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Oxidation of a Monomethylpalladium(II) Complex with O₂ in Water: Tuning Reaction Selectivity to Form Ethane, Methanol or Methylhydroperoxide

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ABSTRACT: Photochemical aerobic oxidation of n-Pr₄N[(dpms)Pd^{II}Me(OH)], **5**, and (dpms)Pd^{II}Me(OH₂), **8**, (dpms = di(2-pyridyl)methanesulfonate) in water in the *pH* range of 6 – 14 at 21 °C was studied and found to produce, in combined high yield, a mixture of MeOH, C₂H₆ and MeOOH, along with water-soluble n-Pr₄N[(dpms)Pd^{II}(OH)₂], **9**. By changing the reaction *pH* and concentration of the substrate the oxidation reaction can be directed toward selective production of ethane (up to 94% selectivity) or methanol (up to 54% selective); the yield of MeOOH can be varied in the range of o-40%. The source of ethane was found to be an unstable dimethyl Pd^{IV} complex (dpms)Pd^{IV}Me₂(OH), **7**, which could be generated from **5** and MeI. To shed light on the role of MeOOH in the aerobic reaction, oxidation of **5** and **8** with a range of hydroperoxo compounds, MeOOH, *t*-BuOOH, H₂O₂, was carried out. The proposed mechanism of aerobic oxidation of **5** or **8** involves predominant direct reaction of excited methylpalladium(II) species with O₂ to produce highly electrophilic monomethyl Pd^{IV} transient that is involved in subsequent transfer of its methyl group to **5** or **8**, H₂O and other nucleo-philic components of the reaction mixture.

INTRODUCTION

Palladium complexes have received much attention as homogeneous catalysts for selective C-H oxidation of organic substrates.1-7 Among such processes oxidation of methane^{1,7} is one of the least developed and one of the most sought after transformations that can be used, in particular, for the development of economically viable routes for "methane upgrade" to higher hydrocarbons,⁸ and value-added oxygenates such as methanol. Taking into account the low cost of some simplest methane derived products MeOH, C₂H₆, etc., oxidants that may be practically important in such processes must be very cheap. In this regard the use of oxygen from the air as a virtually free oxidant is an excellent choice.^{7,9} While direct oxidation of palladium(o) species with dioxygen has been studied in some detail so allowing for substantial advances in aerobic C-H bond oxidations involving Pd°/Pd^{II} couple,⁴ direct aerobic oxidation of organopalladium(II) complexes, especially chemistry involving palladium transients in higher oxidation states, is poorly explored. As a result, the use of dioxygen in catalytic mediator-free chemistry of Pd^{II} compounds remains very limited.¹⁰⁻¹² There are only a few reports on the reactivity of Pd^{II}CH₃ complexes toward O_2 .¹³⁻¹⁵ The reported reactions of O_2 insertion into Pd-C bond produce methylperoxo Pd^{II} complexes and employ either a chain radical (Scheme 1, a)¹³ or a non-radical photochemical mechanism (Scheme 1, b).¹⁴ Oxidation of Pd^{II} hydrocarbyl complexes with O, to

generate related Pd^{III} and/or Pd^{IV} species has also been demonstrated (see, e.g., Scheme 1, c).¹⁶⁻¹⁸

Scheme 1. Examples of reactions between O_2 and $Pd^{II}CH_3$ complexes.^{13,14,17}

$$\begin{array}{c} \begin{array}{c} N & Me \\ Pd \\ N & Me \end{array} \begin{array}{c} O_{2}/radical initiator \\ C_{6}H_{6} \end{array} \begin{array}{c} N & O_{2}Me \\ Pd \\ N & Me \end{array} \begin{array}{c} (a) \\ Pd \\ N & Me \end{array} \end{array}$$

As a guideline for possible further development of aerobic organopalladium(II) chemistry one can use an analogy with dioxygen – platinum(II) chemistry. There are a number of parallels here. For instance, a homolytic¹⁹ or non-radical photochemical^{14,20} dioxygen insertion into Pt^{II}-CH₃ bond is also known for platinum analogs of complexes shown in Scheme 1 (a, b). In addition, dimethyl Pt^{II} complexes are known to react with O₂ in protic media to produce corresponding dimethyl Pt^{IV} hydroxo derivatives (Scheme 2, a).²¹ It is also known that the range of Pt^{II}

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complexes which can be involved in aerobic Pt^{II}-to-Pt^{IV} oxidation can be expanded when they are supported by facially chelating ligands such as 1,4,7-triazacyclononane²² or 1,3,5-triaminocyclohexane.²³ Importantly, the Pt^{IV}-C bond of the resulting oxidation products can be functionalized. Such reactions are facilitated when the supporting facially chelating ligands contain a good leaving group, as it is the case of di(2-pyridyl)methanesulfonate, dpms (Scheme 2, b).²⁴⁻²⁶ The dpms-enabled aerobic Pt^{II}-C(sp³) bond functionalization sequence can be very efficient and selective, e.g., MeOH can be produced in >97% yield, along with 3% Me₂O, starting from neutral zwitterionic (dpms)Pt^{II}Me(OH₂) complex 1 or its anionic derivative 2 and O₂ in water via the intermediacy of methyl Pt^{IV} hydroxo species 3.24 Hence, considering the Pt chemistry noted above, it would be interesting to see if a similar aerobic Pd^{II}-CH₂ bond oxyfunctionalization is possible for Pd analogs of complexes 1 and 2. Exploring chemistry of such Pd analogs may be even more intriguing since the selectivity of the oxidation reaction in Scheme 2 is pH – dependent: transformation of 2 to monomethyl Pt^{IV} complex **3** is impeded at $pH \ge 12$ and leads to the predominant Pt^{IV}-to-Pt^{II} methyl group transfer resulting in the formation of dimethyl Pt^{IV} hydroxo derivative 4 (Scheme 2, c).^{25,26} A similar observation has also been recently made by Goldberg using an analog of complex 2 supported by a tripod dipyrazolylacetate ligand.²⁷ Though complex 4 is robust and does not eliminate ethane, the knowledge of the mechanism of its formation may be useful for the possible development of similar palladium - based systems for aerobic methane-to-ethane oxidative coupling. In fact, first examples of oxidative aerobic coupling of dimethyl Pd^{II} complexes to form ethane via intermediacy of Pd^{IV} species were reported recently by Mirica.^{16,18} The same group has described a photochemical elimination of ethane from a monomethyl Pd^{III} complex²⁸ whereas Canty and Sanford have demonstrated oxidative coupling of monomethyl Pd^{II} species to form ethane using some other oxidants.⁸ Notably, though monomethyl Pd^{II} species are usually considered to be most relevant to methane C-H activation by Pd^{II} complexes,^{1,7} oxidative aerobic coupling of monomethyl Pd^{II} complexes to form ethane remained so far unknown.

