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Palladium Complexes

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Facile Hydrolysis and Alcoholysis of Palladium Acetate**

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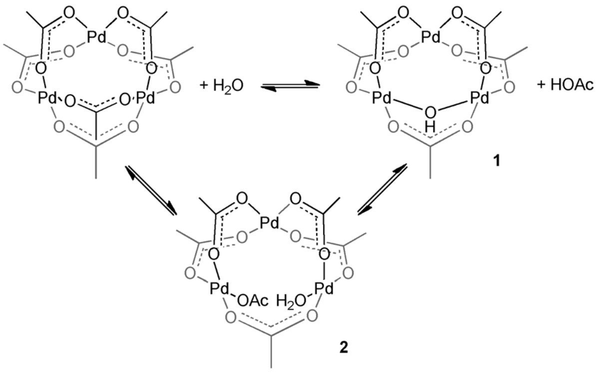
Abstract: *Palladium(II) acetate is readily converted into $[Pd_3(\mu^2\text{-}OH)(OAc)_5]$ (**1**) in the presence of water in a range of organic solvents and is also slowly converted in the solid state. Complex **1** can also be formed in nominally anhydrous solvents. Similarly, the analogous alkoxide complexes $[Pd_3(\mu^2\text{-}OR)(OAc)_5]$ (**3**) are easily formed in solutions of palladium(II) acetate containing a range of alcohols. An examination of a representative Wacker-type oxidation shows that the Pd-OH complex **1** and a related Pd-oxo complex **4** can be excluded as potential catalytic intermediates in the absence of exogenous water.*

When considering the mechanisms associated with a synthetic or catalytic process, for instance the transformation of a pre-catalyst into an active species, it is critically important to be confident of the integrity of the starting material. Palladium(II) acetate is a ubiquitous precursor in an extremely wide range of synthetic and catalytic transformations, yet we show herein that in very many cases what is assumed to be palladium acetate is in fact not.[1] This is because palladium acetate is highly sensitive to moisture in solution, reacting readily with low concentrations of water in a range of common organic solvents, including solvents that have been "dried" over calcium hydride, to give the structurally characterized complex $[Pd_3(\mu^2\text{-}OH)(OAc)_5]$ (**1**).[2] Similarly, reaction with alcohols generates the alkoxide complexes $[Pd_3(\mu^2\text{-}OR)(OAc)_5]$ **3**.

The trimeric structure of palladium acetate in solution—$[Pd_3(\mu^2\text{-}OAc)_6]$—was demonstrated by Wilkinson et al.[3] while a subsequent X-ray crystallographic analysis confirmed the structure in the solid state.[4] Cotton and co-workers were the first to notice that the trimer reacts reversibly with water to generate a new species that, on the basis of ^{1}H NMR spectroscopic analysis, they assigned as the trimetallic complex **2** (Scheme 1),[5] in which water coordinates to one of the palladium atoms, converting a μ^2-acetate ligand into a κ^1-acetate on an adjacent palladium center.[6] Subsequently, Nosova and co-workers postulated, again based solely on NMR studies, that this species was actually the μ^2-hydroxy complex $[Pd_3(\mu^2\text{-}OH)(OAc)_5]$ (**1**).[7] Intrigued by this apparent dichotomy, we examined the reaction of palladium acetate with a large excess of water (10 equiv per Pd) in acetone. This gave essentially quantitative conversion into the μ^2-OH complex **1** as determined by a ^{1}H NMR spectrum of the solution. Complex **1** was isolated in 86% yield as an orange solid containing a small amount (7%) of palladium acetate. A single-crystal X-ray crystallographic analysis unequivocally confirmed the formulation of **1**, and the molecular structure is shown in Figure 1.[8]



Scheme 1. Equilibrium between $[Pd_3(OAc)_6]$ and $[Pd_3(\mu^2\text{-}OH)(OAc)_5]$ (**1**).

The main structural perturbation on replacing a bridging acetate of the palladium acetate trimer with a μ^2-OH ligand is a decrease in the inter-palladium distances. Thus, although

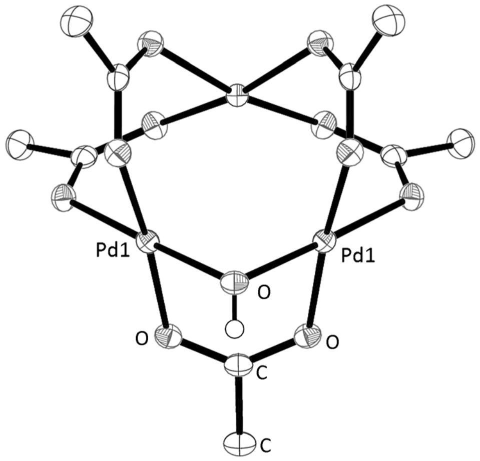


Figure 1. X-ray crystal structure of complex **1**. Thermal ellipsoids set at 50% probability, Me-H atoms omitted for clarity.

