

Dioxygen activation by an organometallic Pd(II) precursor: formation of a Pd(IV)–OH complex and its C–O bond formation reactivity†

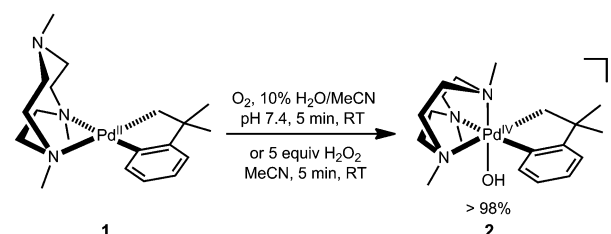
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The complex $(\text{Me}_3\text{tacn})\text{Pd}^{\text{II}}(\text{CH}_2\text{CMe}_2\text{C}_6\text{H}_4)$ is readily oxidized by O_2 or H_2O_2 to yield the $\text{Pd}^{\text{IV}}\text{–OH}$ complex $[(\text{Me}_3\text{tacn})\text{Pd}^{\text{IV}}(\text{OH})(\text{CH}_2\text{CMe}_2\text{C}_6\text{H}_4)]^+$. Thermolysis of this product leads to the selective $\text{C}(\text{sp}^2)\text{–O}$ reductive elimination of 2-*tert*-butylphenol, no $\text{C}(\text{sp}^3)\text{–O}$ elimination product being detected. This system represents a rare example of selective $\text{C}(\text{sp}^2)\text{–O}$ bond formation that is relevant to Pd-catalyzed aerobic C–H hydroxylation reactions.

Palladium-catalyzed C–H functionalization reactions have been developed over the past two decades as important and versatile tools in organic synthesis.^{1–3} Despite the wide range of such synthetic methods, there is a dearth of oxidative C–H functionalization reactions using inexpensive and environmentally friendly oxidants such as O_2 . While the majority of aerobic Pd-catalyzed reactions involve a $\text{Pd}^{\text{0}}/\text{Pd}^{\text{II}}$ catalytic cycle,⁴ several recent studies have proposed high-valent Pd^{III} or Pd^{IV} species as active intermediates in aerobic C–H functionalization reactions.⁵ We have recently employed multidentate flexible ligands to stabilize high-valent Pd^{III} and Pd^{IV} complexes and studied their reactivity in detail.⁶ In addition, such high-valent Pd species can be generated *via* aerobic oxidation of Pd^{II} precursors,^{6c,d,g} which represents an improvement over the expensive and hazardous oxidants typically used to generate high-valent Pd intermediates in catalytic or stoichiometric reactions.⁵ For example, we have reported that $(\text{Me}_3\text{tacn})\text{Pd}^{\text{II}}\text{Me}_2$ can be oxidized by O_2 to generate the isolable $[(\text{Me}_3\text{tacn})\text{Pd}^{\text{IV}}\text{Me}_3]^+$ complex formed by methyl group transfer upon the aerobic oxidation to Pd^{IV} .^{6d} Herein we report the palladacycle complex $(\text{Me}_3\text{tacn})\text{Pd}^{\text{II}}(\text{CH}_2\text{CMe}_2\text{C}_6\text{H}_4)$ (**1**) that undergoes rapid oxidation with O_2 or H_2O_2 to directly form the isolable complex

Scheme 1 Oxidative reactivity of the Pd^{II} complex **1**.

$[(\text{Me}_3\text{tacn})\text{Pd}^{\text{IV}}(\text{OH})(\text{CH}_2\text{CMe}_2\text{C}_6\text{H}_4)]^+$ (**2**) without the need for alkyl group transfer (Scheme 1). Thermolysis of **2** leads to selective formation of 2-*tert*-butylphenol. Additional reactivity studies suggest that the tridentate ligand employed herein leads to selective $\text{C}(\text{sp}^2)\text{–O}$ bond formation, while no C–halide bond formation is observed for the analogous $\text{Pd}^{\text{IV}}\text{–halide}$ complexes, suggesting that ligand denticity can be used to control the selectivity of these high-valent Pd complexes in various C–heteroatom bond formation reactions.