Scheme 2. Aerobic oxidation of dimethyl Pt^{II} complexes (a-c) and functionalization of Pt^{II} -CH₃ bond (b).



It is also important to note that aerobic functionalization of Pd^{II}-CH₃ bond in either mono- or dimethyl Pd^{II} compounds to form MeOH has never been documented. The only example of formation of methanol in a low yield in a photochemical reaction of O₂ with a monomethyl Pd^{III} complex was reported by Mirica.²⁸ Hence, the goal of this work was to find out if the aerobic functionalization in water of a Pd^{II} analog of complex 2, such as 5 (Chart 1), might lead to Pd^{IV} intermediates 6 and 7, analogs of 3 and 4, that can be highly reactive at the production of MeOH and ethane, respectively. We were interested to see if this type of reactivity can compete with or complement the insertion of O₂ into Pd^{II}-C(sp³) bond described in Goldberg or Britovsek's works.^{13,14} In this paper we report results of such study revealing that the aerobic functionalization of the monomethyl Pd^{II} complex **5** is viable and it can lead to selective formation of either ethane or methanol with or without concomitant formation of methylhydroperoxide. We also disclose some means to control the reaction selectivity with respect to each of these three products.

Chart 1. DPMS-supported palladium analogs of complexes 2-4.



RESULTS AND DISCUSSION

a. Oxidation of n-Pr₄N[(dpms)Pd^{II}Me(OH)] with O₂ in water.

a1. Product distribution. The anionic monomethyl Pd^{II} complex [(dpms)Pd^{II}Me(OH)]⁻ in the form of a watersoluble tetra-*n*-propylammonium salt 5 was prepared using standard synthetic protocols (see SI). Similar to the Pt^{II} analog 2, aqueous solutions of 5 are basic; the *pH* of a 4-7 mM solutions typically used in our experiments is ~10.6, which translates to about 6% fraction of the corresponding protonated species (dpms)Pd^{II}Me(OH₂), 8, with an estimated pK_a of 9.4. Exposure of such solutions to air or pure O, atmosphere at 1 atm pressure in a Teflon-sealed NMR tube leads to complete consumption of 5 after 5-6 days at 21 °C accompanied by the formation of dihydroxo Pd^{II} complex **9** and ethane as two major products along with small amounts of an unidentified black solid and methanol (eq 1; Table 1, entries 1-2). No transient Pd complexes were observed in the course of these experiments by means of 'H NMR spectroscopy. Hence, dpms ligand enables an unprecedented selective aerobic oxidative coupling of a monomethylpalladium(II) species to form ethane with 80-90% selectivity. Importantly, this tripod ligand also allows for the formation of methanol, albeit in a low yield, a type of reactivity which, to the best of our knowledge, has never been observed previously in aerobic reactions of methylpalladium(II) compounds.

(c)

Table 1. Summary of product distribution in complete oxidation of *n*-Pr₄N[(dpms)Pd^{II}Me(OH)], 5, in NMR tube under O₂ atmosphere and 20 °C.^a

Entry	Conditions	Reaction time	C ₂ H ₆ , %-/ CH ₄ , %	MeOH, %	MeO ₂ H, %	Other Products, %
1	Air, <i>pH</i> 10.6	5 days	89 ± 3	9 ± 2	0	9 , 8 ₃ ± 5 ^b
2	O ₂ , <i>pH</i> 10.6	6 days	82 ± 4	16 ± 3	0	9 , 83 ± 5 ^b
3	O₂, <i>pH</i> 14.0 ^c	4 days	44 ^d	54 ± 2	4 ± 1	9 , 83 ± 5 ^b
4	O ₂ , <i>pH</i> 14.0 ^{c, e}	2 days	31 ^d	49 ± 1	20 ± 1	9 , 71 ± 1 ^b dpms ⁻ , 21 ± 1
5	Ar, <i>pH</i> 10.6 ^a	7 days	55 ± 3 / 43 ± 1	0	0	dpms ⁻ , 47 ^b
6	Ar, <i>pH</i> 10.6, TEMPO ^f	13 days	63 ± 9 / 27 ± 8	0	0	Me-TEMPO, 7 ± 2^{b}

^a All the reactions in Table 1 were carried out under standard ambient fluorescent lamp lighting. Yields are based on initial [Pd^{II}Me]; ^b formation of small amounts of a black solid was observed, which may be the reason for about 15% lower than expected dpms ligand balance; ^c 1.0 M KOH solution; ^d Calculated assuming 100% methyl group balance. Poor solubility of ethane in this solution precluded quantitative determination of ethane yield; ^e Irradiation with 26 W CFL; no stirring ^f 1.9 equiv. of TEMPO additive.