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$[Pd_3(\mu^2\text{-}OAc)_6]$ has an average inter-Pd separation of around 3.15 Å,[4] this is reduced slightly to 3.0113(2) Å for adjacent acetate-only-bridged palladium atoms in **1**, while the Pd1⋯Pd1 separation is only 2.8640(3) Å.

The ^1H NMR spectrum of **1** in [D$_6$]acetone showed three signals at $\delta = 1.794$, 1.860, and 1.887 ppm in a 2:1:2 ratio for the three distinct methyl environments, consistent with the C_s-symmetric structure being preserved in solution.[9] This was supported by the detection of signals indicating three distinct environments for acetate ligands in the ^{13}C NMR spectrum. Further evidence that the Pd_3 structure of **1** is maintained in solution was provided by a DOSY NMR experiment. This gave a diffusion coefficient for **1** in [D$_6$]acetone of $1.7 \times 10^{-9}\ m^2 s^{-1}$, similar to that of $[Pd_3OAc_6]$ which gave a value of $2.0 \times 10^{-9}\ m^2 s^{-1}$ under the same conditions.[10]

Addition of acetic acid (2.2 equiv) to a 93:7 mixture of **1** and $[Pd_3(OAc)_6]$ in [D$_6$]acetone (44.7 mM [Pd]) led to the regeneration of some palladium acetate ($\mathbf{1}:[Pd_3(OAc)_6] = 75:25$), indicating that **1** and palladium acetate are in equilibrium (Scheme 1), possibly via the intermediacy of **2**. Figure 2 shows the effect of adding increasing amounts of water to palladium acetate in various solvents. It is clear that in solvents that are miscible with water (THF, acetone, 1,4-dioxane) the equilibria can be pushed in favor of the essentially quantitative formation of **1**. By contrast the data obtained in solvents in which water is only sparingly soluble (toluene, chloroform, dichloromethane) plateau at less than quantitative conversion.[11]

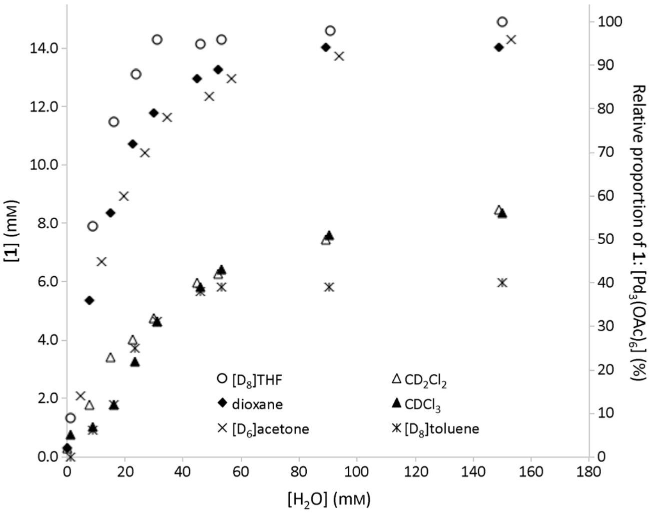
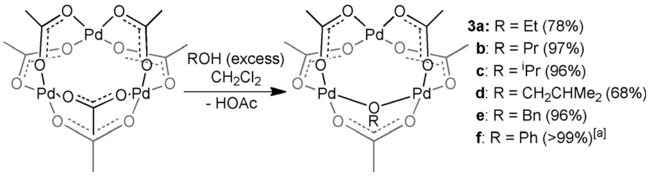


Figure 2. Extent of formation of **1** in representative solvents with increasing water concentration, determined by ^1H NMR spectroscopy after 1 h.

It is important to note that in each case, the first datum for each plot in Figure 2 was obtained from the reaction of residual water in the solvent after it had been dried over calcium hydride.[12] With the exception of toluene, some conversion into the hydroxide **1** was seen in all of the nominally anhydrous solvents. It is clear that solutions of palladium acetate are highly sensitive to traces of water, reacting more extensively and more rapidly than the drying agent, calcium hydride. While solid samples of palladium acetate sealed under air show no increase in the amount of **1** after 3 months, a sample left open to air for only 8 days showed 34 % conversion to **1**.

