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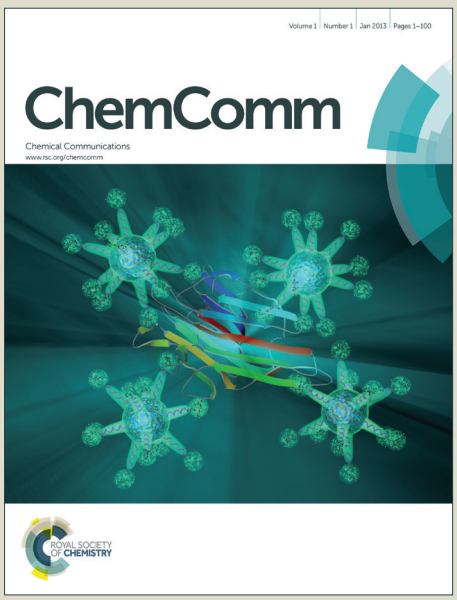

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Dioxygen Activation by an Organometallic Pd(II) Precursor: Formation of a Pd(IV)-OH Complex and Its C-O Bond Formation Reactivity

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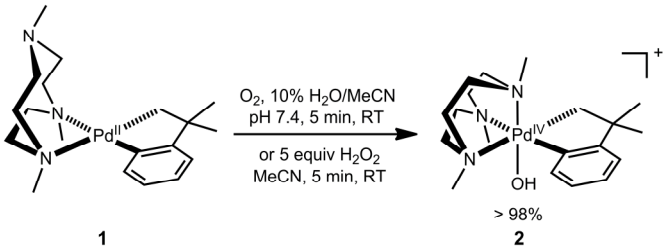
The complex $(Me_3tacn)Pd^{II}(CH_2CMe_2C_6H_4)$ is readily oxidized by O_2 or H_2O_2 to yield the Pd^{IV}-OH complex $[(Me_3tacn)Pd^{IV}(OH)(CH_2CMe_2C_6H_4)]^+$. Thermolysis of this product leads to the selective $C(sp^2)$-O reductive elimination of 2-*t*-butyl-phenol, no $C(sp^3)$-O elimination product being detected. This system represents a rare example of selective $C(sp^2)$-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.[1,2,3] 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 Pd^0/Pd^{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 in detail their reactivity.[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 $(Me_3tacn)Pd^{II}Me_2$ can be oxidized by O_2 to generate the isolable $[(Me_3tacn)Pd^{IV}Me_3]^+$ complex formed upon methyl group transfer upon the aerobic oxidation to Pd^{IV}.[6d] Herein we report the palladacycle complex $(Me_3tacn)Pd^{II}(CH_2CMe_2C_6H_4)$ (**1**) that undergoes rapid oxidation with O_2 or H_2O_2 to directly form the isolable complex $[(Me_3tacn)Pd^{IV}(OH)(CH_2CMe_2C_6H_4)]^+$ (**2**) without the need for alkyl group transfer (Scheme 1). Thermolysis of **2** leads to selective formation of 2-tert-butyl-phenol. Additional reactivity studies suggest that the tridentate ligand employed herein leads to selective $C(sp^2)$-O bond formation, while no C-halide bond formation was observed for the analogous Pd^{IV}-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 $(COD)Pd(CH_2CMe_2C_6H_4)$ 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 $(Me_3tacn)Pd^{II}Me_2$ complex.[6d] The Pd-C distances are 2.010 Å and 2.016 Å, respectively, similar to those found for other palladacycles 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 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 Pd-CH_2CMe_2 and Pd-CH_2CMe_2 at 1.80 and 1.26 ppm, respectively.



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

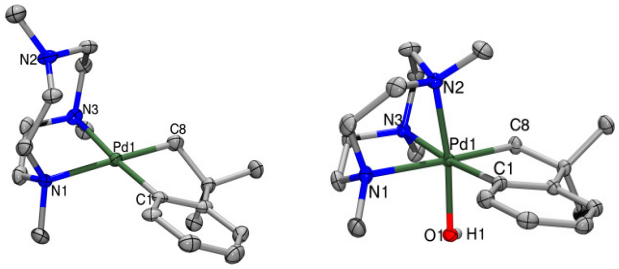
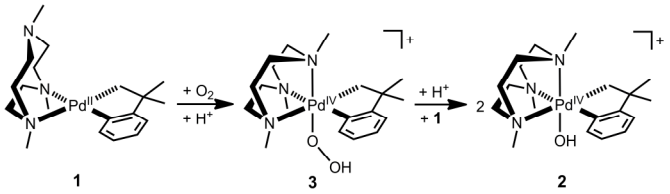


