6a** are about 0.04 Å and 0.015 Å smaller than those in **2**. The Pd–C distances are nearly identical in the

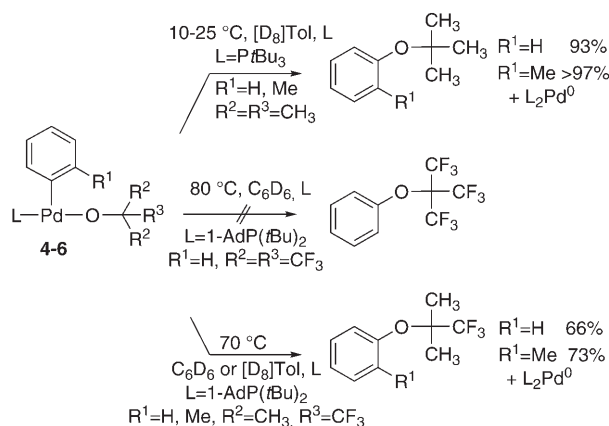
two complexes. One might envision that an *o*-tolylpalladium alkoxide containing a single phosphine ligand would be stabilized by an agostic interaction with a C–H bond of the *o*-tolyl group. However, the solid-state structure of **6b** is nearly identical to that of **6a**. The same close Pd–H distance to the adamantyl methylene hydrogen atom (2.156 Å) was observed, and there was no evidence for an interaction of palladium with the C–H bond of the *o*-tolyl group.

The reductive eliminations of complexes **2–6** are summarized in Equations (1) and (2) and in Scheme 2. Heating of



hindered phenoxide **2** in C_6D_6 with added 1-AdPtBu_2 formed the Pd^0 complex $[\text{Pd}(1\text{-AdPtBu}_2)_2]$, but no biaryl ether. Biphenyl and 2,4,6-tri-*tert*-butyl phenol were formed instead [Eq. (1)].^[22] However, heating of the less hindered phenoxide **3** in $[\text{D}_8]\text{toluene}$ with added PtBu_3 at 70 °C generated diphenyl ether in 67% yield and $[\text{Pd}(\text{PtBu}_3)_2]$ in 79% yield.

Several of the alkoxide complexes also underwent reductive elimination (Scheme 2). Warming C_6D_6 solutions of the *tert*-butoxide complexes **4a** and **4b** generated in situ with added PtBu_3 led to the formation of ArOtBu ($\text{Ar} = \text{Ph}, o\text{-tol}$) in 93–97% yield at room temperature. Perfluoro-*tert*-butoxide **5** was stable at room temperature and did not form any perfluoroalkyl aryl ether upon decomposition at 80 °C in C_6D_6 . However, heating of arylpalladium trifluoro-*tert*-butoxide complexes **6a** and **6b** at 70 °C with added 1-AdPtBu_2 generated $\text{ArOCMe}_2\text{CF}_3$ ($\text{Ar} = \text{Ph}, o\text{-Tol}$) in 66% and 73% yield. In all cases the $[\text{L}_2\text{Pd}^0]$ species was the only palladium



Scheme 2.

product observed. These results are consistent with the intermediacy of **3** and **4** in the palladium-catalyzed formation of biaryl and *tert*-butyl aryl ethers from aryl halides and NaOAr^[5,6,9,14] and NaOtBu.^[10,23,24] Complexes **6a** and **6b** constitute rare isolated and fully characterized alkoxide complexes that reductively eliminate ether.

Most importantly, the stability of trifluoro *tert*-butoxides **6a,b** at room temperature allowed kinetic data to be obtained without potential complications from impurities.^[2] Kinetic data on the reactions of **6b** were consistent with direct reductive elimination from the isolated complex. Reaction of **6b** (12 mM in C₆D₆) at 73 °C in the presence of 1, 5, and 10 equivalents of added 1-AdPrBu₂ occurred with rate constants of 4.6 ± 0.4 , 4.2 ± 0.3 , and $5.8 \pm 0.8 \times 10^{-4} \text{ s}^{-1}$, respectively. Thus, the reaction is zero-order in added ligand, and reversible dissociation or association of ligand does not occur prior to C–O bond formation.