The surprisingly facile solvolytic reactivity of palladium acetate in solution is not limited to hydrolysis. By NMR spectroscopy, we find that the equivalent μ-OEt complex **3a** is formed quantitatively on dissolving palladium acetate in a mixture of 10 % (v/v) ethanol in [D$_2$]dichloromethane (Scheme 2). Similarly the formation of **3a** from palladium acetate also proceeded quantitatively within 5 min on reaction with 10 % mixtures of ethanol in [D$_6$]acetone, dioxane, [D$_8$]THF, $CDCl_3$, and [D$_8$]toluene.[13] Interestingly a solution of palladium acetate (14.9 mM) in reagent-grade dichloromethane also showed a significant amount of **3a** (approximately 90 %), as a result of the 0.2 % of ethanol used as a stabilizer for the solvent.



Scheme 2. Formation of μ^2-alkoxide complexes **3**. [a] Spectroscopic yield (^1H NMR), product contains residual phenol.

In an analogous manner, excess propanol, isopropanol, isobutanol, benzyl alcohol, and phenol all reacted with palladium acetate in dichloromethane solution to give spectroscopically the quantitative formation of alkoxides **3b–f** (Scheme 2). These reactions can be performed in air, except for the formation of the phenoxide complex **3f**, which is air-sensitive. Solid samples of **3a–e** could be isolated in a greater than 95:5 ratio of $\mathbf{3}:[Pd_3(OAc)_6]$.[14] The single-crystal X-ray structure of complex **3a** is shown in Figure 3 and is very similar to that of the μ-hydroxo complex **1** (Figure 1).[8]

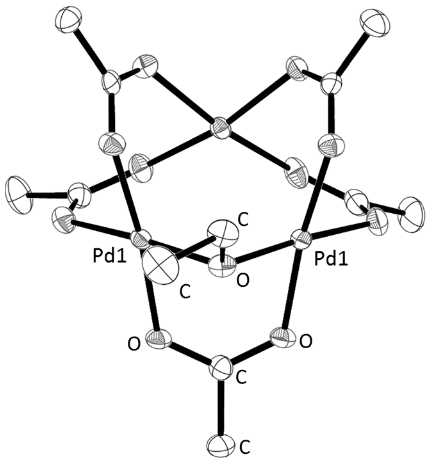
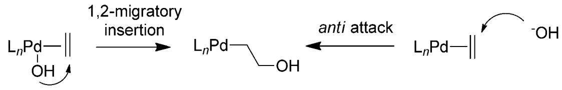


Figure 3. X-ray crystal structure of complex **3a**. Thermal ellipsoids set at 50 % probability, Me-H and Et-H atoms omitted for clarity.

The μ-hydroxo and μ-ethoxide complexes **1** and **3a** can be interconverted by reaction with excess ethanol and water respectively, although the reactions are slow. Thus, **1** reacts with ethanol (30 equiv) to give a 1:3 mixture of **1** and **3a** after 18 h, while **3a** reacts with H_2O (30 equiv) giving **1a** quantitatively. A ^{1}H NMR spectrum of a competition reaction between palladium acetate and 10 equivalents per palladium of both water and ethanol in [D_6]acetone showed quantitative conversion into a 1.89:1 mixture of **1** and **3a** within 30 min, indicating that the equilibria lie in favor of the μ-hydroxo species.[15]

Finally, with complex **1** in hand, we turned our attention to trying to resolve an issue that remains somewhat contentious, namely whether or not palladium hydroxide complexes play any role in the Wacker oxidation of alkenes. There is still some debate as to whether the oxygen is incorporated into the product by *anti* addition of an external oxygen nucleophile (H_2O or OH^-) to the coordinated alkene or by 1,2-migratory insertion of the coordinated alkene into the Pd–O bond of a hydroxide complex (Scheme 3).[16]

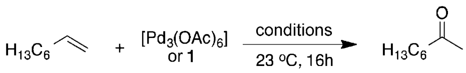


Scheme 3. Potential mechanisms for the C–O bond-forming step in the Wacker oxidation of alkenes.