Fig. 1 ORTEP representation of **1** (left) and the cation of **[2]**ClO_4 (right). Selected bond lengths (Å) and angels (°): **1**, Pd1-C1, 2.015(3); Pd1-C8, 2.010(6); Pd1- N1, 2.215(4); Pd1-N3, 2.240(3); C1-Pd1-C8, 78.99(14); **2**, Pd1-C1, 2.024(2); Pd1-C8, 2.061(2); Pd1-O1, 2.0185(17); Pd1-N1, 2.263(2); 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).

The cyclic voltammogram (CV) of **1** in 0.1 M Bu_4NPF_6/MeCN shows a reversible oxidation wave at $E_{1/2}$ = −0.53 V (ΔE_p = 71 mV) vs. Fc^+/Fc,[7] which is significantly lower than those for analogous $Pd^{II}Me_2$ complexes with bidentate N-donor ligands,[6c] and only slightly higher than our previously reported complex $(Me_3tacn)Pd^{II}Me_2$.[6d] We attribute the low redox potential of **1** to the ability of the Me_3tacn 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]

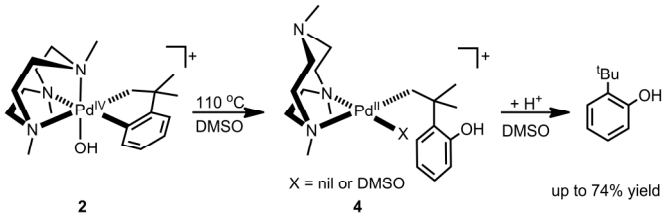
The observed low redox potential for **1** prompted us to study its oxidation by O_2. Exposure of a colorless solution of **1** to O_2 in presence of H_2O (10% H_2O:MeCN v:v) generates rapidly a yellow solution, and ^1H NMR analysis reveals the formation of a new species identified as the Pd^{IV} complex $[(Me_3tacn)Pd^{IV}(OH)(CH_2CMe_2C_6H_4)]^+$ (**2**). The yield of **2** can be increased to >98 % when the oxidation is performed in 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 O_2 reduction, and addition of acid or even use of a buffered solution ensures a rapid reduction of O_2 over the course of the reaction. In addition, complex **2** can also be rapidly generated in almost quantitative yield upon addition of 5 equiv H_2O_2 (Scheme 1). The Pd^{IV} product can isolated as the perchlorate salt, [**2**]ClO_4, 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 Me_2tacn 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 $Pd^{IV}(CH_2CMe_2C_6H_4)$ complex supports 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 of **2** in CD_3CN exhibits two doublets at 4.05 ppm and 3.97 ppm for the Pd-CH_2 group, supporting a geometry lacking a plane of symmetry.[7]



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

On the basis of previous mechanistic studies of the aerobic oxidation of $(Me_3tacn)Pd^{II}Me_2$,[6d] we propose an analogous mechanism for the O_2 activation by **1** that involves the formation of an Pd^{IV}-OOH intermediate followed by the formation 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 $[(Me_3tacn)Pd^{IV}(OH)(CH_2CMe_2C_6H_4)]^+$ (**2**, calcd. m/z 426.1739) and $[(Me_3tacn)Pd^{IV}(OOH)(CH_2CMe_2C_6H_4)]^+$ (**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 aerobic oxidation of $(Me_3tacn)Pd^{II}Me_2$, the oxidation of **1** by O_2 to yield an isolable Pd^{IV} product does not require and alkyl group transfer step that cannot occur for **2**.[6d] Thus, it can expected that O_2 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 from asymmetric dihydrocarbyl-Pd^{IV} complexes are rare.[11] When **2** was heated to 110 °C in DMSO, a new transient species (**4**) is observed followed by formation of 2-tert-butylphenol in up to 74% yield, as determined by NMR and GC-MS (Scheme 3).[12] C-O bond formation was also observed in other polar aprotic solvents: thermolysis in DMF leads to the formation of 2-tert-butylphenol in a comparable yield.[7] Interestingly, the organic product that would result from C(sp^3)-O reductive elimination, $PhCMe_2CH_2OH$, 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.