These rate data were similar to those for reductive eliminations from *tert*-butoxides **4a,b**. Reductive elimination from **4a** was also independent of the concentration of added ligand. Complex **4a** (24 mM in CH₂Cl₂) reacted at 30 °C with rate constants of 2.6 ± 0.2 , 2.4 ± 0.2 , and $2.5 \pm 0.2 \times 10^{-4} \text{ s}^{-1}$, and **4b** (12 mM in [D₈]toluene) reacted at 15 °C with rate constants of 4.1 ± 0.4 , 4.4 ± 0.2 , and $5.3 \pm 0.5 \times 10^{-4} \text{ s}^{-1}$ with 1, 5, and 10 equivalents of added ligand. The faster elimination from these complexes than from trifluoro *tert*-butoxide **6a** is consistent with faster carbon–heteroatom bond-forming reductive elimination from complexes with more electron-rich amido and alkoxo groups.^[25,26]

These data allow comparison of the rate of reductive elimination of ether from a discrete three-coordinate and an isolated four-coordinate palladium alkoxo complex. Reductive eliminations from binap-ligated alkoxides (binap = 2,2'-bis(diphenylphosphanyl)-1,1'-binaphthyl) containing electron-neutral aryl groups occur in low yields. These reactions occur in higher yields from binap-ligated alkoxides containing electron-poor aryl groups. However, the reductive eliminations from alkoxides **4** and **6** containing a single phosphine and an electron-neutral aryl group are comparable or faster than those from binap-ligated arylpalladium complexes generated in situ containing electron-poor aryl groups.^[2,4] Although there are differences between the electron-donating properties of arylphosphines and alkylphosphines and between bisphosphines and monophosphines, this comparison fits the trend of faster reductive elimination from three-coordinate species than from four-coordinate species^[25] observed for alkylpalladium and amidopalladium complexes.^[26]

These data also allow comparison of the rates of reductive elimination from three-coordinate alkoxo and three-coordinate amido complexes. Reductive elimination of *tert*-butyl aryl ether from alkoxide **4a** is slower than reductive elimination of triarylamine from the related diarylamido complex [(PrBu₃)Pd(Ar)(NTol₂)]. Alkoxide **4a** reacted at 30 °C at the same timescale as [(PrBu₃)Pd(Ar)(NTol₂)] reacted at –10 °C.^[16] Further studies are needed to determine if this difference results from steric effects, basicity of alkoxide versus amide ligands, polarizability of the heteroatom, or thermodynamic driving force.

In summary, we have described the direct observation of reductive elimination from a series of monomeric arylpalladium(II) aryloxo and alkoxo complexes, including the first reductive elimination from an isolated T-shaped alkoxo complex. These reactions allow a direct comparison of the rates of these eliminations to related processes and constitute a rare case in which unsaturated intermediates in a catalytic process are observed, isolated, and studied directly.

Experimental Section

Representative procedure for generation and characterization of 4a at low temperature: A 600 μL CD₂Cl₂ solution of [(PrBu₃)Pd(Ph)(Br)] (**1b**) (12.0 mg, 0.0260 mmol) was placed into a screw-capped NMR tube and cooled to 0 °C. To this tube was added by syringe a solution of NaOtBu (216 μL , 0.12 M, 0.026 mmol) in CD₂Cl₂. The reaction mixture was agitated and immediately turned from yellow to deep orange. The tube was placed into a NMR probe that was precooled to –10 °C. The reaction was monitored by ³¹P NMR spectroscopy for approximately 1 h or until [(PrBu₃)Pd(Ph)(Br)] was completely consumed. ¹H NMR (CD₂Cl₂, 400 MHz, –10 °C): δ = 1.06 (s, 9H), 1.41 (d, J = 12.0 Hz, 27H), 6.82–6.85 (m, 3H), 7.34–7.36 ppm (m, 2H); ¹³C{¹H} NMR (CD₂Cl₂, 100 MHz, –10 °C): δ = 31.1 (d, J = 4.0 Hz), 34.5, 38.4 (d, J = 9.6 Hz), 71.0, 122.2, 125.7, 136.0 (d, J = 1.9 Hz), 136.1 ppm (d, J = 5.7 Hz); ³¹P NMR (CD₂Cl₂, 202 MHz, –10 °C): δ = 65.9 ppm.