Based on the fact that the rate and selectivity of the oxidation of the Pt^{II} analog 2 with O₂ are strongly *pH* dependent,²⁶ we hypothesized that the effect of *pH* may also be pronounced in aerobic oxidation of **5**. The effect of the reaction *pH* on the product distribution was probed using 1.0 M KOH (*pH* ~ 14.0) and some buffer solutions. The *pH* change from 10.6 to 14.0 turned out to have the most dramatic effect on the reaction (1) selectivity (Table 1, entry 3 vs. 2): the yield of methanol has almost tripled up to 54% after 4 days and a small amount of methylhydroperoxide (4%) was detected among the reaction products.

All the experiments in Table 1 were conducted using standard borosilicate glass vessels under standard lighting conditions employing fluorescent hood lights as the only light source. In the course of these experiments it was noticed that the reaction rate and selectivity are changed when the mixtures are exposed to more or less light (*vide infra*). Notably, when the reaction was performed under irradiation with 26 W CFL at *pH* 14.0 the yield of methylhydroperoxide could be increased up to 20% (entry 4).

Methane was not detected among reaction products in either of our aerobic experiments. By contrast, when argon was used instead of air or oxygen, methane formed in 43% yield after 7 days (entry 5). Notably, in the presence of 1.9 equivalents of TEMPO formation of Me-TEMPO adduct was detected by means of ¹H NMR spectroscopy and electro-spray mass-spectrometry (entry 6) so suggesting that methyl radicals may be involved in the anaerobic reaction. Formation of methane in the course of decomposition of monomethyl Pd^{II} complexes in the absence of any oxidants was also reported by Sanford.⁸ It is important to note that in all of our closed-vessel experiments where reliable integration of the alkane signals was possible (that is, all experiments except entries 3-4 where 1M KOH was used) the methyl group balance was reasonably close to 100%.

a2. Factors affecting rate of oxidation of complex 5 (eq 1) and possible mechanisms of O_2 activation.

The effect of various factors on the rate of reaction in eq 1 was analyzed next with the goal to get some insight into the reaction mechanism. To maintain a steady concentration of the oxidant in the solution the experiments were carried out with rapid stirring under ambient pressure of oxygen gas at 20 °C. Under these conditions the amount of ethane formed could not be quantified. Hence, the yield of ethane was estimated assuming 100% methyl group balance as it was observed in our sealed flask experiments (Table 1). The oxidation was monitored by 'H NMR spectroscopy for ~3-4 reaction half-lives and was found to follow *first order kinetics* in the complex **5** concentration (Table 2, entries 1-5).

a) Oxygen partial pressure. A comparison of the experiments performed under air and pure O_2 atmosphere at *pH* 10.6 (entries 1 and 2, respectively) shows that an ~5-fold increase in the partial pressure of oxygen leads to only ~25% faster rate of the overall reaction (eq 1) and does not change significantly its selectivity. Hence, for the most of the contributing processes, the rate-determining step of the reaction does not involve O_2 .

b) TEMPO additives. The reaction rate is moderately inhibited by an additive of 2.4 eq of TEMPO (entry 3) pointing to a radical-like reactivity of the reaction intermediates. Formation of Me-TEMPO adduct was detected in those experiments by means of 'H NMR spectroscopy.

c) Solution pH. The most significant change of the rate and/or selectivity of the reaction between 5 and O_2 could

Table 2. Effect of	f various facto	rs on the	kinetics of	f oxidation of	'6 mM	I complex	5 at 20 °C."

Entry	Conditions	$t_{_{1/2}}$, h	MeOH, %	$C_{2}H_{6}^{,b}\%$	MeO₂H, %	Other Products, %
1	Air, <i>pH</i> 10.6	31 ± 1	7 ± 2	94	0	9 , 55 ± 6 ^c
2	O ₂ , <i>pH</i> 10.6	25 ± 1	12 ± 2	88	0	9 , 81 ± 4 $^{\rm c}$
3	O₂, <i>pH</i> 10.6, TEMPO ^d	38 ± 1	11 ± 1	80	о	9 , 89 ± 4 ^c Me-TEMPO, 9 ± 1
4	O ₂ , <i>pH</i> 6.8 ^e	4.8 ± 0.1	10 ± 1	90	0	11 , 70 ± 1 $^{\circ}$
5	O₂, <i>pH</i> 14.0 ^f	16.0 ± 0.2	51 ± 4	44	5 ± 1	9 , 99 ± 5
6	O₂, <i>pH</i> 10.6, 1.0 M KNO₃	15.8 ± 0.3	9 ± 2	91	о	9 , 69 ± 18
7	O₂, <i>pH</i> 14.0, [†] Light ^g	4.4 ± 0.1	41 ± 1	45	14 ± 2	9 , 98 ± 2 $^{\circ}$
8	O₂, <i>pH</i> 14.0, ^f Dark ^h	187	6	94	0	dpms ⁻ , 70 ^c

^a Yields are based on the amount of **5**; typical concentration [**5**] 6-7 mM;^b calculated assuming 100% methyl group balance; ^c formation of black solid was observed; ^d 2.4 equiv. of TEMPO; ^e KH₂PO₄/K₂HPO₄ buffer; ^f 1.0 M KOH solution; ^g Reaction mixture was irradiated with 26 W fluorescent lamp; ^h reaction flask wrapped with aluminum foil.

be achieved by changing its pH from the "native" value of 10.6 to either lower or higher side. A 5-fold acceleration without change in the selectivity in MeOH was observed at a lower pH 6.3 (entry 4). In turn, a 4-fold increase in selectivity with respect to MeOH with a modest 30% increase of the reaction rate was seen at pH 14.0 (entry 5 vs. 2). The effect of the ionic strength of 1.0 M KOH solution may be responsible for the latter reaction rate increase but not its selectivity change, as it is seen from the results of oxidation at pH 10.6 in the presence of 1.0 M KNO₃ (entry 6 vs. 2).

d) Effect of light. Finally, the photochemical nature of the reaction in eq 1 was demonstrated by i) running it in the presence of 26W CFL bulb placed near temperature – controlled reaction flask; the reaction rate increased ~5-fold (entry 7) and ii) running the oxidation in the dark (aluminum foil wrapping; entry 8). In the latter case the reaction was slowed down more than tenfold.