Complex **1** was prepared by reacting Me_3tacn with $(\text{COD})\text{Pd}(\text{CH}_2\text{CMe}_2\text{C}_6\text{H}_4)$ in diethyl ether.⁷ The single crystal X-ray characterization of **1** reveals a square planar geometry around the Pd^{II} center that is bound to two C and two N atoms, while the third N atom of the Me_3tacn ligand points away from the Pd center (Fig. 1, left), similar to the previously reported $(\text{Me}_3\text{tacn})\text{Pd}^{\text{II}}\text{Me}_2$ complex.^{6d} The Pd–C distances are 2.010 Å and 2.016 Å, respectively, similar to those found for other palladacycle complexes supported by N-donor ligands.⁸ NMR analysis reveals one singlet peak for the three *N*-methyl groups of the Me_3tacn ligand, indicating that the three *N*-Me groups are rapidly exchanging on the NMR timescale. In addition, the dynamic behavior of Me_3tacn leads to a plane of symmetry incorporating the palladacycle fragment, as suggested by the singlet NMR peaks observed for $\text{Pd}\text{–CH}_2\text{CMe}_2$ and $\text{Pd}\text{–CH}_2\text{CMe}_2$ at 1.80 and 1.26 ppm, respectively.

The cyclic voltammogram (CV) of **1** in 0.1 M $\text{Bu}_4\text{NPF}_6/\text{MeCN}$ shows a reversible oxidation wave at $E_{1/2} = -0.53$ V ($\Delta E_p = 71$ mV) *vs.* Fc^+/Fc ,⁷ which is significantly lower than those for analogous $\text{Pd}^{\text{II}}\text{Me}_2$ complexes with bidentate N-donor ligands,^{6c} and only slightly higher than our previously reported complex $(\text{Me}_3\text{tacn})\text{Pd}^{\text{II}}\text{Me}_2$.^{6d}

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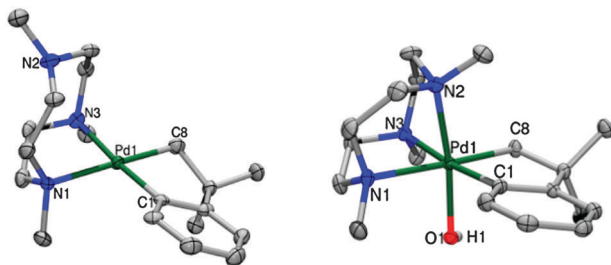
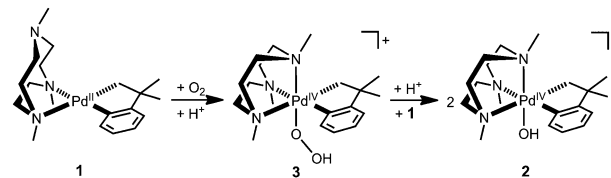


Fig. 1 ORTEP representation of **1** (left) and the cation of **[2]ClO₄** (right). Selected bond lengths (Å) and angles (°): **1**, Pd1–C1, 2.015(3); Pd1–C8, 2.010(6); Pd1–N1, 2.215(4); Pd1–N3, 2.240(3); C1–Pd1–C8, 78.99(14); **2**, Pd1–C1, 2.024(2); Pd1–C8, 2.061(2); Pd1–O1, 2.0185(17); Pd1–N1, 2.263(2); Pd1–N2, 2.117(2); Pd1–N3, 2.227(2); O1–Pd1–C1, 87.29(9); O1–Pd1–C8, 90.02(8); C1–Pd1–C8, 81.36(9).

We attribute the low redox potential of **1** to the ability of the Me₃tacn ligand to provide an axial donor atom and thus stabilize the oxidized high-valent Pd species that generally adopt a geometry with a higher coordination number.⁶ⁱ

The observed low redox potential of **1** prompted us to study its oxidation by O₂. Exposure of a colorless solution of **1** to O₂ in the presence of H₂O (10% H₂O–MeCN v/v) generates, rapidly, a yellow solution, and ¹H NMR analysis reveals the formation of a new species identified as the Pd^{IV} complex [(Me₃tacn)Pd^{IV}(OH)(CH₂CMe₂C₆H₄)]⁺ (**2**). The yield of **2** can be increased to >98% when the oxidation is performed in the presence of either 10% 1.0 M phosphate buffer (pH 7.4) or a slight excess of acid.⁷ These results suggest that aerobic oxidation of **1** requires the presence of protons for O₂ reduction, and addition of acid or even the use of a buffered solution ensures a rapid reduction of O₂ over the course of the reaction. In addition, complex **2** can also be rapidly generated in almost quantitative yield upon addition of 5 equiv. of H₂O₂ (Scheme 1). The Pd^{IV} product can be isolated as the perchlorate salt, **[2]ClO₄**, and characterized by X-ray crystallography, NMR, and ESI-MS.⁷ X-ray analysis reveals an octahedral Pd center with the two C atoms and two N atoms in the equatorial plane, while the third N donor from Me₃tacn and the hydroxide ligand occupy the axial positions (Fig. 1, right). The Pd–C distances (2.024 Å and 2.061 Å) are similar to the only other Pd^{IV}(CH₂CMe₂C₆H₄) complex supported by a tridentate N-donor ligand,⁹ while the Pd–OH distance (2.018 Å) is similar to those of other palladacycle Pd^{IV}–OH complexes.^{8a} The ¹H NMR spectrum of **2** in CD₃CN exhibits two doublets at 4.05 ppm and 3.97 ppm for the Pd–CH₂ group, supporting a geometry lacking a plane of symmetry.⁷