Preparation of 6b: In a glovebox, [(1-AdPrBu₂)Pd(*o*-tol)(Br)] (**1c**, 31 mg, 0.055 mmol) and NaOC(CH₃)₂(CF₃) (8.5 mg, 0.057 mmol) were dissolved in toluene (2 mL), and the solution was stirred. In a separate vial, silver triflate (15 mg, 0.058 mmol) was dissolved in toluene (1 mL). The triflate solution was added dropwise to the stirred solution of palladium and alkoxide. A precipitate formed immediately. The reaction was stirred for an additional 5 min. After this time, the reaction mixture was filtered through celite, and all of the toluene was evaporated under reduced pressure. The resulting yellow-orange residue was dissolved in a minimum amount of ether (ca. 2 mL), layered with pentane (ca. 6 mL), and cooled at –35 °C. After 24 h, yellow crystals were collected, washed quickly with pentane, and dried under vacuum to yield 60 % of **6b**. ¹H NMR (C₆D₆, 500 MHz): δ = 1.13 (d, J = 12.5 Hz, 9H), 1.15 (d, J = 13 Hz, 9H), 1.43 (s, 3H), 1.44–1.52 (m, 6H), 1.59 (s, 3H), 1.71 (brs, 3H), 2.01–2.14 (m, 6H), 3.26 (s, 3H), 6.77–6.79 (m, 1H), 6.86–6.90 (m, 2H), 7.45 ppm (d, J = 8 Hz, 1H); ¹³C{¹H} NMR (C₆D₆, 126 MHz): δ = 27.0, 27.4, 28.9 (d, J = 7.8 Hz), 29.0, 31.9, 32.0, 36.3, 39.0 (d, J = 9.8 Hz), 39.2 (d, J = 9.8 Hz), 41.2, 45.8 (d, J = 9.8 Hz), 75.55 (q, J = 25 Hz), 123.7, 124.2, 128.9, 130.90 (q, J = 290 Hz), 136.3 (d, J = 4.9 Hz), 137.4 (d, J = 1.9 Hz), 142.5 ppm; ³¹P NMR (C₆D₆, 202 MHz): δ = 64.5 ppm. ¹⁹F NMR (C₆D₆, 376 MHz) δ = –82.5 ppm. Elemental analysis calcd (%) for C₂₉H₄₆F₃OPd: C 57.57, H 7.66; found: C 57.53, H 7.84.

Crystal data for **2**: M_r = 725.33, monoclinic, space group *C2/c*, a = 36.023(7), b = 9.6881(19), c = 22.328(5) Å, α = 90°, β = 92.06(3), γ = 90°, V = 7787(3) Å³, Z = 8, ρ = 1.237 Mg m^{–3}, μ = 0.547 mm^{–1}, T = 183(2) K, crystal dimensions: 0.20 × 0.20 × 0.15 mm. Of 8881 reflections measured, 5397 unique reflections were used in refinement. Final R = 0.0544, (R_w = 0.1119). Crystal data for **6a**: M_r = 591.00, monoclinic, space group *P2(1)/c*, a = 13.887(3), b = 11.847(2), c = 17.853(4) Å, α = 90°, β = 112.79(3), γ = 90°, V = 2707.9(9) Å³, Z = 4, ρ = 1.450 Mg m^{–3}, μ = 0.784 mm^{–1}, T = 183(2) K, crystal dimensions: 0.30 × 0.25 × 0.25 mm. Of 6687 reflections measured, 5250 unique reflections were used in refinement. Final R = 0.0363, (R_w = 0.0850). Crystal data for **6b**: M_r = 605.03, monoclinic, space group *P2(1)/c*, a = 10.6142(3), b = 18.5875(6), c = 14.9558(5) Å, α = 90°, β = 103.338(2), γ = 90°, V = 2871.06(16) Å³, Z = 4, ρ = 1.400 Mg m^{–3}, μ = 0.741 mm^{–1}, T = 193(2) K, crystal dimensions: 0.59 × 0.48 × 0.06 mm. Of 43885 reflections measured, 8368 unique reflections were used in refinement. Final R = 0.0316, (R_w = 0.0765). CCDC-651861 (**2**), 651862

(6a), and 651863 (6b) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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