Discussing possible mechanisms of O_2 activation in our system it worth noting that the formation of MeOOH, the effects of TEMPO additives and light on the reactivity of complex **5** are reminiscent of a chain radical O_2 insertion into Pd^{II}-CH₃ bond observed for a bipyridyl dimethyl Pd^{II} complex (Scheme 1a).¹³ The methylhydroperoxide may be released into the reaction mixture as a result of subsequent reaction with the solvent (eq 2).

$$\begin{array}{c} H \xrightarrow{SO_3^{\bigcirc} n_{\mathsf{P}}r_4 N^{\oplus}} \\ N \xrightarrow{N} Pd^{\parallel} \xrightarrow{\mathsf{Me}} \\ \mathbf{5} \end{array} \xrightarrow{\mathsf{O}_2, hv} \xrightarrow{\mathsf{N}} Pd^{\parallel} \xrightarrow{\mathsf{O}_2 Me} \\ N \xrightarrow{\mathsf{N}} Pd^{\parallel} \xrightarrow{\mathsf{O}_2 Me} \\ \mathbf{0} H \xrightarrow{\mathsf{H}_2 O} \\ \mathbf{9} + \mathsf{Me}O_2 H \quad (2) \end{array}$$

At the same time, a modest inhibition of the reaction (1) by TEMPO and the lack of noticeable changes in its selectivity in the presence of TEMPO (entry 3 vs. 2) support the notion that the chain radical O_2 – insertion is not the major mechanism of O_2 activation in reaction (1) under ambient-light conditions.

A non-radical photochemical O_2 insertion into Pd^{II} - CH_3 bond described by Britovsek (Scheme 1b)¹⁴ may be considered as another possible mechanism of O_2 activation in reaction (1) also leading to the formation of Pd^{II} -OOMe species via a Pd^{IV} peroxo methyl intermediate. The Britovsek's reaction model suggests an involvement of a dinuclear excited triplet species which, if applied to our system, translates into second order rate of disappearance in [5]. This mechanism is also unlikely to be predominant in our system since reactions listed in Table 2 (entries 1-5) follow first order kinetics in [5].

Since none of the reaction models above can account for our experimental observations, we propose that a direct photochemical oxidation of 5 to produce an electrophilic Pd^{IV} complex 6 (Chart 1; see section f) might constitute a third mechanistic possibility for O_2 activation in reaction (1). In such a case the aerobic reaction (1) would follow a first order dependence in [5], consistent with our observations. In this mechanism formation of MeOOH may result from a nucleophilic attack of H₂O₂ at the methyl ligand in complex 6 (*vide infra*).²⁹

b. Oxidation of n-Pr₄N[(dpms)Pd^{II}Me(OH)] with ROOH in water (R = Me, *t*-Bu, H).

The fact that methylhydroperoxide is observed as one of the reaction products in our aerobic experiments at pH 14.0 prompted us to consider potential involvement of MeOOH in the oxidation reaction (eq 1) as an intermediate which is more reactive and hence "invisible" at lower pH values. It is worth noting that the ability of H₂O₂ ³⁰ and some alkyl hydroperoxides^{16,28} to oxidize organopalladium(II) complexes has been documented previously.

Since MeOOH is not commercially available and is a dangerous to work with compound, dilute solutions of MeOOH (~0.3 mmol/L) were generated at pH 14.0 using reaction (1) carried out under light. These solutions contained no unreacted complex **5**; dihydroxopalladium(II) **9** was the only soluble Pd-containing complex. The content of CH₃OH and CH₃OOH was quantified using ¹H NMR

Table 3	. Results of the	oxidation of o.6	o mM <i>n</i> -Pr₄N	[(dpms)Pd ¹¹	Me(OH)] with	MeOOH in water	at 20 °C.ª
			4 1	L(F /			

Entry	Conditions	Conversion, % / Reaction time	MeOH, equiv. ^b	Other Products, %
1	<i>pH</i> 14.0, ^c MeOOH (2.5 equiv.)	100 / 16 h	1.62 ± 0.05	-
2	<i>pH</i> 5.7, ^d MeOOH (2.0 equiv.)	100 / 5 h	1.16 ± 0.09	$LPd^{IV}Me_2(OH)$, 28 ± 1

^a Yields are based on the initial [Pd^{II}Me]; ^b The amount of MeOH formed with respect to that of **5**; ^c 1.0 M KOH solution; ^d pH adjusted with aqueous solution of HBF₄.

spectroscopy using 1,4-dioxane as internal standard. Stability of the resulting solutions at pH 14.0 was tested and no noticeable change in MeOOH concentration was observed in the course of at least 2 days (Table S9). Upon mixing of solutions containing 5 and MeOOH to allow for 2.5:1 MeOOH:5 ratio, the pH of the MeOOH solution was adjusted by addition of 50% aqueous HBF₄ when necessary and the mixture was monitored by ¹H NMR spectroscopy.