On the basis of previous mechanistic studies of the aerobic oxidation of (Me₃tacn)Pd^{II}Me₂,^{6d} we propose an analogous mechanism for the O₂ activation by **1** that involves the formation of a Pd^{IV}–OOH intermediate followed by the formation of the Pd^{IV}–OH product (Scheme 2). Indeed, the ESI-MS of the oxidation reaction solution shows two peaks with *m/z* values of 426.1732 and 442.1685, corresponding to [(Me₃tacn)Pd^{IV}(OH)(CH₂CMe₂C₆H₄)]⁺ (**2**, calcd *m/z* 426.1739) and [(Me₃tacn)Pd^{IV}(OOH)(CH₂CMe₂C₆H₄)]⁺ (**3**, calcd *m/z* 442.1688), respectively.⁷ The decrease of the peak intensity of **3** over time is accompanied by an increase of the relative peak intensity of **2**, supporting the intermediacy of **3** during the formation of **2**. A similar mechanism was also proposed for the aerobic oxidation of related Pd^{II} and Pt^{II} organometallic complexes.^{6c,e,g,10} Compared to the



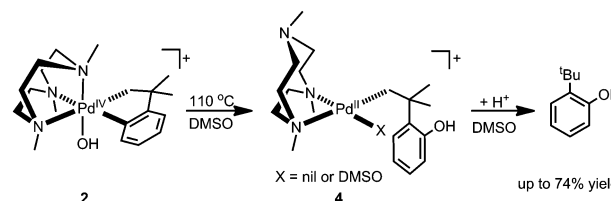
Scheme 2 Proposed mechanism for aerobic oxidation of **1**.

aerobic oxidation of (Me₃tacn)Pd^{II}Me₂, the oxidation of **1** by O₂ to yield an isolable Pd^{IV} product does not require an alkyl group transfer step that cannot occur for **2**.^{6d} Thus, it can be expected that O₂ could be used as an oxidant for oxidatively induced C–heteroatom bond formation reactions (see below).

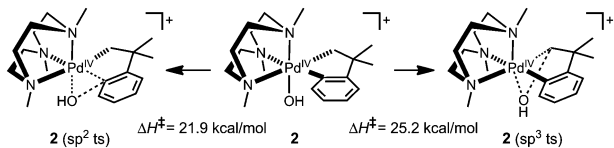
We next sought to study the C–O bond formation reactivity of **2**, especially the selectivity of the C–O bond formation, as C–heteroatom bond formation studies on asymmetric dihydrocarbyl–Pd^{IV} complexes are rare.¹¹ When **2** was heated to 110 °C in DMSO, a new transient species (**4**) was observed followed by the formation of 2-*tert*-butylphenol in up to 74% yield, as determined by NMR and GC-MS studies (Scheme 3).¹² C–O bond formation was also observed in other polar aprotic solvents: thermolysis in DMF led to the formation of 2-*tert*-butylphenol in a comparable yield.⁷ Interestingly, the organic product that would result from C(sp³)–O reductive elimination, PhCMe₂CH₂OH, was not detected under any of the experimental conditions examined. In addition, C–C bond formation to form a benzocyclobutane derivative is unlikely due to the strain of the four-membered ring product.

Complex **4** was tentatively assigned as [(Me₃tacn)Pd^{IV}(CH₂CMe₂-*o*-OH-C₆H₄)]⁺ (or its solvent derivative) based on ESI-MS and NMR studies. ESI-MS of the reaction mixture shows the presence of a peak at *m/z* 426.1717 (calcd [(Me₃tacn)Pd^{IV}(CH₂CMe₂-*o*-OH-C₆H₄)]⁺ 426.1731),¹³ while the ¹H NMR spectrum reveals a singlet at 2.16 ppm for the Pd–CH₂ group, similar to complex **1** (singlet at 1.80 ppm) and in the typical range of 1.96–2.37 ppm for Pd^{II}(CH₂CMe₂Ph)¹⁴ and Pd^{II}(CH₂CMe₂-*o*-C₆H₄)¹⁵ complexes with N donor ligands.