Palladium acetate can be used to good effect in the Wacker oxidation of alkenes to ketones, using benzoquinone as an oxidant in the presence of a strong acid.[17,18] We have previously shown that *p*-toluene sulfonic acid reacts with palladium acetate to give unusual palladacycles in which the toluene ring has undergone orthometallation.[19] By contrast, ^{1}H NMR spectra of reactions of 1-naphthyl, 5-isoquinoline, or 3-pyridyl sulfonic acids in toluene reveal the formation of the μ^2-OH complex **1**, indicating that it can be formed under the acidic conditions often employed in Wacker chemistry with palladium acetate.[17,18]

Table 1 summarizes the results of stoichiometric reactions of palladium acetate or complex **1** with the representative alkene, 1-octene. In the presence of water, the reaction with palladium acetate yields 64 % of the product, 2-octanone. By contrast, the μ-hydroxo complex **1** gives no product under anhydrous conditions, whereas the same reaction repeated in the presence of added water yields 46 % of the ketone. The data from these reactions (entries 1–3) seem to be inconsistent with a 1,2-migratory insertion process involving the species Pd-OH.[20]

Table 1: Oxidation of 1-octene by [$Pd_3(OAc)_6$] or **1** to form 2-octanone.



Entry	Conditions	Yield [%][a]
1	[$Pd_3(OAc)_6$], acetone : H_2O (7:1)	64
2	**1**, anhydrous acetone	0
3	**1**, acetone : H_2O (7:1)	46
4	**1**, 5-isoquinoline sulfonic acid (1 equiv) anhydrous acetone	7

[a] Yield of octanone determined by GC (mesitylene internal standard).

Interestingly, in one instance, on reaction of palladium acetate with 5-isoquinoline sulfonic acid, we obtained crystals of the hexapalladium μ^4-oxo complex [{$Pd_3(OAc)_5$}$_2$(μ^4-O)] (**4**), the crystal structure of which is shown in Figure 4.[8]

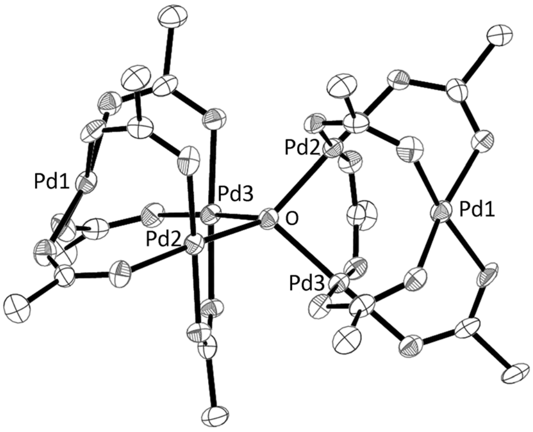


Figure 4. X-ray crystal structure of [{$Pd_3(OAc)_5$}$_2$(μ^4-O)] (**4**). Thermal ellipsoids set at 50 % probability, H atoms omitted for clarity.

Complex **4** is clearly related to the μ^2-hydroxo complex **1**, and indeed may well form via the intermediacy of **1**. The formation of **4** proved to be highly capricious, but its appearance in at least one reaction in the presence of a strong acid could potentially have a bearing on Wacker oxidation.[21,22] However, when this acid was added but water excluded from the alkene oxidation reaction in Table 1 (entry 4), very little ketone formation was detected, effectively precluding this possibility.

In conclusion, palladium acetate should be treated as highly moisture-sensitive in solution and moderately sensitive in the solid state. All reactions performed in aqueous or alcoholic media should be considered to be based on complexes **1** and **3** respectively, not palladium acetate. Does this matter? If the material behaves the way you want it to in a reaction, then it is tempting to say no. However, if you are interested in the mechanism of a process, then it is of course crucial that your considerations are based on what is actually present in the reaction.

Keywords: acetate ligands · homogeneous catalysis · hydrolysis · oxidation · palladium

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[1] Nitrite ion contamination can also play an important role in the chemistry of palladium acetate, for example see: S. E. Bajwa, T. E. Storr, L. E. Hatcher, T. J. Williams, C. G. Baumann, A. C. Whitwood, D. R. Allan, S. J. Teat, P. R. Raithby, I. J. S. Fairlamb, *Chem. Sci.* **2012**, *3*, 1656.

[2] Palladium hydroxide complexes are believed to be important intermediates in many Suzuki cross-coupling reactions. For a recent example with key references, see: A. R. Kapdi, G.

Dhangar, J. L. Serrano, J. Perez, L. Garcıa, I. J. S. Fairlamb, *Chem. Commun.* **2014**, *50*, 9859.

[3] T. A. Stephenson, S. M. Morehouse, A. R. Powell, J. P. Heffer, G. Wilkinson, *J. Chem. Soc.* **1965**, 3632.

[4] A. C. Skapski, M. L. Smart, *J. Chem. Soc. D* **1970**, 658.

[5] V. I. Bakhmutov, J. F. Berry, F. A. Cotton, S. Ibragimov, C. A. Murillo, *Dalton Trans.* **2005**, 1989.