In the reaction carried out at pH 14.0 complex **5** was consumed in the course of 16 h. Intriguingly, the oxidation produced 1.62±0.05 mol of methanol per mol of **5** (Table 3, entry 1). Assuming that 1 equivalent of MeOH is liberated from MeOOH as a result of its reduction with **5** (*vide infra*), the additional 0.62±0.05 equivalents should have originated from the methyl ligands of **5**. We propose that MeOH produced beyond the expected 1 equivalent is derived from complex **6** (see section d), as shown in eqs 3 (R = Me) and 4.



Oxidation of **5** with MeOOH at *pH* 5.7 (Table 3, entry 2) was complete in 5 h, that is noticeably and expectedly²⁶ (using analogy with Pt^{II} complex 1) faster than at *pH* 14.0. The reaction produced 1.16±0.09 mol of methanol per mol of **5**. Importantly, formation of an intermediate dimethyl Pd^{IV} complex 7 along with dihydroxopalladium(II) species **9** (eq 5; R = Me) was also detected. The amount of **7** increased during initial stages of reaction reaching a maximum yield of 28%; the complex disappeared by the end of the reaction.



The reactivity observed in our experiments involving **5** and MeOOH was found to be common also for some other hydroperoxides, *tert*-butylhydroperoxide and hydrogen peroxide (eqs 3-5, R = H, *t*-Bu; see also SI). When either of

these oxidants was used in the reaction with **5** in water at *pH* 5.7, 10.6 and 14.0 formation of MeOH was detected with the highest MeOH yield, 32% for H_2O_2 and $61\pm6\%$ for *t*-BuOOH as oxidant, seen at *pH* 14.0. In the latter case *quantitative* formation of *t*-BuOH (99% NMR yield) was also observed. Notably, one more reaction product, MeOOH, was also detected in the oxidation of **5** with H_2O_2 , and *t*-BuOOMe in the oxidation with *t*-BuOOH when these reactions were carried out at *pH* 14 and 6 (see SI).

Based on these observations and the proposed intermediacy of monomethyl Pd^{IV} complex **6** in the oxidation of **5** with O₂ (eq 1), methanol may result from i) the reduction of transient MeOOH with **5** (eqs 3, 5; R = Me) and ii) from nucleophilic attack by water solvent or OH⁻ at the monomethyl Pd^{IV} complex **6** (eq 4). A similar nucleophilic attack at **6** involving H₂O₂ instead of water would also lead to the formation of MeOOH that we observed at *pH* 14.0.

As in the case of the reaction with MeOOH, the reaction of **5** with H_2O_2 (except at *pH* 14.0) was fast and complete in the course of a few minutes at 21 °C. Formation of the dimethyl Pd^{IV} intermediate **7** was seen in these experiments in yields ranging from 15-50%. The oxidation of **5** with *t*-BuOOH at *pH* ≤ 14.0 was also fast enough to observe transient formation of **7**.

Production of ethane was detected in all the oxidation experiments above where MeOOH, *t*-BuOOH or H_2O_2 were used as oxidants. The source of ethane was found to be the dimethyl Pd^{IV} complex 7. In contrast to its thermally robust dimethyl Pt^{IV} analog 4 (Scheme 1), the Pd^{IV} complex 7 eliminates ethane readily at 21 °C (eq 6). This complex was prepared and characterized independently as described below.



c. Synthesis of (dpms)Pd^{IV}Me₂(OH)

The dimethyl Pd^{IV} complex 7 could be generated by stirring aqueous solutions of complex 5 with methyliodide at 5 °C (eq 7). This reaction can be viewed as a formal $S_N 2$ attack of the nucleophilic methylpalladium(II) species 5 at the electrophilic Mel.³¹ The reaction is relatively slow and elimination of ethane from the thermally unstable 7 (eq 6) is competitive with the formation of 7. As a result,



the fraction of 7 in the reaction mixtures increases in the course of the first 40 min and then remains steady at 40-47% level during the following hour (Chart S4) so allowing for a reliable NMR characterization of 7. According to ¹H NMR spectroscopy, complex 7 is C_1 – symmetric; selective NOE experiments show interaction between the axial methyl ligand (2.91 ppm) and both *ortho*-C-H protons of the dpms ligand pyridine rings (Fig. S12). An interaction between the axial and equatorial (2.51 ppm) methyl ligands is also observed.

Chart 2. NOE interaction in DPMS-supported palladium complex 7.



Notably, complex 7 does not produce any MeOH even at *pH* 14.0. When temperature of the solutions containing 7 is raised to 21 °C, ethane elimination becomes fast with the half-life of 6 min for this first order process (Chart S5). The short reaction half-life suggests that complex 7 can be observed at this temperature only when the rate of its formation is much faster or comparable to that of the ethane elimination. In fact, this condition was never met in our aerobic oxidation experiments as well as in the oxidation of 5 with H_2O_2 at *pH* 14.0 so allowing to account for our failure to detect 7 in the corresponding reaction mixtures.

d. Competitive formation of 7 and methanol via proposed methylpalladium(IV) transient 6.

A much faster conversion of **5** to mixtures of dimethyl Pd^{IV} complex **7**, dihydroxo Pd^{II} derivative **9** and MeOH can be achieved using a more efficient oxidant, $NaIO_4$ (eq 8; R = H).