The selective formation of 2-*tert*-butylphenol from **2** represents a rare example of C–OH elimination from an organometallic Pd^{IV} complex. While C_{aryl}–O bond formation reactions from Pd^{IV} have been reported (e.g., C_{aryl}–OH bond formation from Pd^{IV} monoaryl complexes¹⁶ or C_{aryl}–carboxylate elimination from Pd^{IV} bis-aryl complexes¹⁷), the selective C_{aryl}–O vs. C_{alkyl}–O bond formation reactivity has not been observed before. The mechanism of this reaction likely involves a concerted C_{aryl}–O elimination from a Pd^{IV} center, as proposed recently.¹⁶ Moreover, the effect of the concentration of **2** on the yield of 2-*tert*-butylphenol suggests that a bimolecular mechanism for C_{alkyl}–O bond formation is unlikely.



Scheme 3 Aryl C–O bond reductive elimination upon thermolysis of **2**.



Scheme 4 Calculated activation parameters for the C(sp²)-O vs. C(sp³)-O bond formation reactivity of **2**.

In order to provide insight into the observed selective C(sp²)-O vs. C(sp³)-O bond formation reactivity for **2**, DFT calculations were employed to determine the activation parameters for the two possible C-O bond formation steps. First, the geometry optimized structure of **2** was determined using the M06/CEP-31G level of theory and with solvent correction,⁷ and then the transition states for both C(sp²)-O vs. C(sp³)-O bond formation reactions were calculated to yield ΔH^\ddagger values of 21.9 and 25.2 kcal mol⁻¹, respectively (Scheme 4 and Fig. S27, ESI[†]). The lower enthalpy of activation, by 3.3 kcal mol⁻¹, for the former transition state supports the observed selectivity and suggests that C(sp²)-O bond-forming reductive elimination is preferred from a Pd^{IV} center supported by a tridentate ligand. Interestingly, the opposite selectivity was recently observed by Sanford *et al.* for C(sp³)-F vs. C(sp²)-F coupling at a Pd^{IV} center supported by a bidentate ligand (see below).¹¹

The oxidation reactivity of **1** was also tested using other oxidants such as *N*-fluoro-2,4,6-trimethylpyridinium triflate, PhICl₂ and I₂. The corresponding products, [(Me₃tacn)Pd^{IV}(F)(CH₂CMe₂C₆H₄)]⁺ (**5**), [(Me₃tacn)Pd^{IV}(Cl)(CH₂CMe₂C₆H₄)]⁺ (**6**) and [(Me₃tacn)Pd^{IV}(I)(CH₂CMe₂C₆H₄)]⁺ (**7**) were isolated, and [6]ClO₄ and [7]I were structurally characterized to reveal a coordination geometry similar to that of **2** (Fig. S28, ESI[†]).⁷ Interestingly, no C-halide reductive elimination was observed upon prolonged heating of either **5**, **6**, or **7**. By comparison, examples of C(sp³)-F and C(sp²)-F bond formation upon reductive elimination from Pd^{IV} complexes supported by bidentate ligands were recently reported,^{17a,18} and the formation of a five-coordinate intermediate *via* ligand dissociation¹¹ or due to the presence of a hemi-labile sulfonamide ligand¹⁸ was proposed during C-F reductive elimination. This suggests that formation of a five-coordinate Pd^{IV} intermediate is likely a prerequisite for facile C(sp²)-F bond formation reactivity and such an intermediate is not easily accessible for **2**, most likely due to the presence of the three strong amine donors of Me₃tacn. The calculated transition states for the C(sp²)-F and C(sp³)-F bond formation reactions from **5** yield comparable ΔH^\ddagger values of 29.4 and 30.5 kcal mol⁻¹, respectively (Fig. S27, ESI[†]),⁷ strongly suggesting that both types of C-halide bond formation from the (Me₃tacn)Pd^{IV} center are disfavored. Overall, this observed ligand-controlled bond formation reactivity can be exploited for developing selective aerobically induced C-O bond formation catalytic transformations, which are currently being investigated by us.

In summary, we report herein an organometallic Pd^{II} complex **1** that undergoes facile aerobic oxidation to form a stable Pd^{IV}-OH complex **2** that was isolated and fully characterized. The O₂ activation reactivity is due to the low oxidation potential of **1** supported by the tridentate amine ligand Me₃tacn that can effectively stabilize the octahedral geometry of the generated Pd^{IV} center. Interestingly, thermolysis of the organometallic Pd^{IV}-OH complex **2** leads to selective C(sp²)-O vs. C(sp³)-O bond formation and formation of

2-*tert*-butylphenol. This represents a rare example of a selective C_{aryl}-O reductive elimination from a Pd^{IV}-OH complex that is formed *via* aerobic oxidation of a Pd^{II} precursor and thus is relevant to Pd-catalyzed aerobic hydroxylation reactions.¹⁹ Moreover, the observed preference for the C-O vs. C-halide bond formation reactivity is currently explored for the development of selective aerobic C-O bond formation transformations.

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