[6] Complex **2** was also proposed as the intermediate in the hydrolysis of $[Pd_3(OAc)_6]$ to monomeric palladium acetate, see: L. A. Adrio, B. N. Nguyen, G. Guilera, A. G. Livingston, K. K. Hii, *Catal. Sci. Technol.* **2012**, *2*, 316.

[7] V. Nosova, Y. Ustynyuk, L. Bruk, *Inorg. Chem.* **2011**, *50*, 9300.

[8] See Table S3 in the Supporting Information for crystallographic data.

[9] The OH signal is not detected in acetone; seen at $\delta = -0.99$ ppm in $CDCl_3$.

[10] The Stokes–Einstein equation predicts a hydrodynamic radius of approximately 4.0 Å for **1** (see the Supporting Information). For the recent application of the Stokes–Einstein equation to Pd_3 clusters, see: F. Armbruster, J. Meyer, A. Baldes, P. O. Burgos, I. Fernández, F. Breher, *Chem. Commun.* **2011**, *47*, 221.

[11] The coordinating solvents acetonitrile and dimethylformamide give more complicated results: although complex **1** is detected, there is no straightforward correlation with a loss of $[Pd_3(OAc)_6]$ over time, suggesting other reactions are occurring, most likely the formation of lower nuclearity solvent-coordinated complexes. $[Pd_3(OAc)_6]$ in $[D_5]$pyridine (14.9 mM) with $[H_2O] =$ 447 mM, gave no **1** after 1 h, instead ^1H NMR revealed a single signal at $\delta = 2.07$ ppm. On standing, crystals of $[Pd([D_5]Py)_4][HCO_3]_2$ were deposited, and analyzed by X-ray crystallography (see Supporting Information).

[12] Solvents were stirred over CaH_2 overnight, distilled, and stored over 4 Å molecular sieves (except $[D_6]$acetone). Residual water determined by Karl Fischer titration (see the Supporting Information).

[13] **3a** is not stable in EtOH and undergoes rapid decomposition.

[14] See the Supporting Information. With PhOH, the product was contaminated with excess alcohol.

[15] A preference for a Pd-OH species was detected in the equilibrium between a (PCP)Pd-OMe pincer complex and (PCP)Pd-OH in the presence of water. See: G. R. Fulmer, A. N. Herndon, W. Kaminsky, R. A. Kemp, K. I. Goldberg, *J. Am. Chem. Soc.* **2011**, *133*, 17713.

[16] For a discussion and key references, see: N. M. Weliange, P. R. Sharp, *Organometallics* **2012**, *31*, 6823.

[17] D. G. Miller, D. D. M. Wayner, *J. Org. Chem.* **1990**, *55*, 2924.

[18] For representative recent examples, see: a) B. Morandi, Z. K. Wickens, R. H. Grubbs, *Angew. Chem. Int. Ed.* **2013**, *52*, 2944; *Angew. Chem.* **2013**, *125*, 3016; b) G. Zhang, X. Xie, Y. Wang, X. Wen, Y. Zhao, C. Ding, *Org. Biomol. Chem.* **2013**, *11*, 2947; c) B. Morandi, Z. K. Wickens, R. H. Grubbs, *Angew. Chem. Int. Ed.* **2013**, *52*, 9751; *Angew. Chem.* **2013**, *125*, 9933.

[19] R. B. Bedford, M. F. Haddow, C. J. Mitchell, R. L. Webster, *Angew. Chem. Int. Ed.* **2011**, *50*, 5524; *Angew. Chem.* **2011**, *123*, 5638.

[20] At this stage we cannot entirely exclude the possibility that in the presence of exogenous water, complex **1** dissociates to a lower nuclearity palladium-hydroxide species that is itself able to react with alkenes by 1,2-insertion, however in all of the NMR experiments undertaken, including the DOSY diffusion experiments, we see no evidence in support of this suggestion.

[21] The O atom of a Pd-oxo complex could in principle directly add to the double bond of an alkene, mimicking “oxygenase” metalloenzyme activity. For a discussion of oxygenase-like versus oxidase-like activity of Pd catalysts, see: S. S. Stahl, *Angew. Chem. Int. Ed.* **2004**, *43*, 3400; *Angew. Chem.* **2004**, *116*, 3480.

[22] We cannot entirely exclude the possibility that in one or more of the NMR experiments, the species assigned as **1** may in fact be **4**. However, in all cases, the OAc peaks match (within ± 0.009 ppm) those of isolated **1** dissolved in the anhydrous solvent and the DOSY NMR experiments suggest that, in acetone, the product is a Pd_3 rather than a Pd_6 cluster.

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