The oxidation is complete after 11 minutes at pH 10.6 and 21 °C leading to 27% yield of MeOH, 31% yield of 7 and free ethane. Overall, this chemistry is reminiscent of the reactions of **5** with hydroperoxides (eqs 3 and 5) and, presumably, also proceeds via intermediacy of a highly electrophilic monomethyl palladium(IV) complex **6** (eq 9):



An indirect evidence for the transient formation of intermediate **6** can be obtained from the oxidation of **5** with NaIO₄ in D₂O/CD₃OD (eq 9). Analysis of the products by ¹H NMR spectroscopy shows that CH₃OCD₃ (32% yield) is formed along with CH₃OH (32% yield). These products may result from concurrent reactions of **6** with OCD₃⁻ and OH⁻ respectively (eq 10). Remarkably, the Pt^{IV} analog of **6**, complex **3**, is much less electrophilic and is virtually unreactive with respect to such nucleophiles.^{26,29}



Our attempts to observe formation of **6** in reactions between **5** and **3** equiv. NaIO₄ were unsuccessful even at temperatures as low as -60 °C using D₂O-CD₃OD mixtures. Complex **5** was fully consumed within first 5-10 minutes producing the dimethyl Pd^{IV} complex **7** and two more C_1 - symmetric *d*imethylpalladium(IV) species (dpms)PdMe₂X in a 54% combined yield (see SI); here X was presumed to be OMe (eq 8; R = Me) and IO₄. All three (dpms)PdMe₂X complexes decompose rapidly at 21 °C with elimination of ethane with a half-life ranging between **3** and 6 min.

It is also apparent that, similar to (dpms)Pt chemistry,²⁶ a Pd^{IV}-to-Pd^{II} methyl transfer from the electrophilic methyl Pd^{IV} complex **6** to a nucleophilic species **5** may be involved (eq 11). The Pd^{IV}-to-Pd^{II} methyl transfer reaction (11) occurs concurrently with reactions (4) and (10) where **6** reacts with hydroxide and methoxide anions, respectively, acting as nucleophiles.



e. Mechanism of oxidation of Pr₄N[(dpms)Pd^{II}Me(OH)] via O₂ insertion into Pd^{II}-C bond

As discussed in section (b), MeOH and ethane in reaction (1) may form both via intermediacy of MeOOH and monomethylpalladium(IV) transient **6**, respectively. Scheme 3 summarizes the hypotheses concerning a possible mechanism of such photo-induced transformations. The first step is the photo-excitation of **5** to produce, after a spin interconversion, a triplet spin-isomer ³[5] (step *a*). This photo-excitation should be rate-limiting consistent with the observed first order of reaction (1) in complex **5**. Subsequent fast trapping of ³[5] with O₂ leads to the O₂ insertion into Pd-CH₃ bond of ³[5] to form a palladium(II) methylperoxo species (step *b*; see section *g* for more de-

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58 59 60 tail). Hydrolysis of the palladium(II) methylperoxo species generates free methylhydroperoxide (step *c*). The MeOOH is then converted to MeOH by another equivalent of **5** to produce a highly electrophilic monomethylpalladium(IV) transient **6** (step *d*). This *pH* – dependent reaction is fast at $pH \le 11$ so that MeOOH does not accumulate in the mixtures and is undetectable by means of ¹H NMR spectroscopy. By contrast, the reaction is slow enough at *pH* 14.0 so that MeOOH is an observable product of photo-oxidation (1).

The transient **6** may be involved in two concurrent processes: i) a nucleophilic reaction with the solvent or hydroxide anion (S_N 2) leading to a second equivalent of MeOH (step *e*) and ii) a Pd^{IV}-to-Pd^{II} methyl transfer reaction leading to a dimethyl Pd^{IV} intermediate **7** (step *f*) that is responsible for ethane production (step *g*) in this reaction sequence.

If the step *f* fully outcompetes *e*, the MeOH : C_2H_6 ratio is expected to be 1 : 1, whereas if step *e* is also competitive, the MeOH : C_2H_6 ratio should be greater than 1 : 1. In the latter case this ratio is expected also to grow as *pH* increases since greater concentration of the nucleophile, OH⁻, involved in the reaction *e*, becomes available. Indeed, when ROOH are used as oxidants (R = H, Me, *t*-Bu) in their reactions with complex **5** (see Table 3), both pathways, *e* and *f*, are operational and competitive. For instance, when MeOOH is used at *pH* 14.0, the observed MeOH : C_2H_6 ratio is about 1.62 : 0.38 = 1.6 times greater contribution of the reaction *e* vs. *f*, so that in 1.0 M KOH solution the hydroxide anion is about 1.6 times more competitive than ~5mM **5** in the reaction with **6**. Hence, **5** is (1.0 / 0.005) / 1.6 \approx 100 times more nucleophilic than OH⁻. In turn, at *pH* 5.7 the observed MeOH : C₂H₆ ratio is 1.16 : 0.84 = 58% : 42% which suggests that ~5 mM complex (dpms)Pd^{II}Me(OH₂), **8**, is about 0.84 / 0.16 = 5.3 times more competitive than 55 M H₂O in their reaction with **6**. Hence, **8** is (55 / 0.005) × 5.3 \approx 60000 times more nucleophilic than H₂O.

We can now compare MeOH : C_2H_6 ratios in reactions of **5** at pH 14.0 when O_2 is the oxidant that range from 49 : 31 to 54 : 44 (Table 1, entries 4 and 3, respectively) vs. 80 : 20 (see above) when MeOOH is the oxidant. These ratios at a lower $pH \sim_7 are 10$: 90 with O₂ as oxidant (Table 2, entry 4) vs. 58 : 42 when MeOOH is the oxidant. In both cases in the aerobic reaction the observed fraction of MeOH is always lower than in the analogous reactions utilizing MeOOH as oxidant. The observed dramatic difference in the reaction selectivity implies that the predominant mechanisms leading to the formation of MeOH and ethane do not involve intermediacy of MeOOH either at pH 14.0 or pH 6-7. Therefore, the mechanism in Scheme 3 can have only a minor contribution to the overall reaction (1). Hence, we propose another mechanism leading to complex 6 as discussed in the following section.

f. Direct photochemical formation of complex 6 with O_2 as oxidant

The alternative mechanism for the formation of MeOH and ethane is given in Scheme 4 for the methylpalladium(II) aqua complex **8** as an example. A similar reaction sequence can be written for its hydroxo derivative 5.