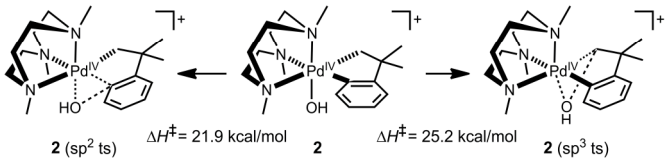


Scheme 3 Aryl C-O bond reductive elimination upon thermolysis of **2**.

The complex **4** was tentatively assigned as $[(Me_3tacn)Pd^{II}(CH_2CMe_2$-*o*-OH-$C_6H_4)]^+$ based on ESI-MS and NMR. ESI-MS of the reaction mixture shows the presence of a peak at m/z 426.1717 (calcd. $[(Me_3tacn)Pd^{II}(CH_2CMe_2$-*o*-OH-$C_6H_4)]^+$ 426.1731),[13] while the ^1H NMR spectrum reveals a singlet at 2.16 ppm for the Pd-CH_2 group, similar to complex **1** (singlet at 1.80 ppm) and in the typical range of 1.96-2.37 ppm for $Pd^{II}(CH_2CMe_2Ph)$[14] and $Pd^{II}(CH_2CMe_2$-*o*-$C_6H_4)$[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 complexes[16] or C_{aryl}-carboxylate elimination from Pd^{IV} bis-aryl complexes[17]), 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 concentration of **2** on the yield of 2-tert-butylphenol suggests that a bimolecular mechanism for C_{alkyl}-O bond formation is unlikely.

In order to provide insight into the observed selective C(sp^2)-O vs. C(sp^3)-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(sp^2)-O vs. C(sp^3)-O bond formation reactions were calculated to yield $\Delta H^{\ddagger}$ values of 21.9 and 25.2 kcal/mol, respectively (Scheme 4 and Figure S27). The lower enthalpy of activation by 3.3 kcal/mol for the former transition state supports the observed selectivity and suggests that C(sp^2)-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(sp^3)-F vs. C(sp^2)-F coupling from a Pd^{IV} center supported by a bidentate ligand (see below).[11]



Scheme 4 Calculated activation parameters for C(sp^2)-O vs. C(sp^3)-O bond formation reactivity of **2**.

The oxidation reactivity of **1** was also tested using other oxidants such as N-fluoro-2,4,6-trimethylpyridinium triflate, $PhICl_2$ and I_2. The corresponding products, $[(Me_3tacn)Pd^{IV}(F)(CH_2CMe_2C_6H_4)]^+$ (**5**), $[(Me_3tacn)Pd^{IV}(Cl)(CH_2CMe_2C_6H_4)]^+$ (**6**) and $[(Me_3tacn)Pd^{IV}(I)(CH_2CMe_2C_6H_4)]^+$ (**7**) were isolated, and **[6]ClO$_4$** and **[7]I** were structurally characterized to reveal a coordination geometry similar to that of **2** (Fig. S28).[7] Interestingly, no C-halide reductive elimination was observed upon prolonged heating of either **5**, **6**, or **7**. By comparison, examples of C(sp^3)-F and C(sp^2)-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 dissociation[11] or the presence of a hemi-labile sulfonamide ligand[18] 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(sp^2)-F bond formation reactivity and such intermediate is not easily accessible for **2**, most likely due to the presence of the three strong amine donors of Me_3tacn. The calculated transition states for the C(sp^2)-F and C(sp^3)-F bond formation reactions from **5** yield comparable $\Delta H^{\ddagger}$ values of 29.4 and 30.5 kcal/mol, respectively (Figure S27),[7] strongly suggesting that both types of C-halide bond formation from the $(Me_3tacn)Pd^{IV}$ 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 O_2 activation reactivity is due to the low oxidation potential of **1** supported by the tridentate amine ligand Me_3tacn 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(sp^2)-O vs. C(sp^3)-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 C-O vs. C-halide bond formation reactivity is currently explored for the development of selective aerobic C-O bond formation transformations.

Notes and references

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† Electronic Supplementary Information (ESI) available: Experimental details, spectroscopic characterization, computational details, and X-ray crystallographic data. See DOI: 10.1039/c000000x/

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13. The starting material **2** also has an m/z of 426.1739. However, the peak observed by ESI-MS persists even after **2** has reacted completely based on 1H NMR, indicating that a new product with a similar mass is formed (m/z calcd for **4**: 426.1731).
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