^{hv} → ³[(dpms)Pd<mark>Me</mark>(OH)]⁻ (dpms)Pd^{II}Me(OH)⁻ (a) Photo-excitation (RDS): 5 ³[5] → (dpms)Pd^{II}(OH)(O₂Me)⁻ (b) ³[(dpms)PdMe(OH)]⁻ O₂ insertion: ³[5] Formation of MeOOH: $(dpms)Pd^{II}(OOMe)(OH)^{-} + H_2O$ (dpms)Pd^{II}(OH)₂⁻ + MeOOH (C) 9 eO₂H. H₂ (d) Reduction of MeOOH to MeOH: (dpms)Pd^{II}Me(OH) MeOH 5 óн - OH[.] 6 Elimination of MeOH from MePd^{IV}: OH⁻ or H₂O (competitive at pH 14.0) MeOH (e) 9 or 11 + S_N2 ÓН 6 Pd^{IV}-to-Pd^{II} methyl transfer: (predominant at pH 6.7) 5 or 8; - 9 or 11 (f) OH⁻ or H₂O Ethane elimination from Me₂Pd^{IV}: (g) 9 or 11

Scheme 3. Mechanism of MeOOH and MeOH formation in reaction (1) via initial photochemical O₂ insertion into Pd^{II}-C bond.

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Complex 8 is expected to be the predominant (> 99%) palladium - containing species in ~ 6 mM solution at pH 6.7; this complex should be a minor (~6%) species at pH10.6 and a trace component at pH 14. According to the mechanism in Scheme 4, the Pd^{II} complex 8 is photoexcited (a formal rate-determining step of the overall oxidation reaction) to produce, after a spin interconversion, a triplet spin-isomer ³[8] (vide infra). The triplet transient is trapped by O₂ to form a derived hydroperoxo methylpalladium(IV) species 10. In support of the viability of the formation of Pd^{IV} intermediates in direct aerobic oxidation of palladium(II) methyl species, precedents involving dimethyl Pd^{II} complexes were reported earlier by Mirica.¹⁶⁻¹⁸ In contrast to these previous observations, the aerobic oxidation in Scheme 4 is photo-induced and involves monomethyl palladium(II) species.

Scheme 4. Direct photochemical oxidation of 5 or 8 with O_2 to produce complex 6.



As in the case of the monomethyl hydroxopalladium(IV) **6** (Scheme 3), several competing reactions are possible that involve **10**. Among them are: i) a nucleophilic attack by methylpalladium(II) complex **8** (paths *a*, *b*) leading to a Pd^{IV}-to-Pd^{II} methyl transfer product **7**; H_2O_2 is another expected product here (path *a*), or/and an OH-group transfer via O-O cleavage to produce **6** (path *b*), and ii) a nucleophilic attack by water and/or H_2O_2 to produce MeOH and/or MeOOH, respectively (path *c*). The path-

way (c) with H_2O_2 as a nucleophile may serve for the MeOOH production in our reaction mixtures at *pH* 14.0, besides insertion of O_2 into Pd^{II}-C bond (eq 2).

g. Time-dependent DFT analysis of ³[5] and ³[8].

To shed light on the anticipated reactivity toward O_2 of the triplet species 3 [5] and 3 [8] that are expected to result from photo-excitation and spin interconversion involving 5 and 8, respectively, we used methods of time-dependent Density Functional Theory (TDDFT). The geometry optimization for 5 and 8 and calculations of the 30 lowest energy singlet and triplet excited states were done for water as a solvent (see SI for details).

The calculated UV-VIS spectrum of the anionic complex 5 contains multiple electronic metal-to-ligand charge transfer (MLCT) transitions in the range of wavelengths 420 – 600 nm. Most of the excitations correspond to the transitions of the metal electrons promoted from its 4d orbitals to the π^* orbitals of the pyridine rings (see SI). In particular, the lowest energy excitation at 549 nm leading to a singlet spin-isomer ¹[5549] involves an electron transition from the metal d_{zz} orbital to a π^* pyridine rings molecular orbital. A higher energy excitation at 355 nm leading to a spin-isomer ¹[5355] corresponds to a transition from the metal d_{z_2} orbital to a predominantly Pd-C σ^* orbital. Analysis of the triplet excitations of 5 allows to find the triplet excited states with similar spin populations (see SI for details). For instance, the lowest energy triplet excited state 3[5,77] has two singly occupied molecular orbitals, SOMO, which is predominantly the metal $4d_{z2}$ orbital, and SOMO+1, which is one of the pyridine π^* -orbitals (Fig. 1, a-b).

Similar analysis was performed for the aqua complex **8**. Compared to **5**, the absorption bands of the MLCT are blue-shifted spanning from 350 - 550 nm (Fig. 1). The lowest energy excitation at 512 nm leading to a spin-isomer $[\mathbf{8}_{512}]$ involves an electron transition from the metal d_{zz} orbital to a π^* pyridine rings orbital (89% contribution) and a Pd-C σ^* -orbital (11%).

Since a fluorescent lamp light spectrum has greatest intensity in the visible range, we may limit our analysis to the MLCT transitions above. For both lowest energy triplet excited states, ${}^{3}[\mathbf{5}_{575}]$ and ${}^{3}[\mathbf{8}_{582}]$ (Fig. 2), the highest energy SOMO+1 is predominantly one of the pyridine π^* -orbitals where the unpaired electron can be "picked up" by an O₂ molecule to produce a superoxide anion-radical and a corresponding Pd^{III} metal-radical (Scheme 5). In the case of the reaction sequence involving ${}^{3}[\mathbf{8}_{582}]$ a subsequent radical pair collapse may be assisted by a proton transfer from the nearby aqua ligand to give the Pd(IV) intermediate **10**. Such reaction sequence may be less efficient for ${}^{3}[\mathbf{5}_{575}]$ at *pH* 14.0 and the corresponding spinisomer ${}^{3}[\mathbf{5}_{575}]$ may decay back to **5**.

A higher-energy spin-isomer of 3 [5], 3 [5₄₅₅], with the SOMO+1 being essentially a Pd-CH₃ antibonding orbital, is expected to have a weakly bound Me ligand which may be abstracted by O₂ to form eventually a Pd^{II}

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Figure 1. Singly occupied molecular orbitals, SOMO and SOMO+1, corresponding to a triplet excited spin-isomer ${}^{3}[5_{575}]$ (a, b) and ${}^{3}[8_{582}]$ (c, d).





methylperoxo complex. A similar methyl radical abstraction reaction may lead to Me-TEMPO when TEMPO is present in reaction mixtures. Similar pathways may be considered for ${}^{3}[8_{582}]$ as well.

We hypothesize that in the absence of O_2 some of the spin-isomeric triplet species ${}^{3}[5]$ and ${}^{3}[8]$ may be involved in a homolytic Pd^{III}-CH₃ bond cleavage resulting in a hydrogen atom abstraction / methane formation.

Table 4. Effect of $[Pd^{II}Me]$ on the product distribution in the oxidation of *n*-Pr₄N[(dpms)Pd^{II}Me(OH)] with O₂ in water at *pH* 14.0.^{a,b}

Entry	[5], mM	Conversion / Reaction time	MeOH (%)	MeOOH (%)	C ₂ H ₆ ^c (%)	Other Products (%)
1	13.2	98 % / 4 days	54 ± 2	4 ± 1	42	9 , 82 ± 5
2	1.3	100 % / 4 days	44 ± 2	30 ± 1	26	9 , 92 ± 6
3	0.7	100 % / 4 days	43 ± 1	40 ± 3	17	9, 69 ± 2 dpms ⁻ , 27 ± 7

^a Yields are calculated based on initial [Pd^{II}Me]; ^b 1.0 M KOH solution; ^c Calculated assuming 100% mass balance.

h. Controlling the C_2H_6/MeX and MeOH/MeOOH ratios: effect of $[Pd^{II}]$ on product distribution

Three organic products of aerobic Pd^{II} -CH₃ bond functionalization resulting from reaction (1), MeOH, MeOOH and ethane, could be produced in different ratios in our experiments. Some results pertinent to control of the reaction selectivity are summarized here. With the goal to maximize the yield of the oxygenated products, MeOH and MeOOH, resulting from reaction (1), one should perform the aerobic oxidation of **5** at *pH* 14.0 (Table 2, entry 5).

Since the rate of formation of ethane is expected to be second order in [5] (Scheme 4, path *a*), one would expect that at a lower [5] formation of ethane should become less competitive as compared to MeOH (Scheme 4, path *c*) which is expected to be first order in [5]. In fact, decreasing concentration of the methylpalladium(II) complex 5 about 10-20 – fold from 13.2 mM (Table 4, entry 1) to 1.3 mM (entry 2) and 0.7 mM (entry 3) allows to decrease the yield of ethane from 42% to 17% while maintaining the yield of MeOH at the 43-54% level.

Similarly, if the major pathway for the reduction of MeOOH to MeOH involves its reaction with **5** (eq 3), by lowering [**5**] one can increase the MeOOH : MeOH ratio. Indeed, this ratio could be raised from 0.07 (Table 4, entry 1) to 0.93 (entry 3) as a result of about 20-fold decrease of [**5**].

CONCLUSIONS

In this work the first example of aerobic oxidation of monomethyl palladium(II) complexes has been demonstrated. The reaction is photochemical in nature and can lead to the formation of three organic products, ethane, methanol and methylhydroperoxide. By varying the solution *pH* and concentration of methylpalladium(II) species the reaction selectivity can be tuned to favor the formation of predominantly ethane (<94%) or methanol $(\leq 54\%)$. The fraction of methylhydroperoxide could also be changed from o to 40% using solution *pH* and light as key tools. A reaction mechanism is proposed that includes photochemical oxidation of monomethyl palladium(II) complexes to their monomethylpalladium(IV) derivatives (major reaction path) and O₂ insertion into Pd^{II}-C bond (minor path). The methylpalladium(IV) complexes are proposed to be highly electrophilic and responsible for concurrent methyl group transfer to nucleophiles present,

e.g., water or hydroxide anion would form methanol, hydrogen peroxide would form methylhydroperoxide and another methylpalladium(II) species would produce a dimethylpalladium(IV) intermediate. The dimethylpalladium(IV) complex was detected in some reaction mixtures, was prepared independently and shown to be highly reactive in ethane reductive elimination. The knowledge gained in this work may be useful for the development of selective photochemical aerobic oxidation of methane to value-added oxygenates or ethane.

ASSOCIATED CONTENT

Supporting Information. Experimental details regarding the synthesis and characterization of the ligands and metal complexes, and TDDFT calculations. This material is available free of charge via the Internet at <u>http://pubs.acs.org</u>.

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Notes

The authors declare no competing financial interests.

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29. We cannot exclude that such a nucleophilic attack involves a C_s - symmetric isomer of **6**, which results from fast isomerization of **6** and is expected to be much more electrophilic than **6** itself, as it is observed in for their Pt^{IV} analogs (ref. 24).

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